IJNRD.ORG ISSN : 2456-4184
INTERNATIONAL JOURNAL OF NOVEL RESEARCH AND DEVELOPMENT (IJNRD) | IJNRD.ORG
An International Open Access, Peer-reviewed, Refereed Journal

Use of various traditional remedies in PCOS (polycystic ovary syndrome).

VARSHA RANI, SHIVANI, AKANKSHA, PANKAJ KUMAR
STUDENT
GAUTAM COLLEGE OF PHARMACY (HMR) (HIMACHAL PRADESH)

Abstract

Polycystic ovarian syndrome (PCOS) is a neuroendocrine metabolic disorder characterized by an irregular menstrual cycle. Treatment for PCOS using synthetic drugs is effective. However, PCOS patients are attracted towards natural remedies due to the effective therapeutic outcomes with natural drugs and the limitations of allopathic medicines. In view of the significance of herbal remedies, herein, we discuss the role of different herbs in PCOS. In this review, we discuss the significance of herbal remedies in the treatment of PCOS. This review article explain that various traditional remedies may helps to cure PCOS without any sideeffects.

Keywords

Infertility , Estrogen , Insulin .

Introduction

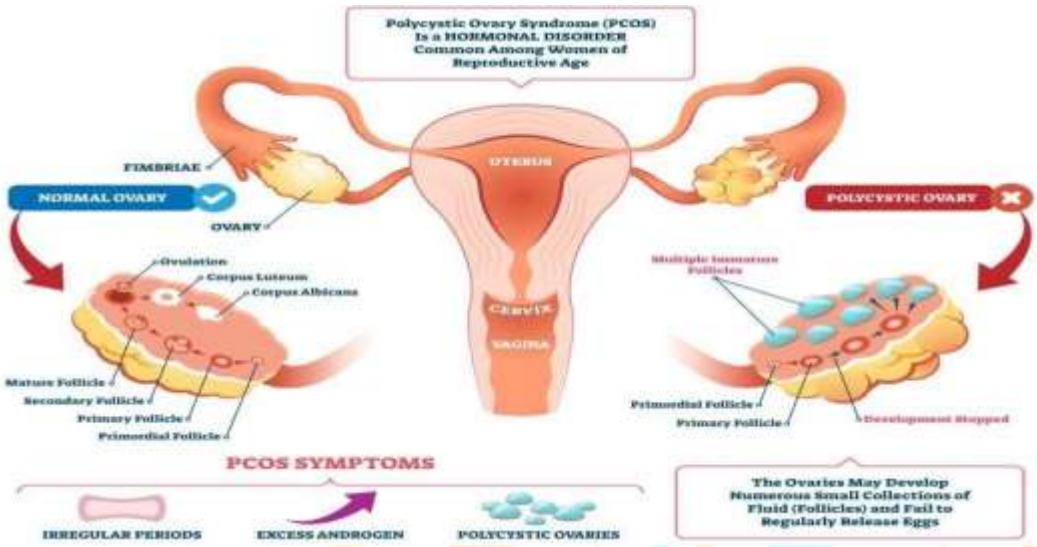
Polycystic ovary syndrome (PCOS) is characterized by endocrine, metabolic, and genetic disorders, chronic absence of ovulation of polycystic ovary, and clinical and biochemical presentations of

hyperandrogenism .The high levels of androgens especially testosterone in PCOS, their role in lack of ovulation, and disrupted synthesis of sex hormones, which causes clinical symptoms and dysfunction of genital tract in the patients, are the main reasons for infertility in reproductive-age women .PCOS is one of the most common gynecological disorders in reproductive-age women with the incidence likelihood of 4–12% . Currently, clomiphene citrate, metformin, and tamoxifen are the most widely used drugs to treat PCOS . Prolonged use of these drugs show major side-effects in our body and we explain how traditional herbs helps to treat PCOS.

What is PCOS?

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder among reproductive-age women, affecting up to 15% of women in this age group. The endocrine disorder affects females under 18–44 age.This disorder manifests itself as menstrual dysfunction, infertility, hirsutism, acne, and obesity .1 : This condition is also named as Schlerocystic Ovaries, Multicystic ovaries, Stein Leventhal Syndrome which was named by an American gynecologist Irving F Stein, SR and Michael L. Leventhal. Globally it affects 5–15% of females .4 : The normal functioning of hormones plays an important role in the ovary functioning and regulation of the menstrual cycle that maintains fertility. If there is a constant disturbance of hormonal level in females then it will disturb ovary functioning which leads to the formation of a cyst inside the sac of an ovary. Whereas androgen which is a male hormone elevated beyond its normal range in females affected with PCOS.The complexity of this condition does not refer to its name, there are many other conditions that are associated with this problem. PCOS patients have numerous cyst 8 mm in size in the sac of their ovary. More than 12 cysts are present in the ovary. About 70% of females are infertile because of

this condition..8 : This condition can be diagnosed on the basis of Rotterdam criteria i.e. irregular menstrual cycle, elevated androgen level, the



presence of cyst.9 :The genetic and environmental factor is responsible for the etiology of this condition. Unhealthy lifestyle, diet or any infectious mediators increase the risk of PCOS.

Common symptoms of PCOS:

Some women start seeing symptoms around the time of their first period. Others only discover they have PCOS after they've gained a lot of weight or they've had trouble getting pregnant.

The most common PCOS symptoms are:

Dermatological feature:Hirsutism (coarse and dark hair on the body areas where men typically grow hair—e.g., the Face, abdomen, chest, and back), acne, and balding/alopecia. In adolescents, some of the Dermatological symptoms may be caused by puberty rather than PCOS.

Menstrual disorders: they may vary, from complete absence of menstruation (amenorrhea) to Menstruation delayed to 35 days or more (oligo menorrhea) to heavy bleeding (menorrhagia). Women with irregular menstrual periods have a 91% chance of having PCOS. Those with PCOS Are 15 times more likely to report infertility.

Disease Pathophysiology:

Across the globe, PCOS affects between 8% and 20% of women of reproductive age annually, according to the diagnostic criteria .The pathophysiology of this condition is influenced by alterations in steroidogenesis, ovarian folliculogenesis, neuroendocrine function, metabolism, insulin production, insulin sensitivity, adipose cell activity, inflammatory factors, and sympathetic nerve function . According to Barre et al., the high consumption of carbohydrates, hyperinsulinemia, hyperandrogenemia, and persistent low-grade inflammation are the four key contributors to pathophysiological alterations in PCOS . (Figure 1).

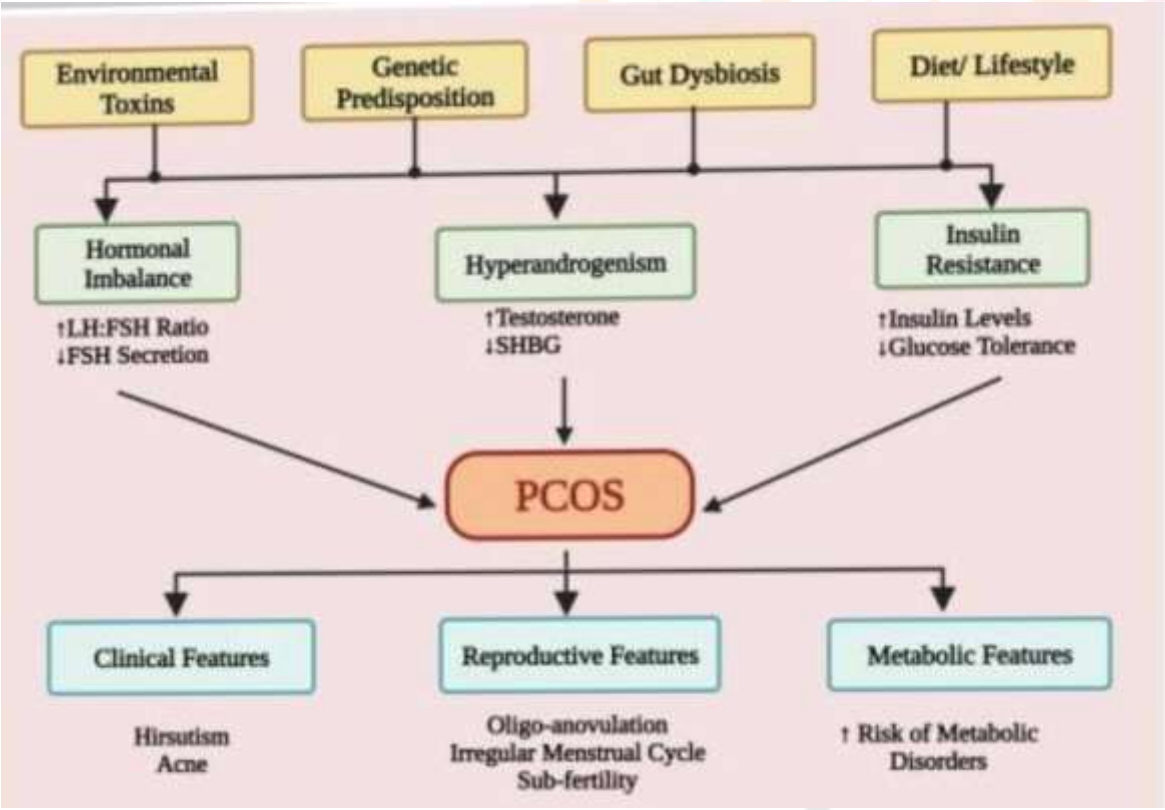


Figure 1. This schematic illustration shows the proposed pathophysiology and features of PCOS. The risk factors like environmental toxins, genetics, gut dysbiosis, and diet responsible for the pathophysiology of the PCOS and subsequent development of clinical, reproductive and metabolic features in PCOS patients. LH: luteinizing hormone; FSH: Follicle stimulating hormone; SHBG: Sex hormone binding globulin.

1.1.Hyperandrogenism

The biochemical hallmark of PCOS is hyperandrogenemia, which manifests clinically as hirsutism, acne, and alopecia. High levels of androgens are observed in 75–90% of PCOS patients with oligomenorrhea, and their concentrations frequently increase with the severity of the phenotype. Excessive androgen synthesis by the ovaries as well as the adrenals contributes to hyperandrogenism . Increased levels of free (unbound) testosterone, a major hormone contributing to the pathogenesis of PCOS, are indicative of hyperandrogenism. Abnormal ovarian or adrenal function leads to the overproduction of androgens. In PCOS, impaired folliculogenesis is the initial effect of excess androgens disrupting normal androgen synthesis. At the early gonadotropin stage, excess androgens encourage the growth of primordial follicles and a rise in the antral follicles . The release of gonadotropin hormones from the pituitary is triggered by GnRH production from the hypothalamus. To increase androgen synthesis in ovarian theca cells, luteinizing hormone (LH) activates the LH receptor. At the same time, follicle-stimulating hormone (FSH) activates the FSH receptor in ovarian granulosa cells to convert androgens into estrogens, which stimulate follicle growth. The dysregulation of the neuroendocrine system is thought to cause an imbalance in the hypothalamic–pituitary–ovarian (HPO) axis, which then leads to an excess of gonadotropin. The rise in GnRH promotes the production of LH over FSH, resulting in a substantial hormonal surge in the LH:FSH ratio in PCOS . Theca cells in the ovaries undergo hyperplasia as a result of increased LH stimulation, which also causes a build-up of follicular fluid that forms cystic structures along the ovary's periphery, giving it the appearance of a string of pearls. This is because many follicles in the theca cells of the ovaries become arrested, mostly in the preantral and antral stages. Due to a rise in follicles and the expression of essential enzymes involved in

androgen synthesis, an excessive amount of androgens are produced .

An altered cortisol metabolism is another proposed mechanism that contributes to excess androgens in PCOS patients. The enhanced inactivation of cortisol by 5alpha-reductase (5alpha-R), or the impaired reactivation of cortisol from cortisone by 11 beta-hydroxysteroid dehydrogenase type 1 (11beta-HSD1), may cause increased peripheral cortisol metabolism, which results in less negative feedback suppression of adrenocorticotropic hormone (ACTH) secretion while maintaining normal plasma cortisol concentrations at the expense of excess androgens . Various genetic factors are associated with abnormal steroidogenesis. CYP genes involved in steroidogenesis play an important role in androgen production and are considered key players in hyperandrogenism in PCOS .

1.2.Hyperinsulinemia

Insulin is the main hormone in charge of both lipogenesis and glucose homeostasis. Insulin serves as a mitogenic hormone in addition to having an impact on the metabolism of carbohydrates, fats, and proteins. Insulin receptors, which are present in many tissues of the HPO axis, mediate the activities of insulin. Insulin potentiates the corresponding trophic hormones in steroidogenic tissues, such as the ovary and the adrenal cortex, to encourage steroidogenesis . As insulin directly mimics the action of LH and indirectly raises GnRH, hyperinsulinemia is the primary cause of excessive androgen production. Sex hormone binding globulin (SHBG), a key circulatory protein that regulates testosterone levels, is decreased by insulin. Therefore, lower SHBG levels would lead to higher levels of free androgens, which cause clinical symptoms of PCOS, such as hirsutism, alopecia, and acne . Numerous studies have shown that lowering

insulin resistance will ultimately result in reduced androgens and an improvement in the disease condition .

Various Traditional remedies uses in PCOS:

A)Herbs That Increase Ovulatory Cycles:

Changes in prolactin levels and hormonal imbalances will have a significant impact on ovulatory cycles. Decreasing prolactin levels or improving the hormonal balance have a positive impact on ovulatory cycles and the treatment of PCOS. These two activities have the potential to reduce cyst formation, dissolve cysts and improve ovulatory cycles. Turmeric is herbs that show a beneficial effect in PCOS by increasing the ovulatory cycles.

Haldi :In haldi curcuminoids present which have significant effects in the treatment of PCOS. They reduce the follicular sheath and improve the formation of the corpus luteum and the ovulation process. Hence, turmeric improves the histological features of polycystic ovaries. Curcuminoids also suppresses

the SERUM LEVELS OF PROGESTERONE AND ELEVATE THE LEVELS OF ESTRADIOL IN WOMEN WITH PCOS . Furthermore, their estrogenic, antihyperlipidemic, antioxidant and hypoglycemic effects are useful in managing PCOS and preventing ovarian cell dysfunction and thereby improving ovulation and fertility.

B) Herbs with Anti-Androgen Properties:

Elevated blood levels of androgens are also the one of the major etiologies behind PCOS.

Hence, drugs with anti-androgen activity are used in the treatment of PCOS. Herbs including Liquorice, Linseed ,Mentha spicata, Cocus

NUCIFERA AND PUNICA GRANATUM HAVE ANTI-ANDROGENIC ACTION AND THESE HERBS COULD BE USEFUL FOR THE MANAGEMENT OF PCOS.

LIQUORICE:IT ACTS AS A POTENT ANTI-ANDROGEN AND HELPS THE BODY TO MAINTAIN BIOSYNTHESIS AND THE RELEASE OF ESTROGEN. THE FLAVONOIDS OF GLYCYRRHIZA POSSESS ESTROGENIC ACTIVITY AND THEY INTERACT WITH ESTROGENIC RECEPTORS, AND THIS RESULTS IN THEIR ANTI-ANDROGENIC EFFECT. ADDITIONALLY, FLAVONOIDS CAN HELP IN THE SECRETION OF INSULIN, WHICH REDUCES BLOOD SUGAR LEVELS AND CONTRIBUTES POSITIVELY TO THE TREATMENT OF PCOS . IN ADDITION TO ITS BENEFITS IN PCOS, LIQUORICE HAS OTHER THERAPEUTIC ROLES, SUCH AS COUGH SUPPRESSION, ANTIBACTERIAL AND ANTIVIRAL ACTIVITY AND TREATMENT FOR DIGESTIVE ISSUES, HEPATITIS AND MOUTH ULCERS .

LINSEED: THE SECONDARY METABOLITES OF LINSEED REGULATE ESTROGEN PRODUCTION IN THE BODY AND PROMOTE FERTILITY RATE AS WELL AS THE MENSTRUAL CYCLE .THEY DECREASE ANDROGEN LEVELS AND CONSIDERABLY REDUCE ELEVATED LEVELS OF TESTOSTERONE IN THE BLOOD, WHICH IS USEFUL FOR TREATING PCOS . FLAXSEED ALSO REDUCES SYMPTOMS ASSOCIATED WITH PCOS, SUCH AS HYPER ANDROGENISM AND HIRSUTISM. PRECLINICAL STUDIES CONFIRMED THAT THE SUPPLEMENTATION OF FLAXSEED IN THE DIET DECREASED THE ANDROGEN LEVELS IN FEMALE RATS, IMPROVED THE FORMATION OF THE CORPUS LUTEUM AND REDUCED THE NUMBER OF CYSTS IN OVARIAN FOLLICLES .

MENTHA SPICATA : MENTHA REGULATES THE BLOOD RATIO OF LH AND FSH. BASED ON THIS REGULATION OF LH/FSH IN THE BLOOD, IT COULD BE USEFUL FOR THE TREATMENT OF PCOS. SEVERAL PRECLINICAL STUDIES HAVE SHOWN THAT SPEARMINT HAS ANTI-ANDROGEN PROPERTIES .

COCOS NUCIFERA :THE LIPID METHYL (9Z,12Z)-9,12-OCTADECADIENOATE PRESENT IN THIS PLANT POSSESSES ANTI-ANDROGENIC PROPERTIES . C. NUCIFERA REGULATES THE BLOOD LEVELS OF SEX HORMONES SUCH AS FSH AND LH .IT ALSO SUPPRESSES THE WEIGHT OF THE OVARY AND INCREASES THE UTERUS WEIGHT. BASED ON THE REGULATION OF HORMONES, IT COULD BE USEFUL FOR PREVENTING CYST FORMATION IN THE OVARIES. IN INDIA, INFUSIONS OF A COCONUT INFLORESCENCE TAKEN ORALLY ARE USED TO TREAT MENSTRUAL CYCLE DISORDERS .SIMILARLY, UPON ORAL ADMINISTRATION, COCONUT MILK HAS A CONTRACEPTIVE PROPERTY.

PUNICA GRANATUM : IT HAVE GOOD EFFECTS IN REDUCING THE COMPLICATIONS OF PCOS. IN WOMEN WHO INCLUDED PUNICA GRANATUM IN THEIR REGULAR DIET, THE BLOOD LEVELS OF FREE TESTOSTERONE, SERUM ESTROGEN AND ANDROSTENEDIONE HORMONE WERE NORMALIZED . USAGE OF PUNICA GRANATUM REDUCES THE COMPLICATIONS ASSOCIATED WITH PCOS .

C) Herbs That Restore Glucose Sensitivity, Estrus Cyclicity and Enzyme Activity:

DECREASING INSULIN SENSITIVITY AND ELEVATED BLOOD GLUCOSE LEVELS ARE ALSO TWO OF THE MAJOR SYMPTOMS OBSERVED IN WOMEN SUFFERING FROM PCOS. AS A RESULT, DRUGS THAT INCREASE INSULIN SENSITIVITY ARE INCLUDED IN PCOS TREATMENT. HERBS SUCH AS CINNAMOMUM CASSIA AND ALOE VERA, WHICH HAVE THE SAME MECHANISM, CAN REDUCE BLOOD GLUCOSE AS WELL AS REGULATE THE ESTRUS CYCLE AND COULD BE USEFUL.

CINNAMOMUM CASSIA: CINNAMON EXTRACT IMPROVES INSULIN SELECTIVITY IN WOMEN WITH PCOS. THE PROCYANIDINS AND POLYPHENOLS IN CINNAMON ARE RESPONSIBLE FOR THE HYPOGLYCEMIC EFFECT BY STIMULATING THE INSULIN SIGNALING PATHWAY. CINNAMON IS USED AS AN ADJUNCTIVE IN THE TREATMENT OF PCOS THROUGH ORAL SUPPLEMENTATION DURING THE LUTEAL PHASE, WHERE IT COULD REGULATE PROGESTERONE LEVELS. SIMILARLY, TAKING CINNAMON ON A DAILY BASIS WILL HELP TO NORMALIZE THE MENSTRUAL CYCLE AND EFFECTIVELY SUPPRESS POLYCYSTIC OVARY SYNDROME . THE INGREDIENTS POSSESS GOOD ANTI-INFLAMMATORY AND ANTIOXIDANT PROPERTIES. THEY RAISE THE LEVELS OF SUPEROXIDE DISMUTASE (SOD), GLUTATHIONE PEROXIDASE (GPX) AND CATALASE (CAT) IN THE BLOOD, WHILE LOWERING THE LEVEL OF MALONDIALDEHYDE (MDA) AND INCREASING THE LIKELIHOOD OF PREGNANCY .

ALOE VERA :ALOE VERA GEL EXPERIENCED THE PARTIAL REVERSION OF ESTROUS CYCLICITY AND IMPROVED STEROIDOGENIC ACTIVITY. IT ALSO REDUCED THE OVARY WEIGHT, RESULTING IN THE SUPPRESSION OF OVERALL ANDROGEN SECRETION.IT ALSO INCREASED ESTROGEN SYNTHESIS BY STIMULATING THE FLUX OF THE STEROIDOGENESIS PATHWAY. IT CAN RESTORE GLUCOSE SENSITIVITY, THE ESTRUS CYCLE AND THE PLASMA LEVELS OF LIPOPROTEINS, BESIDES SUPPRESSING THE BIOGENESIS OF CHOLESTEROL IN THE LIVER .ALOE VERA ALSO HAS A REGULATING EFFECT ON BLOOD LIPID AND GLUCOSE LEVELS, AND HENCE THIS ACTIVITY IS USEFUL IN TREATING PCOS DUE TO METABOLIC DISTURBANCES.

D) Herbs That Promote FSH and Decrease LH Secretions:

IN PCOS, A COMMON COMPLICATION IS ELEVATED LEVELS OF LH AND DECREASED LEVELS OF FSH. HENCE, DRUGS THAT HAVE THE ABILITY TO ELEVATE THE LEVELS OF FSH AND REDUCE THE CONCENTRATIONS OF LH ARE BENEFICIAL IN THE TREATMENT OF PCOS. HERBS INCLUDING FENNEL, GINSENG, BLACK COHOSH, SWEET CUMIN, FENUGREEK HAVE SUCH ACTIONS; HENCE, THEY ARE USEFUL FOR THE TREATMENT OF PCOS.

FENNEL:FENNEL VITAMINS HAVE HIGH ANTIOXIDANT ACTIVITY AND PROTECT THE CELLS FROM OXIDATIVE DAMAGE. ANETHOLE PROMOTES MENSTRUATION, FACILITATES BIRTH AND ALSO INDUCES ESTROGENIC PROPERTIES IN THE OVARIAN FOLLICLE. ALL THESE MAY CONTRIBUTE TO THE TREATMENT OF PCOS. OTHER PHARMACOLOGICAL PROPERTIES OF FENNEL ARE USEFUL FOR THE TREATMENT OF HELMINTHIC INFECTIONS, NEUROLOGICAL DISORDERS AND HIRSUTISM. FURTHER, IT HAS TUMOR SUPPRESSION, ANTI-DIABETIC AND HEPATOPROTECTIVE PROPERTIES.

GINSENG: THIS CAN SIGNIFICANTLY ELEVATE SERUM ESTRADIOL WHILE SUPPRESSING FOLLICLE-STIMULATING HORMONE (FSH) AND LUTEINIZING HORMONE (LH). A SIGNIFICANT DECREASE IN PLASMA LH LEVELS MAY BE BENEFICIAL AND EFFECTIVE FOR IMPROVING THE FERTILITY RATE IN PCOS ANOVULATION PATIENTS . GINSENG CAN ALSO HELP WITH POSTMENOPAUSAL SYMPTOMS SUCH AS INSOMNIA, ANXIETY AND DEPRESSION. IT IS OFTEN USED AS A NATURAL ESTROGEN REPLACEMENT THERAPY, AS WELL AS BECAUSE IT CAN MODIFY THE ESTRUS CYCLE AND SHOWS SIGNIFICANT ESTROGENIC EFFECTS, AS SUGGESTED BY THE REVERSAL OF ATROPHY OF THE VAGINA AND UTERUS WITH THE UPREGULATED EXPRESSION OF ERA AND ERB IN THE REPRODUCTIVE TISSUE. ALL THE ABOVE-DISCUSSED FEATURES OF GINSENG ARE POSITIVE FACTORS THAT COULD CONTRIBUTE TO THE TREATMENT OF PCOS .

BLACK COHOSH:THESE ARE RESPONSIBLE FOR THE SUPPRESSION OF CYSTS IN THE OVARY. THESE COMPOUNDS EXHIBIT THEIR EFFECTS BY SPECIFICALLY INTERACTING WITH THE HYPOTHALAMUS AND PITUITARY ESTROGEN RECEPTORS (ERA). THE BINDING OF COMPOUNDS TO A-ESTROGEN RECEPTORS IN THE PITUITARY GLAND WILL REDUCE LH PRODUCTION. THE FLAVONOIDS DECREASED THE BLOOD LEVELS OF LH AND ALSO IMPROVED PREGNANCY RATES IN PATIENTS WHO HAD EVER USED CLOMIPHENE DURING A MENSTRUAL CYCLE.

SWEET CUMIN: IT HELPS TO RELIEVE OLIGOMENORRHEA AND IMPROVE QUALITY OF LIFE IN WOMEN WHO ARE UNDERGOING TREATMENT FOR PCOS. THE PHENOLIC INGREDIENTS POSSESS PHYTOESTROGENIC FEATURES, WHICH MAY PLAY A GREATER ROLE IN THE REGULATION AND IMPROVEMENT OF MENSTRUAL CYCLES AND LH/FSH

SECRETION IN WOMEN WITH PCOS AND PLAY AN IMPORTANT ROLE IN RELIEVING PCOS COMPLICATIONS .

FENUGREEK : IT WAS EFFECTIVE IN ALLEVIATING PCOS SYMPTOMS WHEN WOMEN TOOK TWO CAPSULES DAILY THROUGH THE DIET . IT REDUCED THE CYST SIZE, AS WELL AS OVARY VOLUME, IN WOMEN WHO RECEIVED IT DAILY AS A SUPPLEMENT TO THEIR DIET OVER A PERIOD OF 90 DAYS .SIMILARLY, IT ALSO DECREASES THE LH/FSH RATIO; SIGNIFICANT MAINTENANCE OF THE MENSTRUAL CYCLE WAS SEEN FOLLOWING ORAL SUPPLEMENTATION. BASED ON THESE ACTIONS, THIS HERB COULD HAVE A USEFUL AND SIGNIFICANT EFFECT ON PCOS .

E) Effective Ovulation Induction Agents:

The most common complication of PCOS is infertility or frequent pregnancy termination due to the patient's lack of carrying capacity. As a result, drugs used to stimulate ovulation are included in PCOS treatment. Herbs such as ginger and gokhru, which have the same action and promote ovulation, might be useful for the treatment of PCOS.

Ginger: It contains flavonoids and phenolics that are beneficial in PCOS. Gingerol and shogaol are potent antioxidant compounds, along with zingerone and a mild amount of oily resin ginger; all of these have demonstrated an anti-prostaglandin effect by inhibiting prostaglandin production and suppressing arachidonic acid production (Figure 18) . Ginger will increase the fertility index, the testosterone level in serum and the testes and seminal vesicle weight, and increase the motility of sperm as well as the

SPERM COUNT IN MALES. THE FLAVONOIDS AND PHENOLIC COMPOUNDS IN GINGER COULD MAINTAIN THE BALANCE OF ESTROGEN AND PROGESTERONE, WITH THEIR SPECIFIC PHARMACOLOGICAL AND PHYSIOLOGICAL EFFECTS. SIMILARLY, THEY COULD REGULATE THE SEX HORMONES IN THE BLOOD . GINGER'S PHYTOESTROGEN COMPONENT CAN BALANCE THE ESTROGEN TO PROGESTERONE RATIO, AND THUS IT COULD BE USED TO TREAT PCOS .

GOKHRU: IT SIGNIFICANTLY REDUCED THE SERUM GLUCOSE LEVEL, SERUM TRIGLYCERIDE LEVEL AND SERUM CHOLESTEROL IN A STUDY. IT NORMALIZED ESTROUS CYCLICITY, STEROIDAL HORMONAL LEVELS AND OVARIAN FOLLICULAR GROWTH. MANY COMPOUNDS FROM TRIBULUS ARE EFFECTIVE OVARIAN STIMULANTS AND ACT AS FERTILITY TONICS FOR WOMEN, MAKING IT A GOOD CHOICE FOR WOMEN WITH POLYCYSTIC OVARIES .

Conclusion:

PCOS is the most common hormonal illness in women from adolescence to pre-menopause, with a variety of complications, including infertility, metabolic and cardiovascular issues and long-term health issues that can last a lifetime. Synthetic medications have shown excellent management for the treatment of PCOS, but substantial adverse drug reactions make their value for long-term cure questionable. To enhance recovery rates and acceptance, patients are increasingly relying on herbal therapy as an alternative to synthetic medications for the control and treatment of PCOS. The current review provides a thorough review of herbs that are beneficial for PCOS and related complications. We have reviewed various key medicinal herbs, their primary chemical constituents and their specialized significance in PCOS management. We are certain that our evaluation will be of significant use to researchers working on herbal therapies to treat PCOS.

References :

1.Witchel SF. Puberty and polycystic ovary syndrome. Mol Cell Endocrinol 2006;254–255:146–53

2. ***Mastorakos G, Lambrinoudaki I, Creatsas G. Polycystic ovary Syndrome in adolescents: current and future treatment options. Paediatr Drugs 2006;8:311–***

3. *Hassa H, Tanir HM, Yildiz Z. Comparison of clinical and Laboratory characteristics of cases with polycystic ovarian syndrome based on Rotterdam's criteria and women whose only Clinical signs are oligo/anovulation or hirsutism. Arch Gynecol Obstet 2006;274:227–32.*

4.Jakubowski L. Genetic aspects of polycystic ovary syndrome. Endokrynol Pol 2005;56:285–93 [in Polish].

5. Kent SC, Legro RS. Polycystic ovary syndrome in adolescents. Adolesc Med 2002;13:73–88, vi.

6.Borini A, Dal Prato L. The pathogenesis of infertility and early Pregnancy loss in polycystic ovary syndrome. In: Allahbadia GN, Agrawal R, editors. Polycystic ovary syndrome. UK: Anshan Publishers; 2006. P. 221–32.

7.Bozdag G, Mumusoglu S, Zengin D, Karabulut E, Yildiz BO. The prevalence and phenotypic features of polycystic ovary syndrome: a systematic review and meta-analysis. Hum Reprod. 2016;31:2841–55.

8.Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group . Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome (PCOS). Hum Reprod. 2004;19:41–7.

9.R.S. Legro Stein-Leventhal syndrome. Encyclopedia britannica

(2009)

10.Motlagh Asghari, K.; Nejadghaderi, S.A.; Alizadeh, M.; Sanaie, S.; Sullman, M.J.M.; Kolahi, A.-A.; Avery, J.; Safiri, S. Burden of polycystic ovary syndrome in the Middle East and North Africa region, 1990–2019. Sci. Rep. 2022, 12, 7039.

11.R.S. Legro Stein-Leventhal syndrome. Encyclopedia britannica (2009)

12.M.D. Ricardo Azziz M.P.H. Introduction: determinants of polycystic ovary syndrome.

13.K. Ranjith reddy, et al.POLYCYSTIC Ovary Syndrome: ROLE OF AROMATASE GENE VARIANTS IN SOUTH INDIAN WOMEN Int J Pharma Bio Sci, 6 (2) (2015) Fertil Steril, 106 (July (1)) (2016)

14.E.D.A. Diamanti-Kandarakis Insulin resistance and the polycystic ovary syndrome revisited: an update on mechanisms and implications

Endocrinology, 33 (2012), pp. 981-1030

15.group TREA-sPcw Revised 2003 consensus on diagnostic criteria and longterm health risks related to polycystic ovary syndrome (PCOS) Hum Reprod, 10 (1) (2003), pp. 41-47

group TREA-sPcw Revised 2003 consensus on diagnostic criteria and longterm health risks related to polycystic ovary syndrome (PCOS) Hum Reprod, 10 (1) (2003), pp. 41-47

6. ***Mea Goodarzi Polycystic ovary syndrome: etiology, pathogenesis and diagnosis Nat Rev Endocrinol, 7***
(4) (2011), pp. 219-231

18.Kumarapeli et al., 2008. PubMed ID: 18550559

19. Joham et al., 2015. PubMed ID: 25654626

20.Witchel, S.F.; Oberfield, S.E.; Peña, A.S. Polycystic Ovary Syndrome: Pathophysiology, Presentation, and Treatment With Emphasis on Adolescent Girls. J. Endocr. Soc. 2019, 3, 1545–1573

21.Ibáñez, L.; Oberfield, S.E.; Witchel, S.; Auchus, R.J.; Chang, R.J.; Codner, E.; Dabadghao, P.; Darendeliler, F.; Elbarbary, N.S.; Gambineri, A.; et al. An International Consortium Update: Pathophysiology, Diagnosis, and Treatment of Polycystic Ovarian Syndrome in Adolescence. Horm. Res. Paediatr. 2017, 88, 371–395.

22.Barrea, L.; Marzullo, P.; Muscogiuri, G.; Di Somma, C.; Scacchi, M.; Orio, F.; Aimaretti, G.; Colao, A.; Savastano, S. Source and amount of carbohydrate in the diet and inflammation in women with polycystic ovary syndrome. Nutr. Res. Rev. 2018, 31, 291–301.

23.Kanbour, S.A.; Dobs, A.S. Hyperandrogenism in Women with Polycystic Ovarian Syndrome: Pathophysiology and Controversies. Androg. Clin. Res. Ther. 2022, 3, 22–30.

24.Bulsara, J.; Patel, P.; Soni, A.; Acharya, S. A review: Brief insight into Polycystic Ovarian syndrome. Endocr. Metab. Sci. 2021, 3, 100085.

25.Walters, K.A.; Gilchrist, R.B.; Ledger, W.L.; Teede, H.J.; Handelsman, D.J.; Campbell, R.E. Metabolism. New perspectives on the pathogenesis of PCOS: Neuroendocrine origins. Trends Endocrinol. Metab. 2018, 29, 841– 852.

26.Ashraf, S.; Nabi, M.; Rasool, S.u.A.; Rashid, F.; Amin, S. Hyperandrogenism in polycystic ovarian syndrome and role of CYP gene variants: A review. Egypt. J. Med. Hum. Genet. 2019, 20, 25.

27.Tsilchorozidou, T.; Honour, J.W.; Conway, G.S. Altered cortisol metabolism in polycystic ovary syndrome: Insulin enhances 5alpha-reduction but not the elevated adrenal steroid production rates. J. Clin. Endocrinol. Metab. 2003, 88, 5907–5913.

28.Ding, H.; Zhang, J.; Zhang, F.; Zhang, S.; Chen, X.; Liang, W.; Xie, Q. Resistance to the Insulin and Elevated Level of Androgen: A Major Cause of Polycystic Ovary Syndrome. Front. Endocrinol. 2021, 12, 741764.

29.Marshall, J.C.; Dunaif, A. Should all women with PCOS be treated for insulin resistance? Fertil Steril 2012, 97, 18–22.

30.De Leo, V.; la Marca, A.; Petraglia, F. Insulin-Lowering Agents in the Management of Polycystic Ovary Syndrome. Endocr. Rev. 2003, 24, 633–667.

31.Jimenez A.S., Monroy A., Alavez S. Curcumin and insulin resistance-molecular targets and clinical evidences. Biofactors. 2016;42:561–580. Doi: 10.1002/biof.1302.

32.Baby B.T., Rani S., Rasheed S.P., Bency B. Polycystic ovarian syndrome: Therapeutic potential of herbal remedies—A review. Int. J. Herb. Med. IJHM. 2016;91:91–96.

33.Yadav K., Ghadge P., Langeh A., Kalbhare S., Phadtare P., Bhoite R. A Review on Herbal Medicinal Plant for Treatment of Polycystic Ovarian Syndrome (PCOS) Asian J. Pharm. Res. Dev. 2020;8:83–87.

34.Jelodar G., Masoomi S., Rahmanifar F. Hydroalcoholic extract of flaxseed improves polycystic ovary syndrome in a rat model. Iran. J. Basic Med. Sci. 2018;21:645–650. Doi: 10.22038/IJBMS.2018.25778.6349.

35.Aziz E., Ameer K., Elham A., Solmaz M.D., Amir H., Magali C. Phytochemical and nutra-pharmaceutical attributes of Mentha spp.: A comprehensive review. Arab. J. Chem. 2021;14:103106.

36.Kamel H.H. Role of phyto-oestrogens in ovulation induction in women with polycystic ovarian syndrome. Eur. J. Obstet. Gynecol. Reprod. Biol. 2013;168:60–63. Doi: 10.1016/j.ejogrb.2012.12.025.

37.Xueli C., Chong T., Jingyi W., Baochang H., Jinbang X. Meta-analysis of therapeutic efficacy and effects of integrated traditional Chinese and Western medicine on coagulation and fibrinolysis system in patients with threatened abortion and polycystic ovary syndrome. Am. J. Transl. Res. 2022;14:2768–2778.

38.Escalante Erosa F., Gamboa-León M.R., Lecher J.G., Arroyo-Serralta G.A., Zizumbo-Villareal D., OropezaSalín C., Peña-Rodríguez L.M. Major components from the epicuticular wax of Cocos nucifera. Rev. Soc. Quím. Mex. 2002;46:247–250.

39.Lima E.B.C., Sousa C.N.S., Meneses L.N., Ximenes N.C., Júnior S., Vasconcelos G.S., Lima N.B.C., Patrocínio M.C.A., Macedo D., Vasconcelos S.M.M. Cocos nucifera (L.) (Arecaceae): A phytochemical and pharmacological review. Braz. J. Med. Biol. Res. 2015;48:953–964. Doi: 10.1590/1414-431x20154773.

40.Bhandary M.J., Chandrashekar K.R., Kaveriappa K.M. Medical ethnobotany of the Siddis of Uttara Kannada district, Karnataka, India. J. Ethnopharmacol. 1995;47:149–158. Doi: 10.1016/0378-8741(95)01274-H.

41..Brondegaard V.J. Contraceptive plant drugs. Planta Med. 1973;23:167–172. Doi: 10.1055/s-0028-1099428.

42.Sachs M., von Eichel J., Asskali F. Wound management with coconut oil in Indonesian folk medicine. Chirurg. 2002;73:387–392. Doi: 10.1007/s00104-001-0382-4.

43.Hirschhorn H.H. Botanical remedies of the former Dutch East Indies (Indonesia). Part I: Eumycetes, Pteridophyta, Gymnospermae, Angiospermae (Monocotyledones only) J. Ethnopharmacol. 1983;7:123–156. Doi: 10.1016/0378-8741(83)90016-8.

44.Hossein K.J., Leila K., Ebrahim T.K., Nazanin S.J., Farzad P., Elham R. The effect of pomegranate juice extract on hormonal changes of female Wistar rats caused by polycystic ovarian syndrome. Biomed. Pharmacol. J. 2015;8:971–977. Doi: 10.13005/bpj/849.

45.Wang J.G., Anderson R.A., Graham G.M., Chu M.C., Sauer M.V., Guarnaccia M.M. The effect of cinnamon extract on insulin resistance parameters in polycystic ovary syndrome: A pilot study. Fertil. Steril. 2007;88:240– 243. Doi: 10.1016/j.fertnstert.2006.11.082.

46.Khodaeifar F., Fazljou S.M.B., Khaki A., Torbati M., Ouladsahebmadarek E., Khaki A.A. Investigating the Role of Hydroalcoholic Extract of Apium graveolens and Cinnamon zeylanicum on Metabolically Change and
Ovarian Oxidative Injury in a Rat Model of Polycystic Ovary Syndrome. Int. J. Women's Health Reprod. Sci. 2019;7:92–98. Doi: 10.15296/ijwhr.2019.15.

47.Ainehchi N., Farshbaf-Khalili A., Ghasemzadeh A., Hamdi K., Khaki A., Ouladsahebmadarek E., Delazar A.,
Bakhtyari F., Mazandarani M. The Effect of Herbal Medicine Supplementation on Clinical and Para-clinical Outcomes in Women with PCOS: A Systematic Review and Meta-analysis. Int. J. Women's Health Reprod. Sci. 2019;7:423–433. Doi: 10.15296/ijwhr.2019.72.

48.Desai B.N., Maharjan R.H., Nampoothiri L.P. Aloe barbadensis Mill. Formulation restores lipid profile to normal in a letrozole-induced polycystic ovarian syndrome rat model. Pharmacogn. Res. 2012;4:109–115. Doi:
10.4103/0974-8490.94736.

49.Farideh Z.Z., Bagher M., Ashraf A., Akram A., Kazem M. Effects of chamomile extract on biochemical and clinical parameters in a rat model of polycystic ovary syndrome. J. Reprod. Infertil. 2010;11:169–174.

50.Badgujar S.B., Patel V.V., Bandivdekar A.H. Foeniculum vulgare Mill: A review of its botany, phytochemistry, pharmacology,

contemporary application, and toxicology. BioMed Res. Int. 2014;2014:842674. Doi: 10.1155/2014/842674.

51.Shahidi F., Hossain A. Bioactives in spices, and spice oleoresins: Phytochemicals and their beneficial effects in food preservation and health promotion. J. Food Bioact. 2018;3:8–75. Doi: 10.31665/JFB.2018.3149.

52.Sadrefozalayi S., Farokhi F. Effect of the aqueous extract of Foeniculum vulgare (fennel) on the kidney in experimental PCOS female rats. Avicenna J. Phytomed. 2014;4:110.

53.Pak S.C., Lim S.C., Nah S.Y., Lee J., Hill J.A., Bae C.S. Role of Korean red ginseng total saponins in rat infertility induced by polycystic ovaries. Fertil. Steril. 2005;84:1139–1143.

54.Wuttke W., Seidlova W.D., Gorkow C. The Cimicifuga preparation BNO 1055 vs. Conjugated estrogens in a double-blind placebo-controlled study: Effects on menopause symptoms and bone markers. Maturitas. 2003;44((Suppl. 1)):67–77. Doi: 10.1016/S0378-5122(02)00350-X.

55.Frei K.S., Schaffner W., Rahlfs V.W., Bodmer C., Birkhäuser M. Cimicifuga racemosa dried ethanolic extract in menopausal disorders: A double-blind placebo-controlled clinical trial. Maturitas. 2005;51:397–404. Doi: 10.1016/j.maturitas.2004.10.003.

56.Dayani S.A., Karunathilaka L.P., Kodituwakku N.D., Karunarathne Y.A. Clinical efficacy of Ayurveda treatment regimen on Subfertility with Poly Cystic Ovarian Syndrome (PCOS) Ayu. 2010;31:24–27. Doi: 10.4103/0974-8520.68203.

57.Bhingardive K.B., Sarvade D.D., Bhatted S. Clinical efficacy of Vamana Karma with Ikshwaaku Beeja Yoga followed by Shatapushpadi Ghanavati in the management of Artava Kshayawsr to polycystic ovarian syndrome. Ayu. 2017;38:127–132. Doi: 10.4103/ayu.AYU_192_16.

58.Anand S., Amrita J., Sushil K.G., Manashi B., Pawan K., Harry G., Debasis B. Efficacy of a Novel Fenugreek Seed Extract (Trigonella foenum-graecum, Furocyst TM) in Polycystic Ovary Syndrome (PCOS) Int. J. Med. Sci. 2015;12:825–831. Doi: 10.7150/ijms.13024.

59.Atashpour S., Kargar J.H., Kargar J.Z., Maleknasab M. Comparison of the effects of ginger extract with clomiphene citrate on sex hormones in rats with polycystic ovarian syndrome. Int. J. Reprod. Biomed. 2017;15:561–568. Doi: 10.29252/ijrm.15.9.561.

60.Ali B.H., Blunden G., Tanira M.O., Nemmar A. Some phytochemical, pharmacological and toxicological properties of ginger (Zingiber officinale Roscoe): A review of recent research. Food Chem. Toxicol. 2008;46:409– 420. Doi: 10.1016/j.fct.2007.09.085.

61.Poojari P., Paramanya A., Singh D., Ali A. Herbal Medicines: A Boon for Healthy Human Life. Academic Press; Cambridge, MA, USA: 2022. Polycystic ovarian syndrome: Causes and therapies by herbal medicine; pp. 435–451.

62.Chhatre S., Nesari T., Somani G., Kanchan D., Sathaye S. Phytopharmacological overview of Tribulus terrestris. Pharmacogn. Rev. 2014;8:45–54. Doi: 10.4103/0973-7847.125530.