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HERBAL REMEDIES FOR THE MANAGEMENT OF POLYCYSTIC OVARY SYNDROME (PCOS); A SYSTEMIC REVIEW AND META- ANALYSIS

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Keywords:

Polycystic ovary syndrome, Hyperandrogenic, Infertility, Insulin resistance, Diabetes, Acne, Excessive hair growth (hirsutism), Antioxidant

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ABSTRACT: Polycystic Ovary Syndrome (PCOS) is a multifaceted endocrine disorder that affects a significant percentage of women of reproductive age, with substantial implications for metabolic, reproductive, and psychological health. This review aims to provide a comprehensive overview of current research on the pathophysiology, diagnosis, and treatment approaches for PCOS. The syndrome is characterized by hyperandrogenism, ovulatory dysfunction, and polycystic ovarian morphology, yet its presentation varies greatly among individuals, complicating diagnosis and management. Key findings from recent studies suggest that genetic predispositions, lifestyle factors, and environmental influences contribute to the heterogeneity of PCOS. Additionally, the review explores the role of insulin resistance and chronic low-grade inflammation in exacerbating the condition. Treatment strategies include lifestyle modifications, pharmacotherapy, and hormonal regulation, tailored to manage symptoms and improve overall quality of life. This article synthesizes current evidence to underscore the importance of an individualized, multidisciplinary approach to PCOS management and identifies gaps in research, emphasizing the need for further investigation into the underlying mechanisms and long-term treatment outcomes.

INTRODUCTION: Polycystic ovary syndrome (PCOS) is a complex endocrine disorder that affects women of reproductive age. It is characterized by a combination of symptoms including irregular menstrual cycles, elevated levels of androgens (male hormones), and the presence of multiple small cysts on the ovaries. PCOS is associated with various metabolic and reproductive complications, such as insulin resistance, obesity, infertility, and an increased risk of type 2 diabetes and cardiovascular disease.

Polycystic ovarian syndrome, first described in 1935 by Stein and Leventhal, is allied with chronic oligoanovulation and polycystic ovarian morphology also with psychological impairments, metabolic derangements mainly insulin resistance and compensatory hyperinsulinemia, which may be responsible for altered androgen production and metabolism reproductive age¹.

This condition is also named as Schlerocystic Ovaries, Multicystic ovaries, Stein Leventhal Syndrome which was named by an American gynaecologist Irving F Stein, SR and Michael L. Leventhal. 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 ². Polycystic Ovarian Disease (PCOD) is a medical condition in which the woman ovaries produce immature or partially mature eggs in large numbers and over the time these become cysts in ovaries. Due to this, ovaries become large and secrete large amount of male hormones (androgens) causing infertility, irregular menstrual cycles, hair loss and abnormal weight gain ³. It is recognized by the presence of enlarged ovaries with multiple small cysts and a hyper vascularized androgen secreting stroma ⁴.

World Health Organization (WHO) estimates that PCOS has affected 116 million women (3.4%) worldwide in 2012 ⁵. Globally, 1.55 million incident cases of PCOS in women of reproductive age (15–49 years) were reported, representing an increase in the rate of 4.47% (2.86–6.37%) from 2007 to 2017 ^{5, 6}. A large-scale survey conducted across India in 2020 showed that around 16% of female respondents between the ages of 20 and 29 years suffered from PCOS ⁷. PCOS are strongly

interlinked by the pathogenesis of various individual disorders; they may be broadly classified into endocrine dysfunction, reproductive dysfunction, metabolic dysfunction and biochemical dysfunction ⁸. It is also associated with psychological impairments including depression and other mood disorders. Most women with PCOS are also overweight or obese, further enhancing androgen secretion while impairing metabolism and reproductive functions and possibly favoring the development of the PCOS ⁹.

Metabolic abnormalities such as dyslipidemia, insulin resistance, therefore, diseases including diabetes, obesity, cancer and infertility as well as coronary heart diseases could be seen along with PCOS ¹⁰. Reactive oxygen species and antioxidants remain in balance in normal individual but when this balance is disturbed, oxidative stress develops ⁹. Which may lead to different disorders. Increased oxidative stress contributes to the risk of cardiovascular disease in women with PCOS ¹¹.

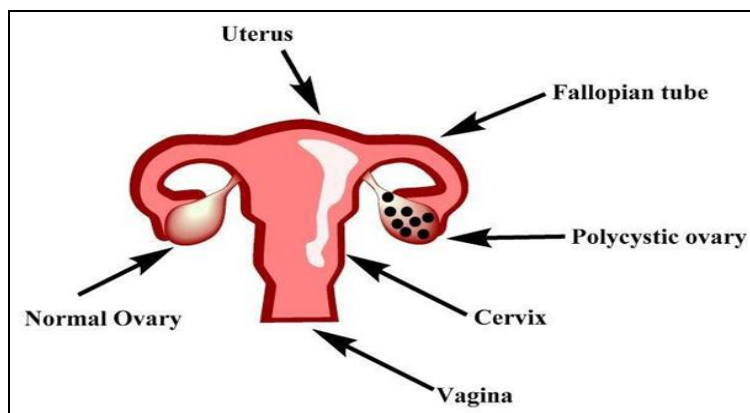


FIG. 1: DIFFERENTIATION BETWEEN A NORMAL AND POLYCYSTIC OVARY

Etiology: The major etiology behind PCOS is primary disordered gonadotropin secretions, ovarian and adrenal hyperandrogenism and disorder of insulin resistance ¹². The regulation of gonadotropin-releasing hormone (GnRH) is uncontrolled, which may lead to increased luteinizing hormone (LH) and decreased FSH; this may lead to the suppression of the response of ovarian follicles to FSH, elevated anti-Müllerian hormone (AMH), follicular arrest and the increased secretion of testosterone, estradiol and dehydroepiandrosterone ¹³. Disrupted ovarian synthesis of steroid hormones in these diseases may result in an increase in circulating androgens,

which may be more pronounced in women with polycystic ovarian syndrome ¹⁴ **Fig. 2.** Hyperinsulinism and hypogonadism are considered as the capability of insulin to stimulate gonadal and adrenal androgen production, and this hyperinsulinism is also one of the major risk factors of PCOS ¹⁵. In PCOS, immature follicle development was observed due to increased LH levels and decreasing levels of FSH. Similarly, the increased production of androgens and reduced blood levels of aromatase were observed. Excessive androgens in PCOS are due to elevated abdominal fat, and this may lead to hyperinsulinemia and dyslipidemia. An increase in

cell androgen production and hyperinsulinemia reduces sex hormone binding globulin (SHBG) to

increase circulating testosterone levels. All these factors may aggravate the disease’s progression ¹⁶.

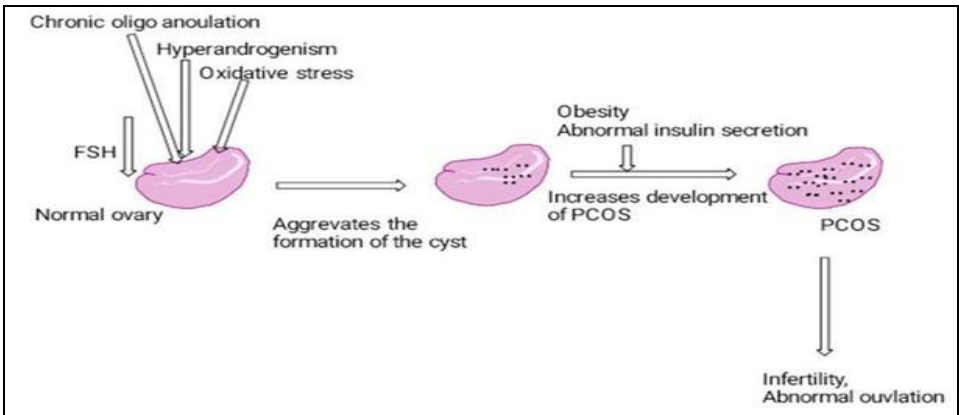


FIG. 2: PATHOGENESIS OF POLYCYSTIC OVARIAN SYNDROME

Pathophysiology: Polycystic ovary syndrome is characterised by increased pulse frequency of gonadotrophin releasing hormone and reduced negative feedback from sex steroids at the level of the hypothalamus ¹⁷. Gonadotrophin releasing hormone is released from neurons in the hypothalamic infundibular nucleus in a pulsatile manner, resulting in increased secretion of luteinising hormone and follicle stimulating hormone. The pulse frequency of gonadotrophin releasing hormone is controlled by multiple upstream endocrine and neural factors, with a higher frequency favouring secretion of luteinising hormone and a lower frequency favouring secretion

of follicle stimulating hormone. In women with polycystic ovary syndrome, raised levels of luteinising hormone cause excess production of ovarian thecal androgens, whereas relative deficiency of follicle stimulating hormone causes follicular arrest, polycystic ovarian morphology, and oligo-ovulation ¹⁸. The reduction in sex steroid feedback on release of gonadotrophin releasing hormone is thought to occur upstream of the hormone itself because gonadotrophin releasing hormone neurons do not have receptors for oestrogens or progesterone ¹⁹ **Fig. 3.** KNDy neurons have an important role in this regard **Fig. 3.**

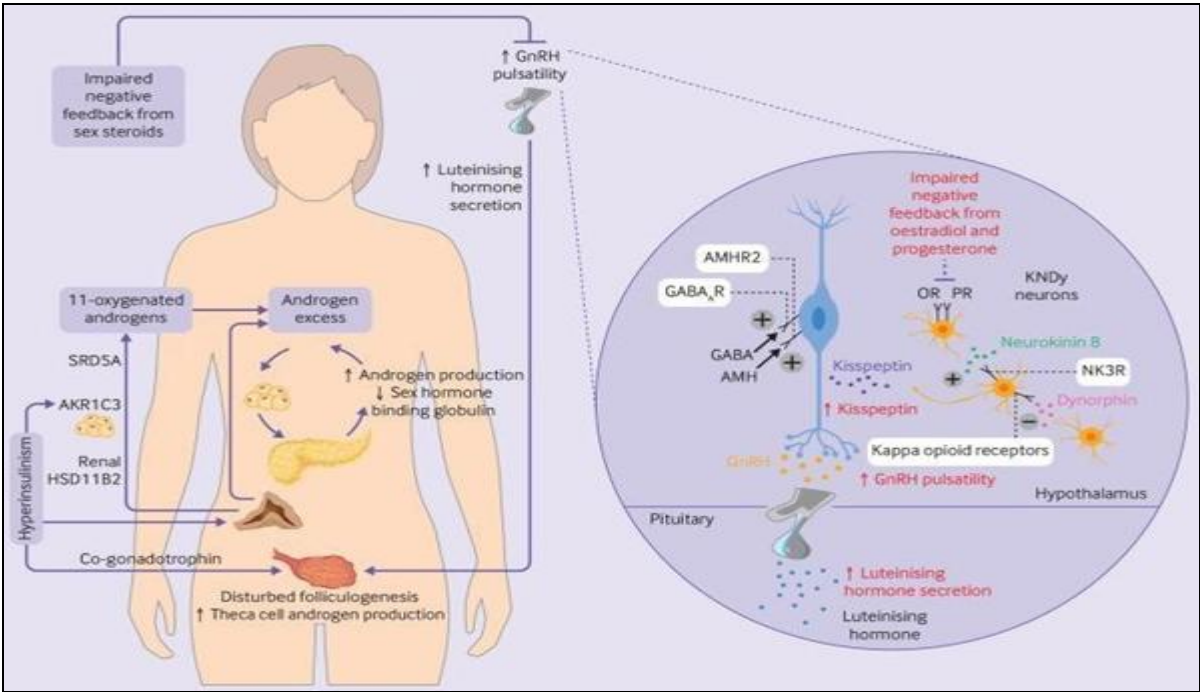


FIG. 3: PATHOPHYSIOLOGY AND NEUROENDOCRINE DISRUPTION OF THE HYPOTHALAMUS-PITUITARY- GONADAL AXIS IN POLYCYSTIC OVARY SYNDROME

Kisspeptins are a family of peptides encoded by the *KISS1* gene which act on the neuronal G protein coupled receptor KISS1R. *KISS1* encodes prepro-kisspeptin, which is cleaved to produce the biologically active peptides KP54, KP14, KP13, and KP10²⁰.

Two discrete neuronal populations exist: neurons in the infundibular nucleus function as the gonadotrophin releasing hormone pulse generator²¹ and mediate negative feedback from oestradiol,²² whereas a separate kisspeptin population located in the preoptic area mediates oestradiol positive feedback to produce the mid-cycle surge in luteinising hormone^{22,23}.

Kisspeptin neurons express sex steroid receptors (progesterone and oestrogen receptors) required for negative feedback on gonadotrophin releasing hormone pulsatility. *KISS1* is also expressed in adipose tissue where it is regulated independently of hypothalamic *KISS1*²⁴. Circulating levels of kisspeptin are higher in patients with polycystic ovary syndrome than in controls²⁵ and although the origin of this excess is not entirely clear, a raised pulse frequency of kisspeptin in women with oligomenorrhoea and polycystic ovary syndrome suggests a hypothalamic source²⁶.

Moreover, physiological coupling of kisspeptin and luteinising hormone pulsatility is lost in these women²⁷. The exact mechanisms for these effects are unclear, with inconsistent data from preclinical models on the existence and direction of dysregulated gonadotrophin releasing hormone pulsatility mediated by kisspeptin²⁸.

Neurokinin B and dynorphin are expressed by KNDy neurons and act in an autocrine and paracrine way to control release of kisspeptin **Fig. 3**. Neurokinin B preferentially binds to the neurokinin 3 receptor (encoded by *TACR3*) to stimulate gonadotrophin releasing hormone pulsatility^{17,29}.

Unlike *KISS1* null mice, mice deficient in components of neurokinin B signalling can still generate surges in luteinising hormone and conceive, suggesting that compensatory pathways exist which contribute to the generation of kisspeptin and gonadotrophin releasing hormone

pulses^{23, 30, 31}. This milder effect of neurokinin B blockade might avoid excessive reduction in gonadotrophin releasing hormone pulsatility, making it an attractive target for treatment¹⁷. Dynorphin, which activates kappa opioid receptors on KNDy neurons to inhibit secretion of gonadotrophin releasing hormone,^{28, 32} has been shown to mediate progesterone negative feedback on gonadotrophin releasing hormone neurons in sheep³³ and humans^{28,34}.

Neuronal activity of gonadotrophin releasing hormone is also regulated by other substances, including γ -aminobutyric acid (GABA) and anti-müllerian hormone, both of which stimulate gonadotrophin releasing hormone neurons directly. GABA exerts an excitatory effect on gonadotrophin releasing hormone neurons through GABAA receptors, and GABA levels in cerebrospinal fluid can be raised in patients with polycystic ovary syndrome³⁵.

Antimüllerian hormone is secreted by ovarian granulosa cells, where raised levels in women with polycystic ovary syndrome disrupt folliculogenesis and ovulation³⁶. Anti-müllerian hormone might also have neuroendocrine effects: 50% of gonadotrophin releasing hormone neurons in mice and humans express anti-müllerian hormone receptor type 2,³⁷ with studies implicating anti-müllerian hormone in neuronal migration of gonadotrophin releasing hormone³⁸, gonadotrophin releasing hormone pulsatility, and secretion of luteinising hormone³⁶.

Clinical Symptoms³⁹:

- ☐ Hyperandrogenism
- ☐ Insulin Resistance
- ☐ Inflammation
- ☐ Ovarian cysts
- ☐ Obesity
- ☐ Irregular periods
- ☐ Infertility
- ☐ Oxidative Stress

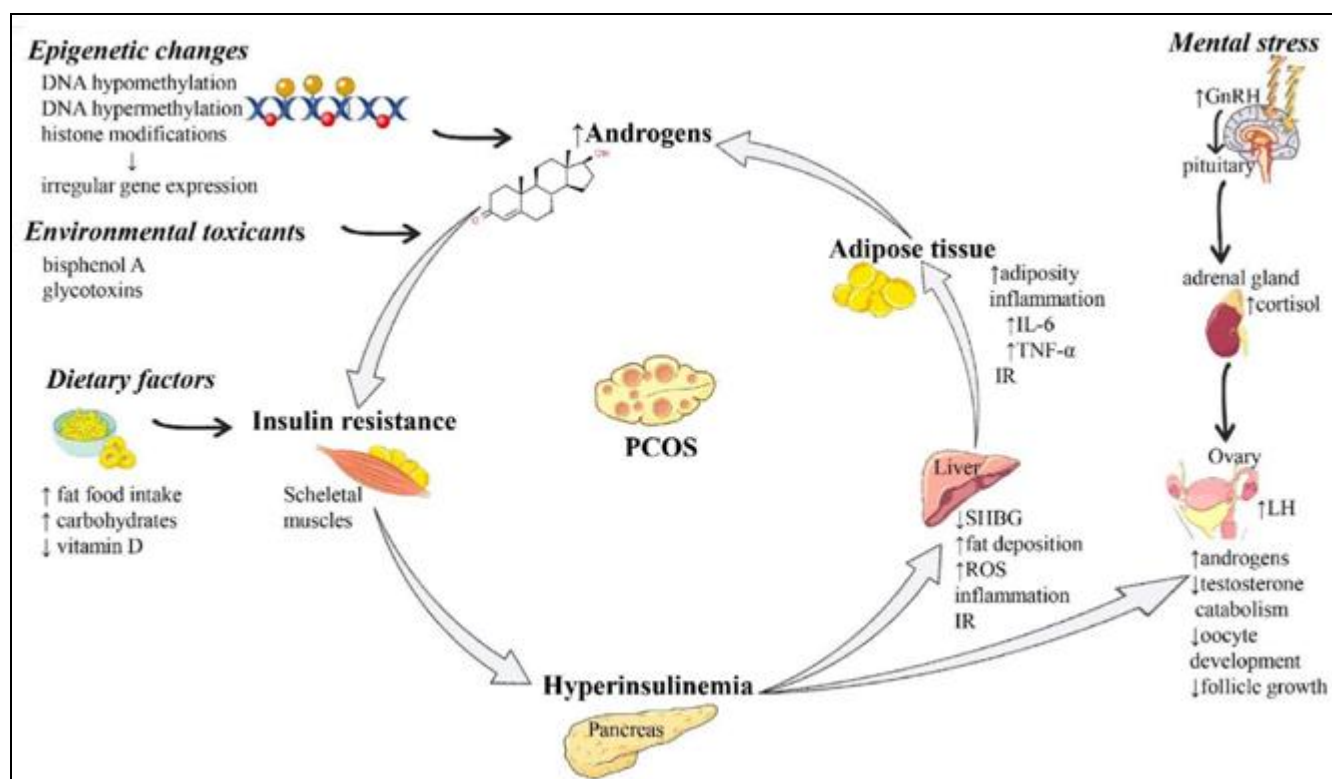


FIG. 4: SUMMARIZED SCHEME REGARDING THE PATHOPHYSIOLOGY AND CLINICAL FEATURES OF PCOS

Management and Treatments:

Weight Loss: The first step for women diagnosed with PCOS would be weight reduction and calorie intake restriction⁴⁰. Many studies demonstrate that even a 5% to 10% reduction in weight can restore the regular menstruation cycle⁴¹. For obese women, it would be best if they could reach their normal range of body mass index (BMI). Along with weight loss, the level of free testosterone decreases, and the incidence of metabolic syndrome reduces⁴².

Exercise: Exercise is the best treatment modality for all the embolic manifestations and is recognized as necessary as food for human health. In PCOS, exercise and weight losing activities have supreme importance because they will help in lowering the adipose tissues having a major contribution to insulin resistance and androgenism^{43,44}.

Pharmacological Mediation: Drug therapy is always considered prime requirement for therapeutic regimens for reproductive abnormalities and metabolic disorders in PCOS, where drugs like;

□ Pioglitazone⁴⁵

□ Inositol⁴⁶

□ Metformin⁴⁷

□ Clomiphene⁴⁸

Oral Contraceptive Pills (OCPs): Oral contraceptives pills (OCPs) are regarded first-line therapy for people with PCOS who are not pursuing pregnancy. Not only are OCPs helpful in regulating the menstrual cycle, but also, they reduce the secretion of androgens and regulate other physical activities⁴⁹. Commonly prescribed Oral contraceptives pills (OCPs) in PCOS;

- Levonorgestrel/Ethinyl estradiol⁵⁰
- Desogestrel/Ethinyl estradiol⁵¹
- Medroxyprogesterone acetate⁵²
- Drospirenone/Ethinyl estradiol⁵³

Laparoscopic Ovarian Drilling (LOD): In 1984, laparoscopic ovarian drilling (LOD) was established to replace the invasive ovarian wedge resection surgery⁵⁴. Currently, this technique is highly recommended and is developing pregnancy in 84% of the PCOS women who are facing infertility problems.

Acupuncture: Acupuncture, a fundamental part of CAM, has been used in China for more than 3000

years⁵⁵. It is a kind of sensory stimulation in which thin needles are placed into the skin and muscles. Acupuncture improves clinical manifestations of PCOS by activating somatic afferent nerves of the skin and muscles, modulating somatic and autonomic nervous system activity and endocrine/metabolic functions⁵⁶.

Dietary Therapy: Dietary therapy to reduce the weight of women with PCOS has a significant impact on metabolic conditions and is recognized to improve many PCOS issues like regulating androgen secretions, reducing insulin resistance, regularity of endocrine secretions, and menstrual cycle regulation^{57, 58}.

Herbal Remedies for PCOS:

Aloe Vera (*Aloe barbadensis miller*):



FIG. 5: ALOE-VERA

Synonyms: Aloe, Indian Aloe, True Aloe

Family: Liliaceae

Biological Source: Aloe vera is a succulent plant species of the genus *Aloe*. The gel and latex derived from its leaves are used medicinally.

Geography: Native to the Arabian Peninsula, but widely cultivated in tropical and subtropical regions worldwide, including Africa, Southern Europe, the Caribbean, and parts of Asia.

Phytoconstituents: Polysaccharides (acemannan), Glycoproteins, Enzymes, Vitamins (A, C, E), Anthraquinone (Aloe-emodin, Barbaloin).

Benefits: Aloe-vera helps in managing blood sugar level, promotes weight loss and also helps in PCOS-related acne.

Usage: It can be applied topically as gels and also taken juice with warm water.

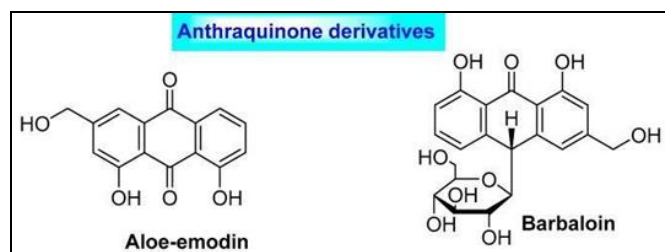


FIG. 6: SECONDARY METABOLITES OF ALOE VERA RESPONSIBLE FOR ALTERING ENZYMATIC ACTIVITY, WHICH COULD BE BENEFICIAL IN PCOS

Amla (*Emblica officinalis*):



FIG. 7: AMLA

Synonyms: Indian gooseberry, *Phyllanthus emblica*.

Family: Phyllanthaceae

Biological Source: The fruit of the *Phyllanthus emblica*, commonly known as Indian gooseberry or amla is rich in vitamin C and used in traditional Ayurvedic medicine.

Geography: Native to India and found throughout tropical and subtropical regions of Southeast Asia, including Pakistan, Sri Lanka, and China.

Phytoconstituents: Vitamin C (ascorbic acid), Polyphenols. (Gallic acid, ellagic acid), Tannins, Flavonoids, Emblicanin A and B (antioxidants).

Benefits: Helps to improve insulin sensitivity, reduce inflammation, detoxifies the body and boosts fertility in women with PCOS.

Usage: Taken in powdered form, capsule, juice and as a supplement

Ashwagandha (*Withania somnifera*):



FIG. 8: ASHWAGANDHA

Synonyms: Ashwagandha, Clustered Winter cherry.

Family: Solanaceae (Nightshade family).

Biological Source: It consists of the dried roots and stem bases of *Withania somnifera* Dunal.

Geography: Native to India, parts of the Middle East, and North Africa.

Phytoconstituents: Alkaloid (withanine), steroid lactone (withanolides), somniferine, pseudowithanine, tropine and pseudotropine

Benefits: Known as an adaptogen, ashwagandha can help reduce stress, balance cortisol levels, and improve mood, which can be beneficial for hormonal balance.

Usage: Taken in powdered or capsule form.

Berberine (*Berberis vulgaris*):



FIG. 9: BERBERINE

Synonyms: Barberry, European Barberry, Pepperidge.

Family: Ranunculaceae (Buttercup family).

Biological Source: Berberine is a bioactive compound extracted from various plants, including *Berberis* species such as *Berberis vulgaris* (barberry), *Coptis chinensis* (goldthread), and *Hydrastis canadensis* (goldenseal).

Geography: Native to South and Southwest Asia, particularly found in countries like India, Turkey, and the Mediterranean region.

Phytoconstituents: Alkaloid (berberine).

Benefits: Berberine helps to reduce elevated androgen levels, and relieve symptoms like excessive hair growth (hirsutism) and acne. It also improves insulin sensitivity and supports in weight loss.

Usage: Typically taken in supplement form

Black Cohos Root (*Cimicifuga racemosa*):



FIG. 10: BLACK COHOS

Synonyms: Fairy Candle, Squawroot

Family: Ranunculaceae

Biological Source: It consists the root of the *Actaea racemosa* (formerly *Cimicifuga racemosa*), a flowering plant in the buttercup family.

Geography: Native to North America, particularly the eastern regions of the United States and Canada.

Phytoconstituents: Triterpene glycosides and phenolic acids, phytoestrogen.

Benefits: Black cohos is often used to induce ovulation, menstrual cycles and helps to balance hormonal levels in women with PCOS.

Usage: Typically taken as a capsule or tincture

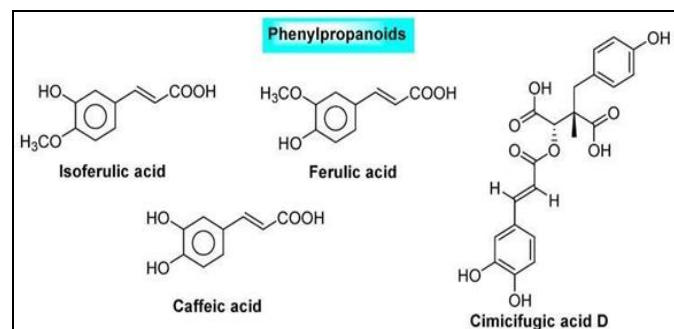


FIG. 11: PHENYLPROPANOIDS PRESENT IN *CIMICIFUGA RACEMOSA*

Black Cumin (*Nigella sativa*):



FIG. 12: BLACK CUMIN

Synonyms: Black seed, Kalonji (Hindi)

Family: Ranunculaceae (Buttercup family)

Biological Source: The seeds of *Nigella sativa*, also known as black seed or black cumin, are used for medicinal purposes.

Geography: Native to South and Southwest Asia, particularly found in countries like India, Turkey, and the Mediterranean region.

Phytoconstituents: Thymoquinone, Nigellidine, Alkaloids.

Benefits: Black cumin helps in regulating hormonal imbalances, which may alleviate symptoms like irregular periods. It also helps to

reduce the oxidative stress, inflammation and improves insulin resistance.

Usage: Can be taken as supplement, capsule, oil or as a raw seed directly

Cinnamon (*Cinnamomum verum*):



FIG. 13: CINNAMON

Synonyms: Ceylon Cinnamon, True Cinnamon

Family: Lauraceae

Biological Source: The inner bark of trees from the *Cinnamomum* genus. Two common types are Ceylon cinnamon (*Cinnamomum verum*) and Cassia cinnamon (*Cinnamomum cassia*).

Geography: Native to Sri Lanka (*Ceylon cinnamon*) and parts of Southeast Asia, especially Indonesia and China (*Cassia cinnamon*).

Phytoconstituents: Cinnamaldehyde, Polyphenols, Manganese and fiber

Benefits: Cinnamon helps to improve insulin sensitivity, which can be beneficial for women with PCOS who are insulin resistant.

Usage: Cinnamon can be taken as a supplement or added to food and beverages.

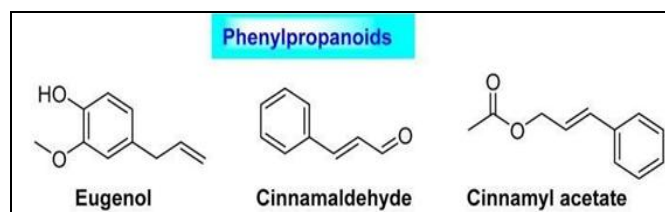


FIG. 14: PHENYLPROPANOIDS OF *CINNAMOMUM CASSIA* THAT EXHIBIT ENZYMATIC ACTIVITY

Flax Seed (*Linum usittatissimum*):



FIG. 15: FLAX SEED

Synonyms: Linseed

Family: Linaceae

Biological Source: The seeds of the flax plant (*Linum usittatissimum*), which are rich in omega-3 fatty acids and dietary fiber.

Geography: Native to the region extending from the eastern Mediterranean to India. It is cultivated globally, with major producers including Canada, Russia, and China.

Phytoconstituents: Lignans (such as secoisolariciresinol diglucoside), Omega-3 fatty acids, Fiber.

Benefits: Flax seeds help to balance hormone by modulating excess estrogen levels, which is often high in PCOS women.

It can also help to improve insulin sensitivity and reduce blood sugar levels, which is key for managing PCOS.

Usage: Used in grounded or powdered form easier digestion and better nutrient absorption.

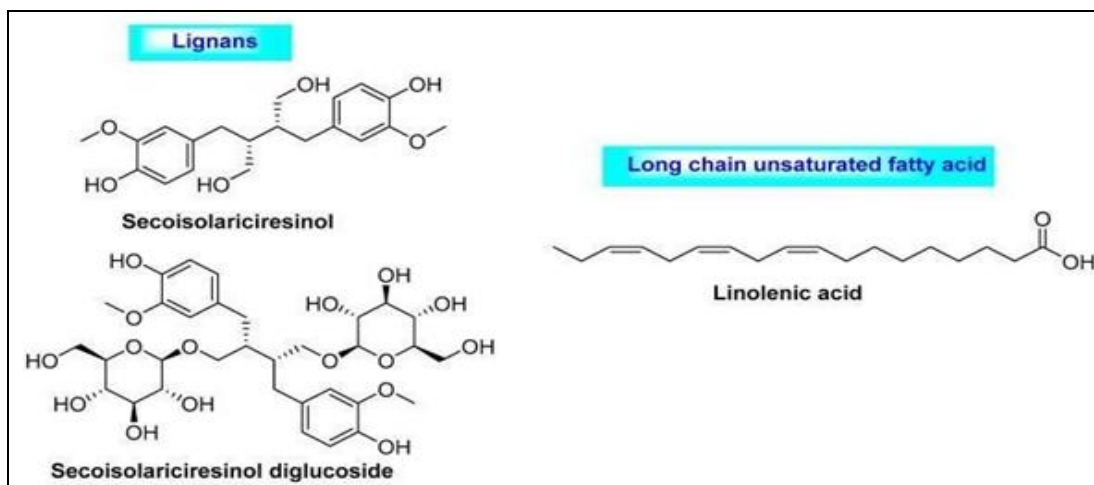


FIG. 16: LIGNANS AND POLYUNSATURATED FATTY ACIDS PRESENT IN *LINUM USITATISSIMUM* WITH ANTI-ANDROGENIC ACTIVITY

Garlic (*Allium sativum*):



FIG. 17: GARLIC

Synonyms: *Allium sativum*, Lasan (in Hindi)

Family: Liliaceae

Biological Source: Garlic comes from the *Allium sativum* plant, a bulbous flowering plant in the amaryllis family.

Geography: Garlic is native to Central and South Asia, and northeastern Iran.

Phytoconstituents: Diallyl thiosulfonate (allicin), diallyl sulfide (DAS), diallyl disulfide (DADS), diallyl trisulfide (DATS), E/Z-ajoene, S-allyl-cysteine (SAC), and S-allyl-cysteine sulfoxide (alliin).

Benefits: It can help reduce insulin resistance and may also improve cardiovascular health, which is often compromised in women with PCOS due to associated conditions like high cholesterol or hypertension.

Usage: Raw garlic or garlic supplements can be incorporated into the diet. Adding garlic to meals, particularly in raw form, may maximize its health benefits.

Ginger (*Zingiber officinale*):



FIG. 18: GINGER



FIG. 19: RESINOUS SUBSTANCES OF *ZINGIBER OFFICINALIS*

Green Tea (*Camellia Sinensis*):



FIG. 20: GYMNEMA SYLVESTRE

Synonyms: Sweet Root, Gan Cao (in Chinese), Gurmar (in Hindi).

Family: Apocynaceae

Biological Source: It consists dried leaves of plant *Gymnema sylvestre* which are primarily used for

Synonyms: Rhizomazingiberis, Zingiber

Family: Zingiberaceae

Biological Source: Ginger consists of the dried rhizomes of the *Zingiber officinale* Roscoe

Geography: Ginger is native to Maritime Southeast Asia and is grown commercially in many tropical and subtropical regions around the world.

Phytoconstituents: Zingerone and shogaol, gingerol, volatile oil (1-2%), pungent resin (5-8%).

Benefits: Ginger is a potent anti-inflammatory and antioxidant. Studies suggested that ginger may reduce insulin resistance, lower androgen levels, and regulate menstruation in women with PCOS. It may also help alleviate digestive issues and reduce pain.

Usage: Ginger can be consumed as ginger tea, added to meals, or taken in supplement form. Fresh ginger can also be used in smoothies or juices.

medicinal purposes, particularly in traditional medicine for managing diabetes.

Geography: Native to the tropical forests of India, Sri Lanka, Africa, and parts of Australia.

Phytoconstituents: Gymnemic acids, saponins, flavonoids.

Benefits: It helps to lower blood sugar levels and reduce sugar cravings, which can aid in weight management and insulin sensitivity.

It may also support overall metabolic health, which is beneficial for women with PCOS.

Usage: *Gymnema* can be taken as a tea or in capsule form. Dosages can vary, but a common recommendation is around 200-400 mg of *gymnema* extract per day.

Jamun Powder (*Syzygium cumini*):**FIG. 21: JAMUN POWDER**

Synonyms: *Syzygiumcumini*, Malabar plum, Java plum, black plum, jamun or jambolana.

Family: Myrtaceae

Biological Source: Jamun obtained from dried fruit of plant *Syzygium jambolan*.

Geography: Found widely in India, Bangladesh, Nepal, Pakistan, and other parts of Southeast Asia. It is also cultivated in South America and parts of Africa.

Phytoconstituents: Jamboline, jambosine, glucoside, ellagic acid, anthocyanins, flavonoids, phenolic compounds.

Benefits: Jamun has properties that help regulate blood sugar levels, making it beneficial for managing insulin resistance.

It also have antioxidant properties which reduce the oxidative stress and inflammation, which may play role in hormone imbalances in PCOS.

Usage: Jamun powder can be mixed with water, smoothies, or yogurt. A common dose is about 1 teaspoon per day.

Liquorice Root (*Glycyrrhiza glabra*):**FIG. 22: LIQUORICE**

Synonyms: Sweet Root, Melethi (in Hindi).

Family: Leguminosae

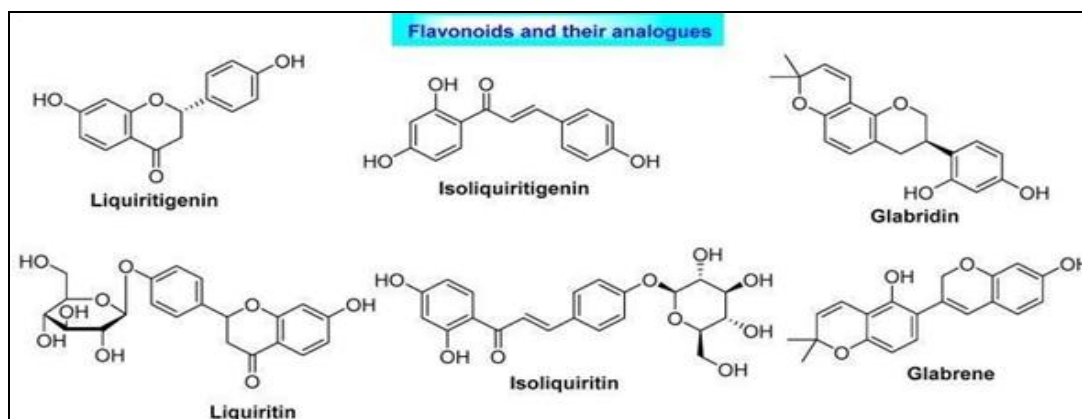
Biological Source: Liquorice consists of peeled and unpeeled roots, stolons, stem of *Glycyrrhiza glabra* Linn.

Geography: Native to Southern Europe, Western Asia, and parts of China. It is also grown in India, Turkey, Iran, and Afghanistan.

Phytoconstituents: Glycyrrhizin (6-8%), flavonoids, saponins, glucose, traces of tannin.

Benefits: Liquorice root may help to lower the testosterone levels, balance hormone, and reduce inflammation related to PCOS in women.

Usage: Can be used in tea or as a supplement, but should be used cautiously in people with high blood pressure.

**FIG. 23: FLAVONOIDS OF LIQUORICE THAT SHOW BENEFICIAL EFFECTS IN PCOS THROUGH ANTIANDROGENIC ACTIVITY**

Puncture Vine (*Tribulus terrestris*):



FIG. 24: PUNCTURE VINE

Synonyms: Tribulus, Gokshura (in Hindi)

Family: Zygophyllaceae

Biological Source: The whole plant, especially the fruit, is used in herbal medicine of plant *Tribulus terrestris*.

Geography: Widely distributed in Southern Europe, Asia, Africa, Australia, and parts of the Americas. It thrives in dry climates.

Phytoconstituents: Protodioscin, saponins, alkaloids, flavonoids.

Benefits: Used in traditional medicine to regulate ovulation and improve fertility in women with PCOS. It may help normalize estrogen and progesterone levels, contributing to more regular menstrual cycles.

Usage: Commonly taken in capsule or tincture form

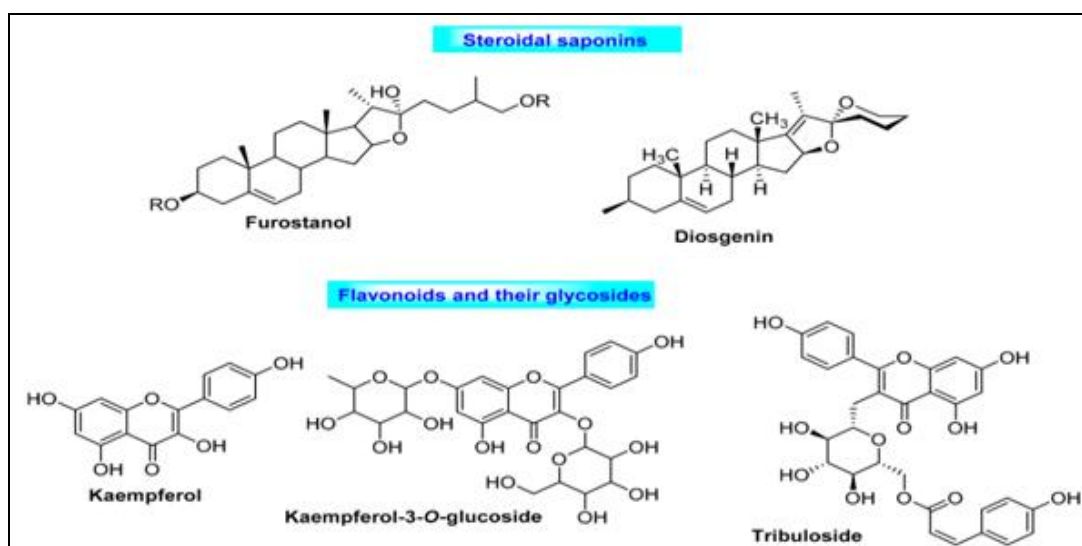


FIG. 25: SAPONINS AND FLAVONOIDS PRESENT IN *TRIBULUS TERRESTRIS* THAT HAVE POSITIVE EFFECTS ON PCOS BY INDUCING OVULATION

Shatavari (*Asparagus racemosus*):



FIG. 26: SHATAVARI

Synonyms: Wild Asparagus

Family: Asparagaceae

Biological Source: The shatavari mostly comprises of the dried roots and the leaves of the naturally occurring plant known as *Asparagus racemosus* Will.

Geography: Native to India, Sri Lanka, and parts of Southeast Asia.

Phytoconstituents: Steriodal saponin, shatavarin IIV (0.2%), shatavarin I.

Benefits: Shatavari is believed to support reproductive health and hormonal balance. It also contains antioxidants that may help reduce oxidative stress and inflammation.

Usage: Shatavari is often taken in powder form mixed with water or milk, or as capsules. A typical dosage ranges from 1-2 teaspoons of powder daily.

Spearmint (*Mentha spicata*):



FIG. 27: SPEARMINT

Synonyms: *Mentha spicata*, Garden Mint

Family: Lamiaceae

Biological Source: Spearmint is a perennial herb and its leaves are commonly used for their aromatic and medicinal properties of plant *Mentha spicata*.

Geography: Native to Europe and Asia, but it is now cultivated in many regions around the world, including North America and Africa.

Phytoconstituents: Rosmarinic acid, flavonoids, carvone, limonene.

Benefits: Spearmint tea has been shown to help reduce testosterone levels in women with PCOS, which can alleviate hirsutism (excess hair growth) and acne. It also has anti-inflammatory properties that may help with the inflammation seen in PCOS.

Usage: Drinking spearmint tea twice a day.

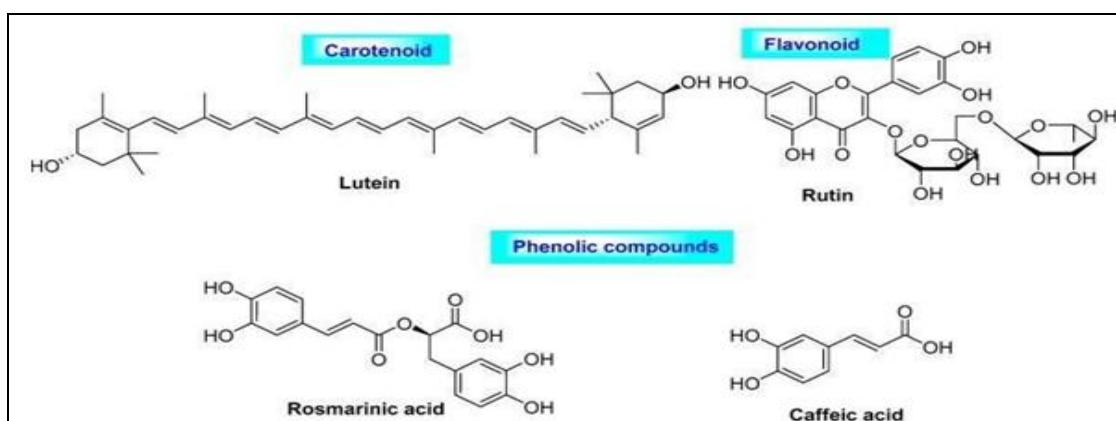


FIG. 28: AN ARRAY OF DIFFERENT SECONDARY METABOLITES OF *MENTHA SPICATA* THAT POSSESS ANTI-ANDROGENIC ACTIVITY

Turmeric (*Curcuma longa*):



FIG. 29: TURMERIC

Synonyms: *Curcuma longa*, Haldi (in Hindi)

Family: Zingiberaceae

Biological Source: Turmeric consists of dried rhizomes of *Curcuma longa*.

Geography: Native to India and Southeast Asia. It is also grown in countries with tropical climates such as China, Indonesia, Sri Lanka, and parts of Africa.

Phytoconstituent: Curcumin, turmerone, zingiberene, sesquiterpenes.

Benefits: Curcumin helps improve insulin sensitivity, reduces oxidative stress and may aid in regulating menstrual cycles. It can also improve mood by reducing inflammation in the brain.

Usage: Turmeric can be used in cooking or taken as supplement. For better absorption, it is often consumed with black pepper (which contain piperine, enhancing curcumin absorption).

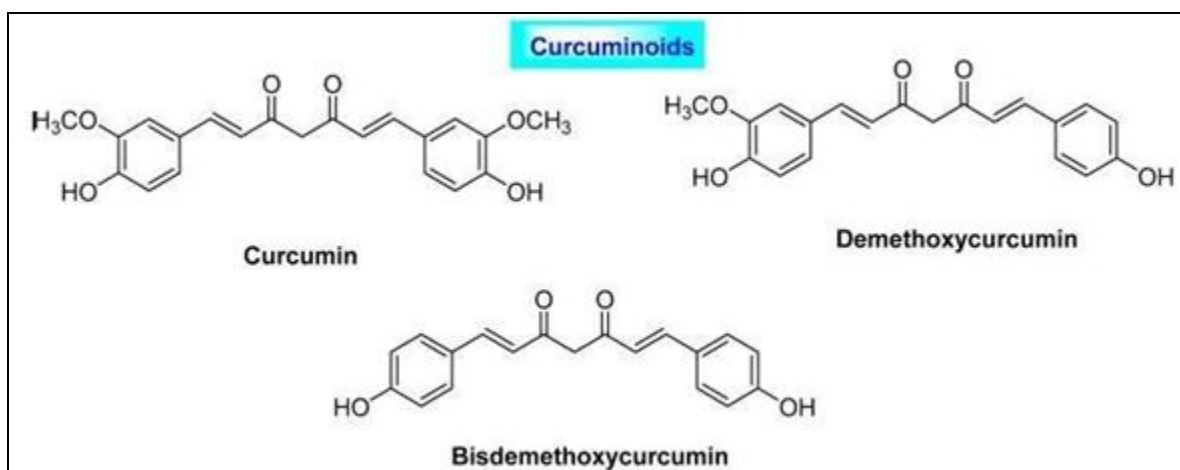


FIG. 30: CURCUMINOIDS SEEN IN *CURCUMA LONGA* RESPONSIBLE FOR IMPROVING THE PCOS CONDITION

Tulsi (*Ocimum sanctum*):



FIG. 31: TULSI

Synonyms: Holy Basil

Family: Lamiaceae (Mint family)

Biological Source: Tulsi, also known as "Holy Basil," belongs to the family *Lamiaceae* which is used as whole plant for its medicinal properties.

Geography: Tulsi is native to the Indian subcontinent and widespread throughout Southeast Asia. It is widely cultivated in India, Nepal, Sri Lanka, and parts of Southeast Asia. Tulsi is also grown in tropical and subtropical regions around the world, such as in Australia, the Middle East, Africa, and some parts of South America.

Phytoconstituents: Eugenol, Ursolic acid, Rosmarinic acid, Flavonoids.

Benefits: Tulsi is known for its anti-androgenic, antioxidant, and anti-inflammatory properties. It helps reduce androgen levels, insulin resistance, and symptoms like hirsutism and acne, which is often in PCOS, thereby improving metabolic health.

Usage: Consuming tulsi tea or using fresh tulsi leaves in foods can help alleviate stress and reduce inflammation. It can also be taken as a supplement in the form of capsules or dried powder

Vitex (*Vitex agnus castus*):



FIG. 32: VITEX

Synonyms: Chasteberry, Monk's Pepper

Family: Lamiaceae

Biological Source: *Vitex agnus-castus* is a small deciduous shrub known for its medicinal fruits, which are used in herbal remedies.

Geography: *Vitex agnus-castus* is native to the Mediterranean region, including Southern Europe and parts of Western and Central Asia.

Phytoconstituents: Agnuside, Aucubin, Casticin, iridoids, diterpenoids.

Benefits: *Vitex agnus-castus* helps to regulate the menstrual cycle by balancing hormones, particularly by promoting the production of progesterone.

Usage: Taken as a supplement or tincture.

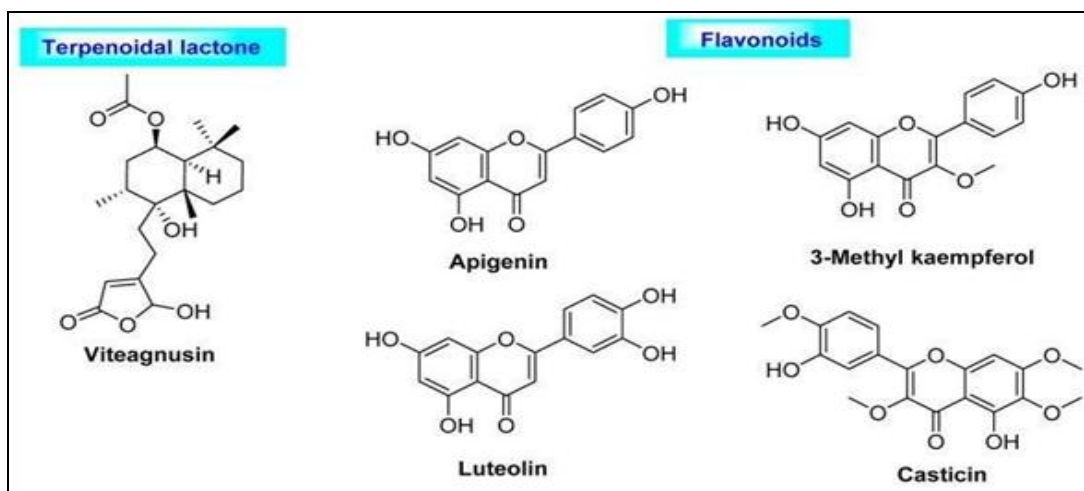


FIG. 33: TERPENOIDAL LACTONE AND FLAVONOIDS OF *VITEX AGNUS-CASTUS* RESPONSIBLE FOR IMPROVING OVULATORY CYCLE

Shortcomings, Challenges, and Future Perspectives: One of the main challenges in the diagnostic therapeutic course of PCOS is the identification of phenotype and the main cause of the disorder. This is a multifactorial etiology condition, often accompanied by signs and symptoms that cannot be directly ascribed to a metabolic alteration. For example, it is important to screen women with PCOS for all complications, including dyslipidemia and psychological distress⁵⁶. Generally, treatment is focused on alleviating symptoms, which can differ substantially among PCOS phenotypes; the woman's needs such as symptoms that cause her the most discomfort or the pregnancy seeking, among the others, cannot be disregarded. Women with PCOS often report significant dissatisfaction with the diagnostic process, the information provided, and the conventional treatment prescribed; moreover, several studies even found increased psychological distress after diagnosis⁵⁷. An additional challenge is choosing the most appropriate nutritional strategy for weight loss, as well as maintaining weight loss. Women with PCOS, indeed, have additional difficulties in weight loss and

maintenance, including insulin resistance, androgen excess, and impaired appetite regulation. Furthermore, there are normal-weight women with PCOS who, however, have been shown to have greater visceral adiposity than normal-weight controls without PCOS⁵⁸; hence, body recomposition and weight gain prevention interventions should be carried out⁵⁹.

It is important, therefore, to dialog with patients and make them understand that PCOS is a long-term illness where it would be desirable to seek a balance between treatment and daily life, in particular regarding nutritional management⁵⁷.

The study of new pharmacological and non-pharmacological therapeutic strategies to provide better treatment of PCOS is the aim of the research, but, to date, studies would seem to be limited by methodological problems, different diagnostic criteria, small sample size, nonrandomized design, and short follow-up⁵⁹. Moreover, not all outcomes have been adequately studied. The weight loss interventions' effectiveness on reproductive function, fertility outcomes, cardiovascular and

psychological health, quality of life, and appetite regulation still requires larger and sufficiently powered studies⁵⁹.

However, a meta-analysis of lifestyle interventions⁶⁰ showed an improvement in the free androgen index by reducing body weight (low-quality evidence), but no specific impact on childbirth or menstrual regularity was detected⁵⁶.

CONCLUSION: PCOS is a complex endocrine disorder affecting reproductive-age women, characterized by hormonal imbalance, insulin resistance, metabolic dysfunction, and psychological effects. Hirsutism, acne, and androgenetic alopecia are common symptoms of hyperandrogenism in women. Although these symptoms may also indicate other underlying diseases, the most common cause of hyperandrogenism in women of childbearing age is PCOS. It is associated with infertility, obesity, cardiovascular risks, and psychological conditions like depression and anxiety. PCOS involves disrupted hormone signaling, including increased gonadotropin-releasing hormone (GnRH) pulsatility, elevated luteinizing hormone (LH), and androgen levels, contributing to ovulatory dysfunction and cyst formation in the ovaries.

A multidisciplinary approach combining lifestyle changes, conventional treatments, and evidence-based herbal therapies is recommended for managing PCOS, highlighting the importance of individualized care. They target specific symptoms of PCOS while promoting overall health and reducing side effects associated with synthetic drugs. The quality of the evidence is variable and strongest for *Vitex agnus-castus* and *Cimicifuga racemosa* in the management of oligo/amenorrhea and infertility as associated with PCOS; and *Cinnamomum cassia* for improving metabolic hormones in PCOS. Berberine and Flaxseed enhances insulin sensitivity and reduces androgen levels. Turmeric and Aloe Vera decreases oxidative stress and inflammation, aiding in hormonal regulation. Ashwagandha reduces stress and supports hormonal balance. The current study gives concise and comprehensive outlook for the understanding of insulin resistance and androgen overexposure. We for the first time reported detailed review on the mechanism,

pathophysiology, and treatment interventions for the insulin resistance and hypersecretion of insulin. *e current study provides better understanding of the PCOS and provides a base for further exploration. There is need for further studies for more clinical trials and research into the mechanisms of PCOS and the long-term efficacy and safety of these herbal treatments, aiming to enhance individualized care protocols.

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CONFLICT OF INTEREST: Nil

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