

A Review on PCOS using *Benincasa Hispida*

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ABSTRACT

Polycystic ovary syndrome (PCOS) is a multifactorial endocrine disorder affecting women of reproductive age, characterized by hyperandrogenism, anovulation, and polycystic ovarian morphology [1]. It is often accompanied by metabolic disturbances such as insulin resistance, obesity, dyslipidemia, and an increased risk of type 2 diabetes and cardiovascular diseases. The etiology of PCOS is complex, involving genetic, hormonal, and environmental factors. Child and adolescent overweight and obesity were associated with significantly increased risk of later polycystic ovary syndrome symptoms [2]. Globally, prevalence estimates of PCOS are highly variable, ranging from 2.2% to as high as 26%. WHO estimates that it affected 116 million women are affected Worldwide in 2012(3.4% of women). In India the prevalence is gradually increasing. It is due to the lifestyle that people have adopted. The prevalence of PCOS among them was 22.5% by Rotterdam and 10.7% by Androgen Excess Society Criteria. Non-obese women comprised 71.8% of PCOS diagnosed by Rotterdam Criteria. Mild PCOS [Oligomenorrhoea and polycystic ovaries on USG] was the most common phenotype (52.6%). Hyperinsulinemia was presenting among 19.2% of diagnosed PCOS causes [3]

Keywords: Polycystic ovary syndrome, *Benincasa Hispida*

INTRODUCTION

The pathophysiology of PCOS involves primary defects in the hypothalamic–pituitary axis, insulin secretion and ovarian function. The various pathogenetic mechanisms of PCOS include abnormal gonadotropin-releasing hormone (GnRH) regulation leading to increased luteinizing hormone (LH) and decreased FSH; decreased response of ovarian follicles to FSH; increased anti-Müllerian hormone, follicular arrest and increased secretion of testosterone, estradiol and dehydroepiandrosterone (DHEA). Obesity, especially abdominal fat deposition, is the major predisposing factor for the metabolic phenotype in PCOS [4]. The insulin play an important role in the molecular mechanisms implicated in the androgenic hypersecretion and also the inhibition of hepatic synthesis of SHBG synthesis in liver cell. It prevents the normal follicular development in granular cell by a decrease in the level of follicle stimulating hormones which leads to follicular arrest [5]. Approximately, 25% to 30% of women with PCOS will show impaired glucose tolerance by the age of 30 and 8% of affected women

will develop type 2 diabetes[6]. Obesity is a common finding in women with PCOS and between 40–80% of women with this condition is reported to be overweight or obese. Familial aggregation of PCOS strongly supports a genetic susceptibility to this disorder [7].

Current pharmacological interventions, depends on the patient's desired outcomes whether the treatment of menstrual irregularity to achieve pregnancy or contraception, the anti- androgenic therapy for hyperandrogenic symptoms like hirsutism, the insulin sensitizer for insulin resistance associated with PCOS, and the ovulation inducer for infertility to induce ovulation[8]. All these therapeutic approaches are short-term symptomatic approaches; hence there is a lack of long-term systemic approaches in the management of PCOS. Consequently, there is a growing interest in exploring alternative and complementary therapies, particularly those derived from natural products.

The usage and acceptability of complementary medicine by women has increased from 26% to 91%

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during the past ten years. Ayurvedic system of medicine has been emerging as one of the most commonly practiced alternative medicine for various health problems, including PCOS [9-10]. Recent day global health debates getting significant attention towards traditional herbal medicines, Ayurveda is one of the most accepted traditional systems of Indian medicine.

Benincasa hispida (Thunb.), commonly known as ash gourd or winter melon is a traditional medicinal plant widely used in Ayurvedic and folk medicine. It belongs to the Cucurbitaceae family and is known for its diverse pharmacological properties including antioxidant, anti-inflammatory, antidiabetic, and diuretic effects. Traditionally used to treat neurological diseases, kidney disease, menstrual disorders, fever, cough accompanied by thick mucus and to fight intestinal worms [11-13]. The fruit is rich in bioactive compounds such as flavonoids, alkaloids, sterols, and phenolic acids, which contribute to its therapeutic potential [14]. Recent studies have indicated that *B. hispida* may exert beneficial effects on metabolic and hormonal imbalances, making it a promising candidate for the management of PCOS.

The letrozole-induced PCOS model in rats is a well-established experimental approach that closely mimics the pathophysiology of human PCOS. Letrozole, an aromatase inhibitor, elevates androgen

levels by blocking the conversion of androgens to estrogens, leading to the development of ovarian cysts and reproductive dysfunction [15]. This model provides a reliable platform for evaluating the efficacy of potential therapeutic agents in alleviating PCOS-associated symptoms.

In light of the above, the present study aims to investigate the therapeutic effect of *Benincasa hispida* fruit extract on letrozole-induced PCOS in female rats. The study also planned to elucidate the potential mechanisms through which *B. hispida* exerts its effects, with a particular focus on its hypolipidemic, anti-diabetic, and hormone-modulatory properties.

POLYCYSTIC OVARY SYNDROME

Polycystic ovary syndrome (PCOS) is a hormonal disorder common among women of reproductive age. Women with PCOS may have infrequent or prolonged menstrual periods or excess male hormone (androgen) levels. The ovaries may develop numerous small collections of fluid (follicles) and fail to regularly release eggs. It may describe in 1935, by F. Stein and Leventhal [16]. PCOS symptoms involve both endocrine and gynecologic system such as Insulin resistance, hyperinsulinemia, dyslipidemia, hypertension, diabetes mellitus, endometrial hyperplasia, cardiac disease, obesity, anovulation and infertility [17].

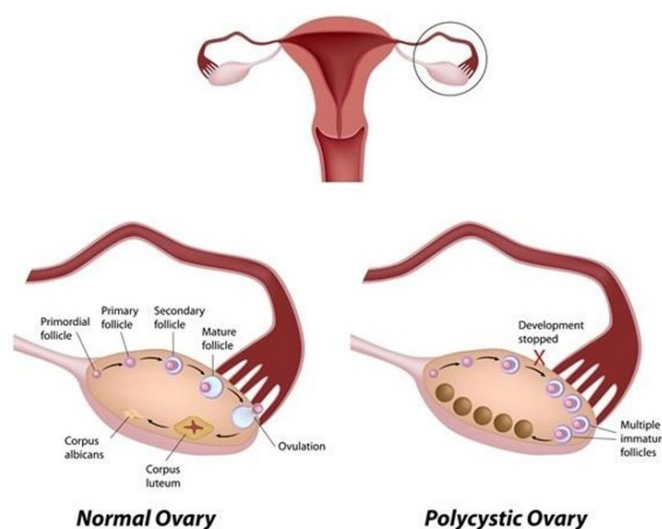


Figure 1: Difference in normal ovary and PCOS ovary

Types of Polycystic Ovary Syndrome

Insulin-Resistant PCOS

Insulin, a pancreas-produced hormone plays a critical role in processing glucose in the bloodstream and turning it into energy for the body. The Body's



primary source of energy is glucose. Commonly, blood glucose is referred to as blood sugar. When the body does not respond to the insulin production this is referred to as insulin resistance. Insulin resistance alters the function of the hypothalamus and the

pituitary gland in the brain, increasing the production of androgenic hormones, which contribute to PCOS. Excessive production of androgenic hormones is an independent risk factor for female infertility and ovarian dysfunction, with or without PCOS [18].

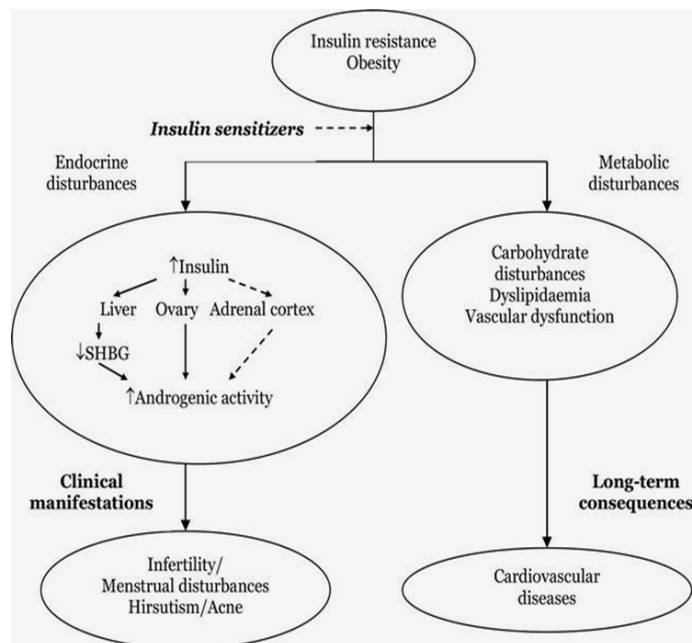


Figure 2: Insulin Resistant Polycystic ovary syndrome

Non-Insulin Resistant PCOS

In this type of PCOS caused by Vitamin D or Iodine deficiency, hormone- disrupting toxins, thyroid disease, and adrenal stress.

Epidemiology & Diagnostic criterion of PCOS

According to the World Health Organization (WHO) statement globally 116 million females (3.4%) are affected by PCOS. Worldwide the prevalence of PCOS is highly variable from a minimum of 2.2% to a maximum of 26.0% [19]. In India, the prevalence ranges from 3.7% to 22.5%. A conducted cross-sectional clinical study reported that the prevalence is about 18% of adolescent women in Tamil Nadu [20].

Table : Diagnostic Criterion of PCOS

Diagnostic criteria	Diagnostic feature
NIH/ NICHD criteria-1992	- Hyperandrogenism - Oligo-ovulation/anovulation (Menstrual dysfunction) - Exclusion of other related disorders
ESHRE/ ASRM Rotterdam Criteria-2003	Two out of three following criteria - Clinical or Biochemical hyperandrogenism - Chronic anovulation or oligomenorrhea - Polycystic ovaries (>10 cysts, 2-8mm in diameter)
AES Criteria-2006	- Hyperandrogenism - Oligo-ovulation/anovulation - Polycystic ovaries - Exclusion of other related disorders
NIH - National Institutes of Health, NICHD- National Institute of Child Health and Human Disease, ESHRE- The European Society for Human Reproduction and Embryology, ASRM- American Society for Reproductive Medicine, AES- Androgen Excess Society	

Pathogenesis and risk factors of PCOS

Ovarian and Adrenal Hyperandrogenism

PCOS is an intrinsic disorder of the ovaries and that the primary defect resides in the increased androgen biosynthesis. Normally, ovarian theca cells produce androgens in response to LH. Androgen production is cyclical and modulated by intra ovaries and extra-ovaries mechanisms. As LH rises, a down regulation of LH receptors and a decrease in CYP17A1 expression occur, minimizing the androgenic production. In contrast, insulin and IGFs stimulate the P450c17 enzyme and up-regulate LH receptor sites. PCOS ovaries are typically hypersensitive to LH, which is caused by partial escape from LH receptor down regulation. The imbalance of the intra-ovarian regulatory system seems to play a role in this increased sensitivity to LH. Exogenous factors, such as insulin resistance and hyperinsulinemia, are examples of extra ovarian modulators that disrupt normal intra- ovarian regulatory mechanisms.

Neuroendocrine axis

The ovarian steroidogenesis is directly related to the gonadotropic stimulus, alterations of LH are indicated as one of the factors involved in the development of PCOS. Progesterone is the primary regulator of GnRH pulsatility. It is known that PCOS patients present a GnRH-generating pulse resistance to negative feedback by progesterone, which results in a higher LH pulses frequency. Therefore alterations of the gonadotropic axis appear to be secondary to hyperandrogenemia. Ovarian and adrenal hyperandrogenism, altered folliculogenesis, increased insulin resistance and neuro endocrine axis dysfunction could have a greater or lesser role in PCOS pathogenesis [21].

Insulin Resistance, Hyperinsulinemia

IR and hyperinsulinemia are commonly detected in women with PCOS; insulin receptor gene mutations are extremely rare among women with PCOS. Insulin is the hormone primarily responsible for glucose homeostasis and lipogenesis. Insulin actions are mediated by insulin receptors, which are found in numerous tissues of the HPO axis. The compensatory hyperinsulinemia associated with IR provokes excessive ovarian/adrenal androgen secretion and decreases hepatic SHBG synthesis with the net result of increasing circulating testosterone concentrations. This leads to the paradox of insulin signaling in PCOS. The transient IR and hyperinsulinemia typical of early puberty may kindle the factors associated with development of PCOS.

Developmental Hypothesis / Fetal Origins

The developmental theory of PCOS proposes that exposure of the female fetus to elevated androgen concentrations contributes to the development of PCOS. Potential mechanisms include effects on steroidogenesis, insulin signaling, pancreatic β -cell function, hypothalamic-pituitary organization, neuroendocrine secretory patterns, and epigenetic modifications. Fetal, neonatal, prepubertal, and/or pubertal ovaries may be genetically predisposed to increased androgen secretion [22].

Obesity

In patients suffering from PCOS, the incidence of obesity is somewhere between 50- 75%, which is higher than in the general population. Not only is obesity more common among women with PCOS, research suggests that obesity may exacerbate many of the manifestations of PCOS including androgen levels and insulin resistance. Obese women suffering from PCOS generally have higher serum androgen concentrations and a reduced response to fertility treatments [23].



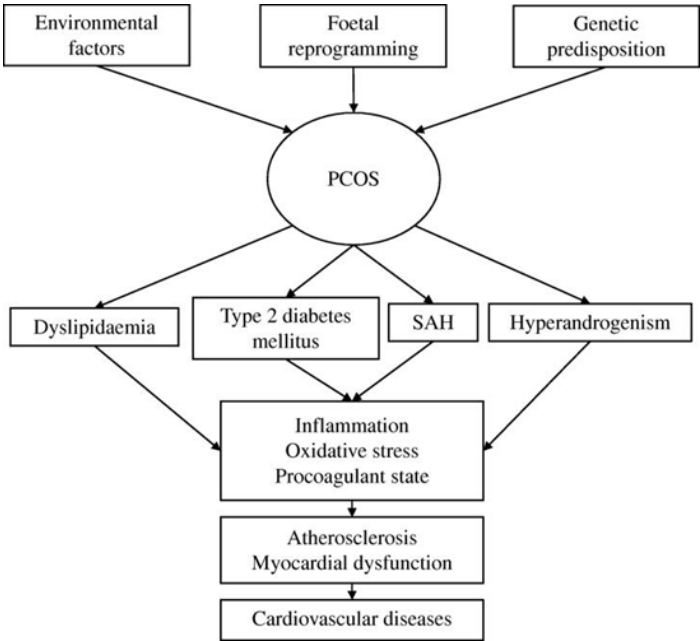


Figure 3: Pathogenesis of Polycystic Ovary Syndrome

Genetics of PCOS:

PCOS is an extremely heterogenetic and complex disease. No single gene has been found to cause PCOS, so the link is likely to be complex and involve multiple genes. Women with PCOS are 50% more likely to have an immediate female relative – mother,

aunt, sister or daughter – with PCOS. Type 2 diabetes is also common in families of those with PCOS. The genetic basis of PCOS is different between families and within families but is related to a common pathway. The genetic susceptibility of different genes is different in patients from the same family [24].

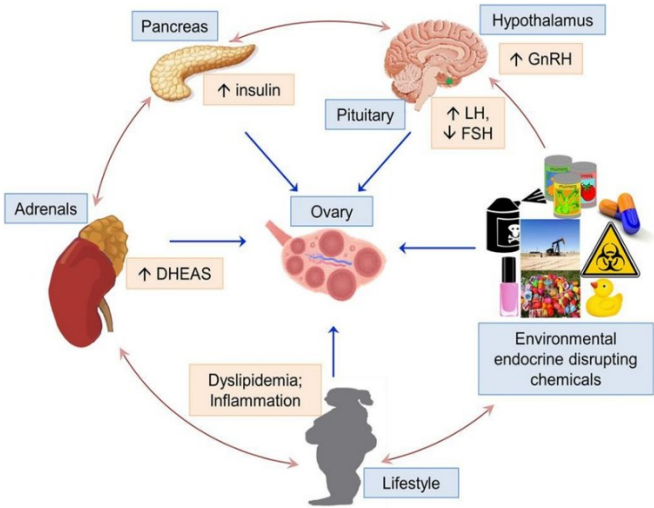


Figure 4: Etiology of Polycystic ovary syndrome

PLANT PROFILE:

Benincasa hispida Fruit

Scientific name	:	<i>Benincasa hispida</i> (Thunb.) Cogn.
Family	:	Cucurbitaceae

Common names	:	Ash gourd, Winter melon, Wax gourd, White pumpkin, Kushmanda (Ayurveda), Dong Gua (TCM)
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Taxonomical Classification

Kingdom	:	Plantae
Subkingdom	:	Tracheobionta (Vascular plants)
Division	:	Magnoliophyta (Angiosperms)
Class	:	Magnoliopsida (Dicotyledons)
Order	:	Cucurbitales
Genus	:	<i>Benincasa</i>
Species	:	<i>Benincasa hispida</i> (Thunb.) Cogn.

Botanical Description

Benincasa hispida (Thunb.) Cogn., commonly known as ash gourd, winter melon, or wax gourd, belongs to the family Cucurbitaceae. It is a climbing annual herb with a hairy stem, large palmately lobed leaves, and yellow unisexual flowers. Large, oblong to round, green when immature, turning pale with a characteristic waxy coating when mature. Pulp is white, watery, and mildly sweet; seeds are numerous, oblong, and white. It is cultivated widely across tropical and subtropical Asia, particularly in India, China, and Southeast Asia.



Figure 6: *Benincasa hispida* Fruit

USES OF BENINCASA HISPIDA:

- In Ayurveda, it is called Kushmanda or Kumra, used as a coolant, diuretic, aphrodisiac, and brain tonic.
- In Traditional Chinese Medicine (TCM), the fruit and peel are prescribed for edema, urinary retention, thirst, and phlegm disorders.

Folk medicine uses include treatment of ulcers, piles, epilepsy, asthma, and as a natural detoxifier

DISCUSSION

Polycystic ovary syndrome (PCOS) is a complex endocrine-metabolic disorder characterized by ovarian dysfunction, hyperandrogenism, and metabolic derangements such as insulin resistance and dyslipidemia [86, 87]. Conventional treatments, including metformin, clomiphene, and letrozole, offer symptomatic relief but are often limited by side effects and lack of holistic efficacy [88]. In this context, herbal medicines have gained attention for their multi-targeted therapeutic actions. *Benincasa hispida* (ash gourd), a member of the Cucurbitaceae family, is traditionally recognized in Ayurveda and Traditional Chinese Medicine for its cooling, diuretic, and restorative properties [89]. Recent pharmacological studies have highlighted its antioxidant, anti-inflammatory, antidiabetic, and antihyperlipidemic activities, making it a promising candidate for PCOS management. Hence, this study is attempted to evaluate *B. hispida* fruit as an effective alternative medicine for PCOS.

SUMMARY:

Polycystic ovary syndrome (PCOS) is a multifactorial endocrine disorder characterized by hyperandrogenism, ovulatory dysfunction, and metabolic abnormalities such as insulin resistance, dyslipidemia, and obesity. Current pharmacological options provide symptomatic relief but are associated with limited long-term efficacy and adverse effects, thereby encouraging the exploration of safer, multi-targeted alternatives.

In the present study, *Benincasa hispida* fruit extract (BHFE) was evaluated for its therapeutic potential in letrozole-induced PCOS in female Wistar rats. Phytochemical analysis of the extract confirmed the presence of bioactive compounds, including alkaloids, flavonoids, phenolic compounds, and sterols, which are known to exert antioxidant, anti-inflammatory, and metabolic regulatory effects.

Acute toxicity studies revealed no adverse effects up to 2000 mg/kg, indicating a favorable safety profile.

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