

Original Research Article

INSIGHTS ON FEVER NUT: THE NEXT GENERATION TREATMENT OF PCOS.

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Abstract

Polycystic ovarian syndrome is a major concern for today's young generation because of unhealthy lifestyle. PCOS is hormone related chronic condition which causes anovulation leading to infertility. It is said to affect the physical and emotional well being of the person who is suffering from it. The approximate percentage of patients suffering from PCOS is around 9-14% many of which are undiagnosed. As such the cause of PCOS is unknown but it is said that women with family history and type 2 diabetes associated with hormonal imbalance, irregular periods, excess androgen levels and cysts in ovaries. *Caesalpinia bonducella* is a smallest tropical leguminous plant that is used by many practitioners for the treatment of various disorders like paralysis, dental caries, leprosy, gum boils etc. The chemical constituent present in *Caesalpinia bonducella* is known to possess anti-estrogenic, antihelmintic, antioxidant, immunomodulatory activity and many more. The review encompasses the contribution of *C. bonducella* in demoting the excess amount of androgen resulting in PCOS.

Keywords: *Caesalpinia bonducella*, PCOS, Chemical Constituents, pharmacological activity.

Introduction

PCOS is a common endocrine condition that commonly affects young women and is marked by hyperandrogenemia, hyperinsulinemia, abnormality in ovarian and hypothalamic-pituitary axis function.^[1] A woman with irregular menstrual bleeding and polycystic ovaries may be designated as having PCOS without any clinical or biochemical evidence of androgen excess.^[2] The clinical presentation is heterogeneous and patients may present some of various signs and symptoms.^[3] This heterogeneity seems to be modulated by multiple factors, such as prenatal androgen exposure, nutritional status in the uterus, genetic factors, as well as ethnicity, insulin resistance of puberty and/or exaggerated adrenarche and changes in body weight^[4]. *Caesalpinia bonducella* is a prickly shrub with synonyms like *Caesalpinia bonduc*, *caesalpinia crista*,^[4] *Guilandina bonduc* belonging to the family -*Caesalpinaceae* which is most commonly found in tropical regions of India, Sri Lanka and Andaman and Nicobar Islands thus widely distributed all over the world.^[4,5] It is found to be effective in treatment of PCOS and an efficient antiseptic, antibacterial, anti-inflammatory, antidiuretic, anthelmintic, antipyretic, anticonvulsant, antidiarrhoeal, antiviral, antiasthmatic, anti-

anaphylactic, antiameobic and antiestrogenic. The pharmacognostic, phytochemical parameters and Quality parameters like microscopic and macroscopic studies were performed following the phytochemical tests carried out with ethanolic extract which revealed the presence of many chemical constituents namely flavonoids, saponins, alkaloids, steroids, resins.^[5,6] PCOS is the primary cause of infertility in person who have it.^[7] Intake of *C.*

bonducella seed kernel has reversed PCOS conditions in many patients as reported by Ayurveda and Siddha practitioners.^[8]

Etiology

High insulin levels lead the ovarian cells to produce more testosterone, less FSH, and have a greater LH/FSH ratio, which in turn contributes to poor follicular development and ovarian abnormalities.^[9] The LH/FSH ratio may also be impacted by changes in the hypothalamus's ability to generate gonadotropin-releasing hormone (GnRH). GnRH stimulates the pulsatile LH and FSH secretion by the pituitary glands.^[10] In certain PCOS individuals, there is low testosterone and too much estrogen. Negative feedback inhibition, brought on by high estrogen levels, stops FSH from being released through the GnRH route.^[10,11] Low FSH and high LH impair follicle maturation.^[12] The incidence of PCOS has been closely related to oxidative stress and chronic low grade inflammation.^[12] Recent 33 studies have demonstrated that the core etiology and primary endocrine characteristics 34 of PCOS are hyperandrogenemia (HA) and insulin resistance (IR).^[15]

Pathophysiology

With a 70% concordance rate in monozygotic twins, PCOS is a highly heritable illness, which raises the possibility that genetics may play a role in its pathophysiology. It has been established that PCOS patients' first-degree male and female relatives both suffer metabolic and reproductive problems.^[14] More specifically, in girls with such genetics, glucose-stimulated hyper- insulinaemia starts to appear as early as age four and lasts into puberty.^[16] Furthermore, fasting indices of insulin resistance and insulin responses during an intravenous glucose tolerance test for the evaluation of b-cell function were used to demonstrate insulin resistance and b-cell dysfunction in such premenarchal girls between the ages of 8 and 14.^[16,17] A deficiency in pancreatic b-cell activity was suggested by a longitudinal follow-up of peripubertal adolescent girls whose mothers had PCOS, which revealed a significantly lower disposition index that remained over 2 years.^[18] One potential genetic reason is the connection between the type 2 diabetes TCF7L2 susceptibility locus and the evidence of b-cell malfunction in adult PCOS women. Epigenetic changes, such as those of the PDX1 gene involved in the regulation of pancreatic development, are also thought to be connected to the b-cell malfunction in girls who are first-degree relatives of people with PCOS. High levels of the adaptor protein Lnk, which suppresses the phosphatidylinositol 3-kinase-AKT and MAPK-ERK signaling response to insulin, are another hereditary factor that may contribute to IR in PCOS patients.^[19] While the role of oxidative stress in the pathogenesis of PCOS is still under study, it was shown to cause altered steroidogenesis in the ovaries, by increasing androgen levels, disturbing follicular development, leading to infertility, Obesity, insulin resistance, and cardiovascular risks were also related to oxidative stress in PCOS women.^[20,21] In multiple investigations, oxidative stress- associated inflammation markers were positively correlated with androgen levels in PCOS patients. ROS exert both negative and positive effects on mammalian ovaries.^[22]

Symptoms

Symptoms of polycystic ovary syndrome can differ from person to person. Symptoms may change over time and often occur without a clear trigger.

Possible symptoms include:

- Heavy, Long, Intermittent, Unpredictable or Absent Periods
- Infertility
- Acne or Oily Skin
- Excessive Hair on the Face or Body
- Male-Pattern Baldness or Hair Thinning
- Weight Gain, Especially around the Belly.

People with PCOS are more likely to have other health conditions including:

- Type 2 Diabetes
- Hypertension (High Blood Pressure)
- High Cholesterol
- Heart Disease
- Endometrial Cancer (Cancer Of The Inner Lining Of The Uterus).^[23]

Diagnosis

Polycystic ovary syndrome is diagnosed by the presence of at least two out of the following:

1. Signs or symptoms of high androgens (unwanted facial or bodily hair, loss of hair from the head, acne or an elevated blood level of testosterone) – after other causes for this have been excluded;^[24]
2. Irregular or absent menstrual periods – after other causes for this have been excluded; and
3. Polycystic ovaries on an ultrasound scan.

When making a diagnosis, doctors also take into account that irregular periods and ovulation can be a normal part of puberty or menopause, having polycystic ovaries may run in families, and women with a family history of PCOS or type 2 diabetes are at higher risk of PCOS^[25]

Since ancient times, plants have contributed significantly to preserving human health and enhancing the quality of human existence by serving as essential ingredients in medications, flavors, beverages, cosmetics, and colours. Herbal medicine is predicated on the idea that plants contain natural compounds that can improve health and treat disease. The study of plants has received more attention recently, and a wealth of data has accumulated to demonstrate the enormous potential of the medicinal plants employed in diverse traditional systems^[26,27]

***Caesalpinia bonducella*: the herb**

Caesalpinia bonducella L., also called "fever nut" According to folklore medicine and historic Ayurvedic texts, bonduc nuts and nicker nuts, which are members of the Caesalpiniaceae family, have medicinal properties.^[27]

The name of the species, "Bonducella," derives from the Arabic word "Bonduce," which means "a little ball" and describes the globular shape of the seed.^[24] *C. bonducella* is a sizable prickly shrub that is endemic to South India, Burma, and Ceylon. It grows best near the shore and up to 2500 feet in mountainous areas. Most plant components have medicinal benefits, according to literature, but the seed and shell have been the subject of extensive research.^[26]

The main alkaloid in *Caesalpinia bonducella* L is known to be natin, which is also present in the shell, seed, and twigs. According to reports, the seed contains a potent glycoside form of the active

chemical, bonducin. It's also known that seeds contain terpenoids and saponins. The shell is reported to include a variety of low molecular weight unsaturated acids, starch, sucrose, phytosterols, stearic, palmitic, oleic, linoceric, and linolenic acids, as well as fatty oils, starch, and sucrose. From 7.430 to 25.346% of the total amino acids are proteins.⁸ The seeds are said to possess anti-diabetic qualities. People of all ages worldwide are affected by type 2 diabetes, a chronic metabolic condition. The blood glucose level rising, which may be multifactorial, is the disease's hallmark. The root causes the decrease or lack of insulin production.^[25]

All of the conducted extracts, with the exception of the hexane for *C. bonducella*, included phenol, according to the qualitative analysis. The seed's kernel is extremely beneficial and excellent for treating all common, ongoing fevers as well as intermittent ones.^[25]

Three times every day, adults and children alike should consume 15–30 grains of the kernel powder combined with equal amounts of black pepper. Asthma patients utilize roasted kernel decoction. To help children who have trouble digesting mother's milk, the extract or powder of the kernel is given to them together with ginger, salt, and honey. Boils and other swellings can be treated with paste made from kernel.^[27] A good treatment for cases of acute orchitis, ovaritis, and scrofula is a cake made of 30 grains of powdered kernels that has been fried in ghee and given twice daily.^[28]

It's important to regulate both b-cell functions and insulin resistance since PCOS is tied to b-cell dysfunction, which is linked to insulin resistance, and common cases of PCOS are linked to hormonal imbalances caused by b-cell dysfunction.^[28]



[A] [B] [C]
Figure : (A) seeds of bonducella in plants. (B) dried seed collected from the plant of *C. bonducella*. (C) diagrammatic representation of polycystic ovarian syndrome.

Phytochemistry

The alkaloids in *Caesalpinia bonducella* L are known to be found in shell, seed and twigs, the predominant one being Natin. The active molecule, Bonducin is reported to be present in the seed as a powerful glycoside. Saponins and terpenoids are also known to be found in seed. The shell is known to contain fatty oil, starch, sucrose, phytosterols, stearic, palmitic, oleic, linoceric, linolenic and a mixture of unsaturated acid of low molecular weights. The protein and amino acid content varies from 7.430 to 25.346%.⁸ The seeds are reported to have anti-diabetic properties.^[29] Type 2 diabetes, a chronic metabolic disorder affects people of all ages across the globe. This disease is characterized by increase in the blood glucose level which may be multifactorial. The primary cause is the decrease or lack of insulin production^[30]

The qualitative analysis has shown the presence of phenol in all the extracts performed other than

the hexane for *C. bonducella*. The kernel of the seed is very much useful and valuable in all ordinary simple, continued and intermittent fevers.^[31]

The kernel powder mixed with equal parts of black pepper is taken thrice a day in a dose of 15-30 grains by adults and 3-4 grains by children.^[33] Decoction of roasted kernels is used in asthma. Children who are unable to digest mother's milk are given the extract of the kernel or its powder along with ginger, salt and honey to get good stomachic effect.^[32] Paste prepared from kernel gives relief from boils and other swellings.^[33] A cake made of 30 grains of powdered kernels, fried in ghee taken twice a day is a valuable remedy in cases of acute orchitis, ovaritis and scrofula.^[35]

Since PCOS is related to the b-cell dysfunction which is linked with insulin resistance and prevalent cases of pcos are associated with the hormonal imbalances due to b-cell dysfunction, its necessary to regulate the b-cell functions along with the insulin resistance.^[36,37]

Plant materials and preparation of extracts

The seeds of *Caesalpinia bonducella* were collected in from Sagar District, Madhya Pradesh, India.^[38] The taxonomical identification of the plant was done at Botanical Survey of India, Pune, India.^[39] The outer shells of the plant seeds were shade-dried, powdered, and an aqueous extract (50 mg/ml) was prepared using gravimetric techniques^[40] The air-dried seeds of *Caesalpinia bonducella* (50 g) were extracted with 500 ml of ethanol by using soxhlet apparatus. The crude extract was filtered, and evaporated under reduced pressure to give a viscous dark mass with a percentage yield of 3.0% (w/w).^[42]

Phytochemical screening

To identify the essential constituents of the ethanolic extract of *Caesalpinia bonducella* seeds such as alkaloids, terpenes and steroids, saponins, flavonoids, polysaccharides and tannins, a preliminary phytochemical screening was carried out using various test methods of Dragendorff's and Mayer's test, Liebermann–Burchard test, foam formation test, lead acetate test, Molisch's and Fehling's test and ferric chloride test, respectively (Trease and Evans, 1983).^[43,44]

Activity

In 1994, Velazquez et al reported for the first time that administration of the insulin sensitizer drug metformin to PCOS patients reduced hyperinsulinemia, insulin resistance, hyperandrogenemia, and systolic blood pressure, while facilitating normal menses and pregnancy^[45,46]. *C. bonducella* can act on the ovary through altered endocrine functions associated with decreased estrogen level. Furthermore, phytoestrogens interfere in estrogen negative feedback by binding with estrogen receptors in anterior-pituitary or hypothalamus and indirectly alter ovarian steroidogenesis estrogen to bind to estrogen receptors^[47,48] There were no uniform variations in serum estradiol and progesterone levels^[49]. When the extract is taken orally (300 mg/kg) it causes anti hyperglycemic action by blocking the glucose absorption and decreases the BUN levels on large scale. The extracts lowered the LDL level and elevated cholesterol in diabetes induced hyperlipidemia.^[50] The effects of ethanolic seed extract of *Caesalpinia bonducella* (ESECB) on in vivo enzymatic and non-enzymatic antioxidant levels and histopathological changes in Mifepristone-induced polycystic ovary syndrome (PCOS) female rats were evaluated.^[50,51]

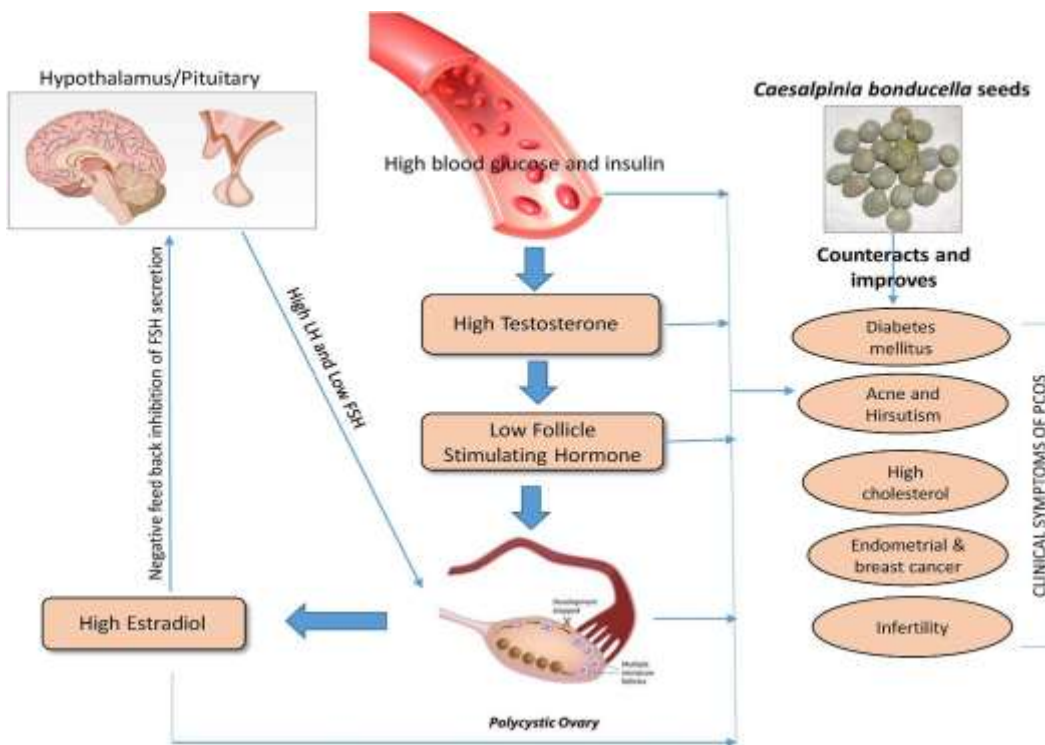


fig: working of C.bonducella[1]

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