

<p>Introduction</p>	<p>Brand Name : Gonadil Therapeutic Category – Nutraceutical [for PCOS]</p> <p>Polycystic ovarian syndrome (PCOS) is universally recognized as the commonest endocrinological disorder in women. Initially thought to be a reproductive disorder, the disorder is more complex, as a number of physiological functions are affected and have a great impact on the health and quality of life of the female. In PCOS, there is an increased androgen [male hormone] synthesis, and disrupted folliculogenesis, irregular menstrual cycles and insulin resistance. In addition to endocrine participation, reproductive and metabolic components also play an active role in PCOS, creating a complex equation to the disorder. The altered metabolic environment, due to PCOS, may have long-term health consequences, leading to chronic conditions such as T2DM and cardiovascular disease.</p> <p>Altered life-styles, junk food, genetics and a host of other conditions add fuel to the fire and have a physiological impact, in the adolescents and women of child-bearing age with PCOS. The manifestations are manifold and include:</p> <ol style="list-style-type: none"> 1. Impaired production of reproductive hormones 2. Disruption of menstrual cycles 3. Reduced rates of fertility and 4. Ovulation [anovulatory states] 5. Weight gain <p>Aetiology & Presentation of PCOS PCOS, is characterized by irregular menstrual cycles, amenorrhoea, hyperandrogenic states such as hirsutism, infertility, caused due to endocrine disruption, with hormonal imbalance. In addition, insulin resistance and hyperinsulinaemia contribute significantly to this chronic disorder and its underlying pathophysiology.</p> <p>In addition to infertility and menstrual cycle disorders, the metabolic manifestations are a major accompaniment in many females with PCOS. that include dyslipidaemias, impaired glucose metabolism and increased cardiovascular risk.</p> <p>Psychological Aspects – In addition to metabolic disturbances, the psychological impact of PCOS, is also plays a major role in the lives of women with PCOS and some the characteristics seen are:</p> <ol style="list-style-type: none"> 1. Low Self-Esteem & Negative body image 2. Depression & Anxiety 3. Mood-Disturbances 4. Physical appearance [Obesity, Hirsutism & Androgenic Alopecia] <p>Investigations in PCOS As PCOS is a complex syndrome, the investigations include:</p> <ol style="list-style-type: none"> 1. Hormonal estimations – LH:FSH ratio, PRL [Prolactin], Thyroid Hormones [T₃, T₄ & TSH] and androgen status [Testosterone, SHBG, and Free Androgen Index] 2. Pelvic Ultra Sound for Ovarian Morphology and Endometrial Thickness 3. Glucose Estimation <p>Despite the best diagnostic facilities, evaluation criteria, the problem of treating PCOS in adolescents and women of reproductive age is a challenge as there is no consensus on the use of contraceptives in adolescents and the use of OCPs for cycle regulation [duration of treatment] in adult women are all a cause of concern for the treating Physician. The use of contraceptives to correct menstrual irregularities, metformin for improving insulin sensitivity, and clomiphene citrate for anovulatory infertility are some of the treatment modalities along with modification in diet and changes in life-styles are some of the treatment measures that are adopted by the Physicians. However compliance is poor, as many patients discontinue the treatment. In lieu of this, many female patients have adopted the use of nutraceuticals, which contain ingredients that have been studied and documented. A combination of anti-androgenic, a cycle regulator and insulin sensitizer is a preferred</p>
<p>Saw palmetto</p>	<p>Proven anti-androgenic properties in a number of human studies, in males with BPH. Disease states in which this natural agent is relevant include Polycystic Ovarian Syndrome, Hirsutism, and Acne. Numerous mechanisms of action of SPB have been proposed, including antiandrogenic effects, inhibition of type 1 and type 2 isoenzymes of 5α-reductase, inhibition of growth factors, and an anti-inflammatory effect. The major components that exert pharmacological activity are Steroids: Sterols, Flavonoids, water soluble polysaccharides and fatty oil. The possible mechanisms :</p> <ol style="list-style-type: none"> 1. Anti-androgenic activity [Saw palmetto inhibits 5-alpha Reductase, therefore inhibiting conversion of testosterone to DHT. Reduces androgen effects there by altering Insulin resistance, contributing to improved Folliculogenesis] 2. Inhibitory effect on type 1 and type 2 iso-enzymes of 5α-reductase 3. Inhibition of prolactin and growth factor-induced cell proliferation 4. Anti-inflammatory effect - The hexane extracts of the herb have demonstrated anti-inflammatory activity. Inhibition of the synthesis of arachidonic acid inflammatory metabolites, through a double blocking of cyclooxygenase and 5-lipoxygenase pathways results in anti-inflammatory properties 5. Anti-oedema Effect
<p>Paeonia lactiflora</p>	<p>Paeonia lactiflora, has been used for more than 1000 years in traditional Chinese medicine for the treatment of gynecological problems, cramp, pain, giddiness, and congestion. Paeoniflorin, Monoterpene glycosides isolated from P. lactiflora, possesses a variety of pharmacological activities. Peony has shown to affect human androgen levels in vitro. Peony has been used for gynecological conditions by both Chinese and Western herbalists, and is used by Western herbalists for PCOS, hyperprolactinemia, endometriosis, ovarian failure and androgen excess. Peony has been shown to positively influence low progesterone, reduce elevated androgens (testosterone) and act to modulate Estrogen and Prolactin. In-vitro, the active constituent paeoniflorin has been shown to affect the ovarian follicle by its action on the aromatase enzyme. Aromatase is important for follicle maturation, ovulation and corpus luteum function, steroid hormone synthesis and the regulation of the conversion of androgens to estrogens. The biofeedback in the pituitary and hypothalamus rely on aromatase to regulate prolactin and GnRH.</p>

	<p>The mechanisms attributed to Paeonia are:</p> <ul style="list-style-type: none"> ▲ Menstrual Cycle Regulator ▲ Follicular phase modulators ▲ Hormone regulator / balancer [Regulation of LH:FSH ratio] 3. Hypothalamic pituitary Ovarian modulator 4. 5. Oestrogen modulator 6. Testosterone /Androgen Inhibition [paeoniflorin, a compound found in white peony that inhibited the production of testosterone and promoted the activity of aromatase, which converts testosterone into estrogen]
Glycyrrhiza glabra	<p>Licorice is a flavorful substance that has been used in food and medicinal remedies for thousands of years. It is also known as “sweet root,” licorice root contains a compound that is about 50 times sweeter than sugar. It has been used in both Eastern and Western medicine to treat a variety of illnesses ranging from the common cold to liver disease. Licorice affects the endocrine system because it contains isoflavones (phytoestrogens), which are chemicals found in plants that may mimic the effects of estrogen and relieve menopausal symptoms and menstrual disorders. Licorice may also reduce testosterone levels, which can contribute to hirsutism in women. The endocrine effect is thought to be due to phytoestrogens and other chemicals found in licorice root, including the steroid glycyrrhizin and glycyrrhetic acid, which also have a weak anti-androgen effect. Licorice could be considered an adjuvant therapy of hirsutism and polycystic ovary syndrome. Licorice extracts have also demonstrated antioxidant, anti-dyslipidemic, hypoglycaemic and anti-inflammatory activity.</p> <p>A synergistic effect was demonstrated by the combination of peony and licorice, and the beneficial effects include:</p> <ol style="list-style-type: none"> 1. Promoting folliculogenesis and at the same time, causing atresia of immature follicles 2. Improving ovarian function, and providing optimum conditions for ovulation 3. Decreasing elevated testosterone, thus normalizing the sex hormone profile
Urtica dioica	<p>Commonly known as stinging nettle, Urtica has proven to have in vitro effects on SHBG. The positive effects of the nettle extract are thought to be due to the lignans, which are predominantly in the glycoside form. The glycosides are cleaved in the digestive process with the intestinal microbial transformation products displaying a binding affinity to SHBG. Furthermore, the lignans may influence the blood levels of free, active steroid hormones by displacing them from the SHBG binding site. Steroid hormones, as well as Urtica lignans, may inhibit the binding of SHBG to its receptor. This reaction would cause an increase in SHBG levels. U. dioica root shows great promise in the treatment of PCOS by up-regulating circulating SHBG. In addition to regulating, SHBG, anti-hyperglycemic and anti-inflammatory effects have also been demonstrated by Urtica dioica</p>
Eugenia jambolana	<p>Eugenia jambolana is commonly called as Jamun, Black plum or Indian Black berry. Eugenia jambolana seeds have hypoglycemic and anti-inflammatory effects in addition to other effects. Eugenia jambolana seed contains several active constituents such as flavonoids, gallic acid, ellagic acid and tannins. The antioxidant potential of Eugenia jambolana seed kernel may be attributed mainly due to the amelioration of hyperglycemia induced oxidative stress by its normoglycemic effect. The presence of flavonoids, further strengthens the efficacy of Eugenia jambolana seed kernel in protecting the tissue defense system against oxidative damage in PCOS. In addition to the anti-hyperglycaemic effect, Eugenia, also demonstrates antioxidant, anti-hyperlipidaemic activities, as demonstrated by in-vivo and in-vitro studies</p>
Emblica officinalis	<p>Although PCOS is not a diabetes like clinical condition, impaired glucose metabolism coupled with insulin resistance is a challenge which many physicians face while treating PCOS. Even though insulin sensitizers such as Metformin, Pioglitazone are used in women with high BMI, compliance remains a big issue. Amongst the portfolio of agents that are used for treating PCOS, Emblica officinalis or the Indian gooseberry is an important addition. Emblica officinalis, contains several biologically active constituents such as flavonoids, gallic acid, ellagic acid, glycosides, triterpenoids and saponins. Emblica officinalis, demonstrates the following actions:</p> <ol style="list-style-type: none"> i. Anti-hyperglycaemic activity [Reduces Insulin Resistance] ii. Anti-oxidant activity and iii. Decreases serum lipid levels
Summary	<p>A non-hormonal, therapy that can be used for long periods of time with no or minimal adverse events is a preferred choice. The drug must exhibit anti-androgenic, metabolic and cycle regulating activities. No single modern medicine has all the abilities, hence extracts of phyto-pharmaceuticals, capable of exerting the actions are gaining popularity amongst the treating physicians.</p> <p>The rationale for the combination of a non-hormonal combination of natural phyto-pharmaceutical ingredients that modulate the physiological activities that are disrupted in PCOS, include:</p> <ol style="list-style-type: none"> 1. Decreases Androgens 2. Cycle Regulation 3. Initiate ovulation, normalise follicle development, tonify the reproductive system and improve fertility [c 4. Decreases LH 5. Improves Hirsutism 6. Supports Adrenal Function 7. Anti-lipidaemic and 8. Antioxidant activity
Indications & Dosage	<p>A “ Non-Hormonal Therapy” for alleviation of symptoms of PCOS, to manage hyperandrogenic states and regulate cycles. 1 Veg, capsule BID for 90-180 days or as advised by the Physician. Treatment may be initiated, after a break, of about 2 weeks</p>
Storage	<p>The capsules must be stored away from direct sunlight and kept in a cool dry place, out of reach from children</p>
Composition	<p>A non-hormonal therapy comprising of:</p> <ol style="list-style-type: none"> 1. Saw palmetto -160 mg 2. Paenia lactiflora – 200 mg 3. Urtica dioica – 100 mg 4. Glycyrrhiza glabra -50 mg 5. Eugenia jambolana – 50 mg

	6. Embelica officinalis – 50 mg
Presentation	Each strip contains 1x10 vegetable capsule and each box contains 10 strips

FAQ's

Definition of PCOS ?

Women are defined to have poly-cystic ovarian syndrome if they have chronic anovulation and evidence of androgen excess for which there is no other cause. This is often referred to as the “NIH Conference” definition.

What is the patho-physiology of PCOS?

The underlying defect in polycystic ovaries remains unknown; however, there is growing consensus that the key features are androgen excess, insulin resistance, and abnormal gonadotropin dynamics

The diagnostic criteria of PCOS?

Clinical Features

1. Abnormal menses – Amenorrhoea, Oligomenorrhoea and Menorrhagia
2. Anovulatory infertility
3. Hirsutism and/or acne and Central Obesity
4. Endocrine abnormalities based on Laboratory Tests
 - △ Elevated androgen levels (testosterone)
 - △ Elevated LH concentration
 - △ Normal to mildly elevated FSH level
5. Insulin resistance with hyperinsulinemia
6. Ultrasound Examination
 - △ Multiple sub-cortical follicular cysts
 - △ Increased ovarian stromal density and/or volume

What are the treatment modalities in states of PCOS?

The common treatment modalities in treatment of COS include:

1. Life style interventions/ modifications
2. Progesterone for withdrawal bleeding
3. OCP's – Cycle regulation
4. Anti-androgens
5. Insulin Sensitizers
6. Combination of Nutraceutical Extracts [Gonadil]

What is the action of the individual ingredients of Gonadil ?

1. **Saw palmetto** - Exerts anti-androgenic effects by inhibiting Type-I and Type-II iso- enzymes of 5α-reductase. Saw palmetto decreases levels of SHBG and interferes with DHT binding to androgen receptors
2. **Paenia lactiflora** – Works on the HPO-axis, and regulates the cycles [cycle regulator]
3. **Urtica dioica** - Enhances androgen binding to circulating SHBG, prevents conversion to DHT
4. **Eugenia jambolana** - Exerts, hypoglycaemic effects and also demonstrates anti-oxidant activity
5. **Glycrhizza glabra** – Significantly reduces, androgen levels, and also demonstrates hypoglycaemic and ant-oxidant effects
6. **Emblca officinalis** - Exerts antihyperglycaemic effect [↓ Insulin Resistance] and demonstrates anti-oxidant activity with mild reduction in LDL levels

Can Clomiphene citrate[CC] and Metformin be administered along with Gonadil Capsules?

CC and Metformin can be used along with Gonadil, but a pharmacological gap of at least 3-4 hours must be maintained to avoid drug interactions if any.[No drug interaction details are available of the individual ingredients] with CC and Metformin

What is the dosage & duration of Gonadil capsules?

The suggested dosage is one vegetable capsule at bed-time with warm milk or water. The duration of treatment is a minimum of 3 months and if required can be continued even after 3 months[a gap of 2 - weeks is suggested] and thereafter continue the treatment

When can the the signs of improvement be seen once a patient with PCOS is asked to Gonadil capsules?

Unlike conventional drugs, the onset of action of Gonadil is slower if not all individuals, but many individuals. The expected results can be seen within 2-3 weeks after initiation of the treatment

Have any side-effects been reported with Gonadil or its individual constituents ?

As per available literature, no known adverse drug events have been reported with the combination of any of its individual ingredients

Are there any compliance issues with Gonadil ?

Unlike contraceptives, anti-androgens or Metformin, which are known to cause severe GI upsets and other effects such as spotting, Gonadil is devoid of side-effects making it more palatable as compared to the other drugs used to treat PCOS

What are the distinct advantages of Gonadil from a patients point of view?

The safety aspects of Gonadil and its continued use make this therapy patient compliant as Gonadil is wholesome non-hormonal therapy containing:

1. Anti-androgens
2. Cycle regulator
3. Hypoglycaemic effects [reducing insulin resistance] and
4. Anti-oxidant activity

Does Gonadil confer any weight loss advantage?

Gonadil a non-hormonal therapy, is primarily indicated for PCOS and not weight-loss therapy, however during the treatment period, a weight loss of 1-2 kg. Has been reported in some individuals