



MEDSITOL SACHETS: Restores fertility, regulates menstruation, Prevents endometrial hyperplasia and endometrial cancer.

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ABSTRACT

Polycystic ovary syndrome (PCOS) is a disorder characterized by hormonal imbalance, irregular menstrual periods, excess hair growth, and obesity. Women with PCOS typically have numerous cysts on the ovaries. PCOS is the most common hormonal disorder among women of reproductive age, affecting an estimated 5–10 percent of Indian population. In PCOS, the body produces an excess number of androgens, and the ratio of luteinizing hormone to follicle-stimulating hormone is abnormally high. Ovulation occurs less frequently, or the ovaries don't release eggs at all. In the absence of ovulation, the menstrual cycle is irregular or absent, and cysts containing the immature eggs form on the ovaries. This causes the ovaries to enlarge. Research suggests that PCOS may result from excess insulin, which boosts male hormone production (androgens), leading to menstrual cycle disturbances, acne, and coarse hair growth. Genetic factors may also be at play since this occurs more commonly in those with a family history. Early diagnosis and treatment of PCOS is important to improving quality of life and reducing the risk of long-term complications, such as diabetes and heart disease. Research Studies concluded that medsitol Sachets may regulate menstrual cycles and improve ovulation, medsitol sachets appears to be effective in improving hormonal disturbances of PCOS. The present paper Reviews the Role of medsitol sachets developed by R&D cell of Lactonova Nutripharm Pvt Ltd. Hyderabad in hormonal disturbances of PCOS, to regulate menstrual cycles and to improve ovulation, Restores fertility, regulates menstruation, prevents endometrial hyperplasia and endometrial cancer.

Keywords: Medsitol Sachets, Ovulation, Hormonal disturbances, PCOS

INTRODUCTION



Fig.1 Female Reproductive system showing polycystic ovaries

Polycystic ovary syndrome (PCOS) is a set of symptoms due to elevated androgens (male hormones) in females. Signs and symptoms of PCOS include irregular or no menstrual periods, heavy periods, excess body and facial hair, acne, pelvic pain, difficulty getting pregnant, and patches of thick, darker, velvety skin [1-3]. Associated conditions include type 2 diabetes, obesity, obstructive sleep apnea, heart disease, mood disorders, and endometrial cancer [14].

PCOS is due to a combination of genetic and environmental factors [6, 7, 15]. Risk factors include obesity, not enough physical exercise, and a family history of someone with the condition [8]. Diagnosis is based on two of the following three findings: no ovulation, high androgen levels, and ovarian cysts [4]. Cysts may be detectable by ultrasound [9]. Other conditions that produce similar symptoms include adrenal hyperplasia, hypothyroidism, and hyperprolactinemia. PCOS has no cure [5]. Treatment may involve lifestyle changes such as weight loss and exercise [10, 11]. Birth control pills may help with improving the regularity of periods, excess hair growth, and acne. Metformin and anti-androgens may also help. Other typical acne treatments and hair removal techniques may be used [12]. Efforts to improve fertility include weight loss, clomiphene, or metformin. In vitro fertilization is used by some in whom other measures are not effective [16].

PCOS is the most common endocrine disorder among women between the ages of 18 and 44 [17]. It affects approximately 2% to 20% of this age group depending on how it is defined [8, 13]. It is one of the leading causes of poor fertility [4]. The earliest known description of what is now recognized as PCOS dates from 1721 in Italy.

COMMON SIGNS AND SYMPTOMS OF PCOS INCLUDE THE FOLLOWING

Menstrual disorders

PCOS mostly produces oligomenorrhea (fewer than nine menstrual periods in a year) or amenorrhea (no menstrual periods for three or more consecutive months), but other types of menstrual disorders may also occur [17].

Infertility

This generally results directly from chronic anovulation (lack of ovulation).

High levels of masculinizing hormones

It Known as hyperandrogenism, the most common signs are acne and hirsutism (male pattern of hair growth, such as on the chin or chest), but it may produce hypermenorrhea (heavy and prolonged menstrual periods), androgenic alopecia (increased hair thinning or diffuse hair loss), or other symptoms [19]. Approximately three-quarters of women with PCOS (by the diagnostic criteria of NIH/NICHD 1990) have evidence of hyperandrogenemia [20].

Metabolic syndrome

This appears as a tendency towards central obesity and other symptoms associated with insulin resistance [17]. Serum insulin, insulin resistance, and homocysteine levels are higher in women with PCOS [21].

Causes of PCOS

PCOS is a heterogeneous disorder of uncertain cause [23, 24]. There is some evidence that it is a genetic disease. Such evidence includes the familial clustering of cases, greater concordance in monozygotic compared-with dizygotic twins and heritability of endocrine and metabolic features of PCOS [7, 23, 24]. There is some evidence that exposure to higher than typical levels of androgens in utero increases the risk of developing PCOS in later life.^[25]

The genetic component appears to be inherited in an autosomal dominant fashion with high genetic penetrance but variable expressivity in females; this means that each child has a 50% chance of inheriting the predisposing genetic variant(s) from a parent, and, if a daughter receives the variant(s), the daughter will have the disease to some extent [24-28]. The genetic variant(s) can be inherited from either the father or the mother, and can be passed along to both sons (who may be asymptomatic carriers or may have symptoms such as early baldness and/or excessive hair) and daughters, who will show signs of PCOS [26, 28]. The phenotype appears to manifest itself at least partially via heightened androgen levels secreted by ovarian follicle theca cells from women with the allele [27]. The exact gene affected has not yet been identified [7, 24, 29]. In rare instances, single-gene mutations can give rise to the phenotype of the

syndrome [30]. Current understanding of the pathogenesis of the syndrome suggests, however, that it is a complex multigenic disorder [31].

The severity of PCOS symptoms appears to be largely determined by factors such as obesity [7, 17, 32].

PCOS has some aspects of a metabolic disorder, since its symptoms are partly reversible. Even though considered as a gynecological problem, PCOS consists of 28 clinical symptoms. Even though the name suggests that the ovaries are central to disease pathology, cysts are a symptom instead of the cause of the disease. Some symptoms of PCOS will persist even if both ovaries are removed; the disease can appear even if cysts are absent. Since its first description by Stein and Leventhal in 1935, the criteria of diagnosis, symptoms, and causative factors

are subject to debate. Gynecologists often see it as a gynecological problem, with the ovaries being the primary organ affected. However, recent insights show a multisystem disorder, with the primary problem lying in hormonal regulation in the hypothalamus, with the involvement of many organs. The name PCOD is used when there is ultrasonographic evidence. The term PCOS is used since there is a wide spectrum of symptoms possible, and cysts in the ovaries are seen only in 15% of people [33].

PCOS may be related to or worsened by exposures during the prenatal period, epigenetic factors, environmental impacts (especially industrial endocrine disruptors [34]. Such as bisphenol A and certain drugs) and the increasing rates of obesity.

PATHOGENESIS OF PCOS



Fig.2 Pathogenesis of PCOS

Polycystic ovaries develop when the ovaries are stimulated to produce excessive amounts of androgenic hormones, in particular testosterone, by either one or a combination of the following (almost certainly combined with genetic susceptibility [27]. The release of excessive luteinizing hormone (LH) by the anterior pituitary gland through high levels of insulin in the blood (hyper-insulinemic) in women whose ovaries are sensitive to this stimulus.

The syndrome acquired its most widely used name due to the common sign on ultrasound examination of multiple (poly) ovarian cysts. These "cysts" are actually immature follicles not cysts. The follicles have developed from primordial follicles, but the development has stopped ("arrested") at an early antral stage due to the disturbed ovarian function. The follicles may be oriented along the ovarian periphery,

appearing as a 'string of pearls' on ultrasound examination.

Women with PCOS experience an increased frequency of hypothalamic GnRH pulses, which in turn results in an increase in the LH/FSH ratio [41].

A majority of women with PCOS have insulin resistance and/or are obese. Their elevated insulin levels contribute to or cause the abnormalities seen in the hypothalamic-pituitary-ovarian axis that lead to PCOS. Hyperinsulinemia increases GnRH pulse frequency, LH over FSH dominance, increased ovarian androgen production, decreased follicular maturation, and decreased SHBG binding. Furthermore, excessive insulin, acting through its cognate receptor in the presence of component cAMP signaling, upregulates 17α -hydroxylase activity via PI3K, 17α -hydroxylase activity being responsible for synthesizing androgen precursors. The combined

effects of hyperinsulinemia contribute to an increased risk of PCOS [42]. Insulin resistance is a common finding among women with a normal weight as well as overweight women [10, 17, 21].

Adipose tissue possesses aromatase, an enzyme that converts androstenedione to estrone and testosterone to estradiol. The excess of adipose tissue in obese women creates the paradox of having both excess androgens (which are responsible for hirsutism and virilization) and estrogens (which inhibits FSH via negative feedback) [43].

PCOS may be associated with chronic inflammation, [44] with several investigators correlating inflammatory mediators with anovulation and other PCOS symptoms [45, 46]. Similarly, there seems to be a relation between PCOS and increased level of oxidative stress [47].

It has previously been suggested that the excessive androgen production in PCOS could be caused by a decreased serum level of IGFBP-1, in turn increasing the level of free IGF-I, which stimulates ovarian androgen production, but recent data concludes this mechanism to be unlikely [48].

PCOS has also been associated with a specific FMR1 sub-genotype. The research suggests that women with heterozygous-normal/low FMR1 have polycystic-like symptoms of excessive follicle-activity and hyperactive ovarian function [49].

MANAGEMENT OF PCOS

The primary treatments for PCOS include: lifestyle changes and medications.

Goals of treatment may be considered under four categories

- Lowering of insulin resistance levels.
- Restoration of fertility.
- Treatment of hirsutism or acne.
- Restoration of regular menstruation, and prevention of endometrial hyperplasia and endometrial cancer.

In each of these areas, there is considerable debate as to the optimal treatment. One of the major reasons for this is the lack of large-scale clinical trials

comparing different treatments. Smaller trials tend to be less reliable and hence may produce conflicting results.

General interventions that help to reduce weight or insulin resistance can be beneficial for all these aims, because they address what is believed to be the underlying cause.

As PCOS appears to cause significant emotional distress, appropriate support may be useful.

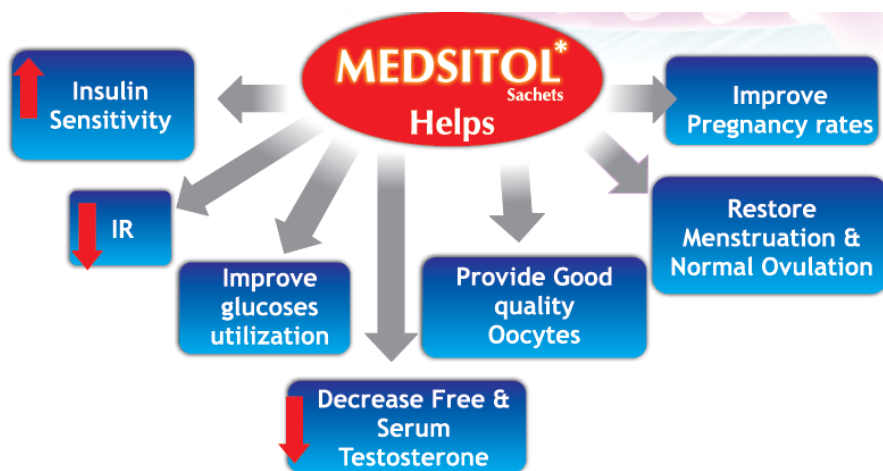
ROLE OF DIET IN MANAGEMENT OF PCOS

Where PCOS is associated with overweight or obesity, successful weight loss is the most effective method of restoring normal ovulation/menstruation, but many women find it very difficult to achieve and sustain significant weight loss. A scientific review found similar decreases in weight and body composition and improvements in pregnancy rate, menstrual regularity, ovulation, hyperandrogenism, insulin resistance, lipids, and quality of life to occur with weight loss independent of diet composition. Still, a low GI diet, in which a significant part of total carbohydrates is obtained from fruit, vegetables, and whole-grain sources, has resulted in greater menstrual regularity than a macronutrient-matched healthy diet.

Vitamin D deficiency may play some role in the development of the metabolic syndrome, so treatment of any such deficiency is indicated. A systematic review found that vitamin D supplementation reduced or mitigated metabolic and hormonal dysregulations in PCOS. Interventions using dietary supplements to correct metabolic deficiencies in people with PCOS had been tested in small, uncontrolled and nonrandomized clinical trials; the resulting data recommend their use.

Medsitol therapy for PCOS

A scientific review concluded that while both myo-inositol and D-chiro-inositol in medsitol Sachets may regulate menstrual cycles and improve ovulation, review have found myo-inositol supplementation in medsitol sachets appears to be effective in improving several of the hormonal disturbances of PCOS.



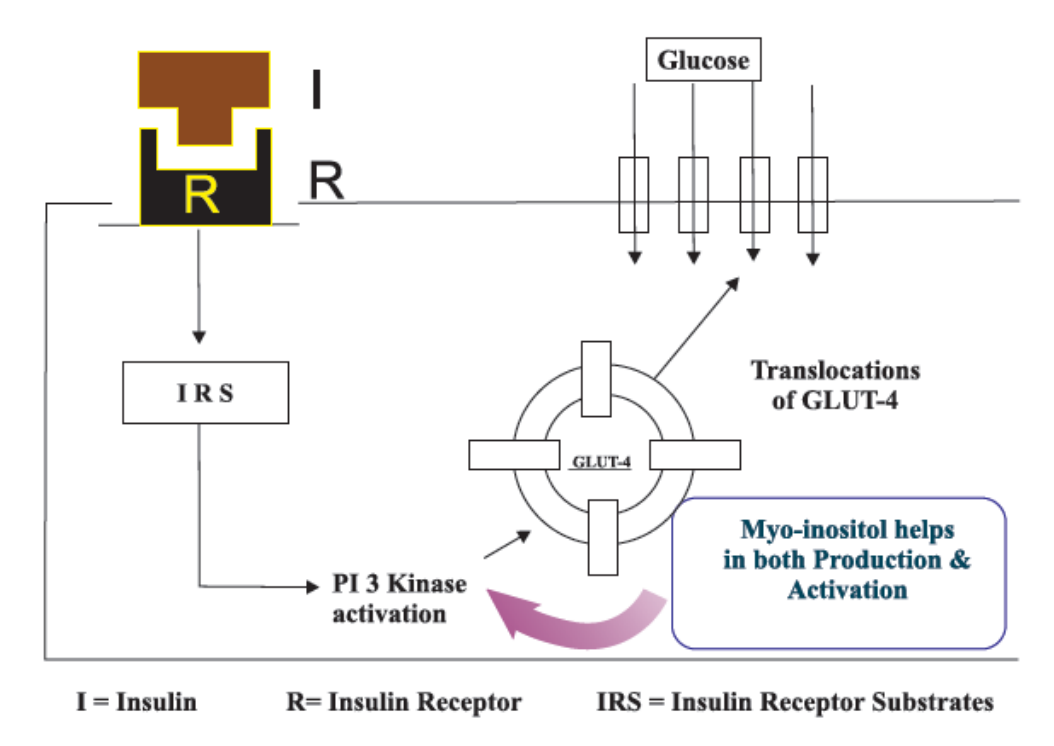
How Medsitol Combats Against POLYCYSTIC OVARY SYNDROME (PCOS)

- Improved insulin action there by improving ovulatory functions and decreasing serum androgen concentration
-Nestler1999
- Prevents hyperhomocysteinemia thereby enhancing oocyte and sperm quality resulting in female fertility
-AM Jclin Nutr 2006; 83:993-1016
- Optimal maintenance of folate levels and assures conception in infertile women
-Cochrane database of systemic review 2010, issue 10
- Preserves reproductive physiology in females through undisruption of estrogen signaling
-Yoshizawa et al, 1997 Panda et al, 2001
- Prevents hyperandrogenism
-Tsilchorozidou, 2004, Jakubowski 2005, Diamanti-kandarakis 2006, Bremer 2008
- Significant improvement in insulin sensitivity and increased frequency of ovulation
- Costantino 2009
- Normalizes menstrual cycles
-Thys- Jacobs, 1999

COMPOSITION

Supplement Facts	
Each sachet contains (approx):	
Myo-Inositol	2gm
D-Chiro-Inositol	50mg
L-Methyl Folate Calcium	1mg
Vitamin D3	1000 IU

MECHANISM OF ACTION



- Promotes production and activation of PI 3 (Phosphoinositide 3) kinase¹
- Promotes synergistic effect of Myo-Inositol and D-Chiro-Inositol in obese patients
- Enhances follicular maturity¹
- Provides good quality oocytes¹
- Prevents genetic polymorphism of MTHFR (Methylenetetrahydrofolate reductase) enzyme²

Mechanism of Action / Pharmacology:

Myo- inositol in **MEDSITOL** is a compound belonging to Vitamin B complex. It is an important constituent of Follicular microenvironment playing the key role in the nuclear and cytoplasmic oocyte development, resulting in good quality oocytes. It also reduces the Luteinizing Hormone (LH) resulting in proper and timely ovulation. It is a key factor in insulin signaling and improves insulin sensitivity.

- L Ciotta, M. Stracquadanio, I. Pagano, A. Carbonaro, M. Palumbo, F.Gulino, 2011; 15:509-514

D-Chiro-Inositol is a bioactive form of inositol. It interacts with simple sugar in the body to form conjugates which play a key role in mediating insulin action there by enhancing insulin sensitivity in PCOS.

- Ballargeon 2010, Cheang 2008

L Methylfolate in **MEDSITOL** prevents hyperhomocysteinemia, thereby increasing oocyte quality . It also maintains optimum folate level which results in conception in infertile women.

- AM Jelin Nutr 2006;83:993-1016

Vitamin D3 in **MEDSITOL** lowers the circulating androgens and improves the parameters of ovarian follicles genesis and ovulation. It also significantly improves insulin sensitivity which prevents diabetes.

- Davis JB, Hardin J, Neal-Perry G 2012 Epub

SUPPORTING CLINICAL RESEARCHES

- The active ingredient Vitamin D3 in **MEDSITOL** supplementation for 6 months to women with PCOS resulted in normalization of menstrual cycle in 7 out of 10 oligomenorrhic (PCOS) women.
-Thys-Jacobs et al, 1999
- The active ingredient Vitamin D3 in **MEDSITOL** resulted in improving parameters of ovarian folliculogenesis and ovulation.
-Rashidi et al, 2009
- The active ingredient Myo-Inositol in **MEDSITOL** showed improved insulin sensitivity and androgen levels leading to normal menstrual cycles.
-Genazzani 2008
- The active ingredient Myo-Inositol in **MEDSITOL** has shown a reduction in hirsutism and improvement in skin appearance (Prevents ACNE)
-Zacche 2009
- The active ingredient L Methylfolate in **MEDSITOL** supplementation in pre conceptional period has been demonstrated to improve sperm concentration and pregnancy rates .
-Forges T, Monnier-Barbarino P, Alberto JM, Dayal JL, 2007
- D-Chiro-Inositol is a bioactive form of inositol. It interacts with simple sugar in the body to form conjugates which play a key role in mediating insulin action there by enhancing insulin sensitivity in PCOS.
-Ballargeon 2010, Cheang 2008

INDICATIONS

PCOS (Polycystic Ovarian Syndrome)

Contra-Indications

- Known contraindications to any ingredients of the supplement.
- The drug may interact with Anti-Epileptic Drugs.
- Avoid consumption of Alcohol

Dosage and Directions for use

- Take 1-2 sachets two times daily for up to three months.
- Mix one sachet in 100 ml of Water.
- It is taken preferably with meals and/or before or as directed by a physician, licensed nutritionist or medical practitioner.

SAFETY

- It is generally well tolerated and has no severe adverse effect.
- It has an excellent safety record in both animal & human investigations.
- It should be avoided by pregnant women and nursing mothers.

SIDE-EFFECTS

Epigastric pain/tenderness, heartburn, diarrhea and nausea vomiting etc.

SPECIAL PRECAUTIONS

Take with or directly after meals to lessen the possibility of gastrointestinal upset.

STORAGE CONDITIONS

- Store in a cool & dry place below temperature 25°C, protected from light.
- Keep out of reach of children.

STORAGE LIFE IS 2 YEARS

The preparation should not be used after the expiry date.

SUMMARY & CONCLUSION

Polycystic ovary syndrome (PCOS) is a disorder characterized by hormonal imbalance, irregular menstrual periods, excess hair growth, and obesity. Women with PCOS typically have numerous cysts on the ovaries PCOS is the most common hormonal disorder among women of reproductive age, affecting an estimated 5–10 percent. In PCOS, the body produces an excess number of androgens, and the ratio of luteinizing hormone to follicle-stimulating hormone is abnormally high. Ovulation occurs less frequently, or the ovaries don't release eggs at all. In the absence of ovulation, the menstrual cycle is irregular or absent, and cysts containing the immature eggs form on the ovaries. This causes the ovaries to

enlarge. Research suggests that PCOS may result from excess insulin, which boosts male-hormone production (androgens), leading to menstrual cycle disturbances, acne, and coarse hair growth. Genetic factors may also be at play since this occurs more commonly in those with a family history. Early diagnosis and treatment of PCOS is important to

improving quality of life and reducing the risk of long-term complications, such as diabetes and heart disease. Research Studies concluded that medsitol Sachets may regulate menstrual cycles and improve ovulation, medsitol sachets appears to be effective in improving several of the hormonal disturbances of PCOS.

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