ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XII Issue IV April 2025

Unraveling the Therapeutic Role of Myoinositol in Polycystic Ovary Syndrome

Malak Shariff*[1], Dr. Mamta Saraf[2], Valanka Melicia Fernandes[3], Zoya Sadaf[4], Bhalavikashini D R[5], Sai Krishna Mohana Kondra[6], Rohan K[7], Samuel Bilgates Brettlee[8]

[1]Department of Cardiac Care Technology, Jain University, Bengaluru, Karnataka, India

[2]Department of Clinical Diagnostics, Jain University, Aurangabad, Maharashtra, India

[3]Department of Psychology, Jain University, Shiroda, Goa, India

[4]Department of Psychology, Jain University, Ramnagar, Karnataka, India

[5]Department of Psychology, Jain University, Bengaluru, Karnataka, India

[6]Department of Psychology, Jain University, Rajamahendravaram, Andhra Pradesh, India

[7]Department of Cardiac Care Technology, Jain University, Bengaluru, Karnataka, India

[8]Department of Psychology, Jain University, Bengaluru, Karnataka, India

DOI: https://doi.org/10.51244/IJRSI.2025.12040112

Received: 21 April 2025; Accepted: 28 April 2025; Published: 17 May 2025

ABSTRACT

Polycystic ovary syndrome (PCOS) is a multifaceted endocrine disorder affecting a significant number of women of reproductive age. It is characterized by irregular menstrual cycles, hyperandrogenism, and polycystic ovaries, contributing to infertility and metabolic disturbances. Inositol, particularly myo-inositol (MI), has emerged as a promising therapeutic approach for managing PCOS symptoms. Myo-inositol is an essential component of cell membranes and a precursor to several important signaling pathways. Recent studies have highlighted its beneficial effects on insulin sensitivity, ovarian function, and hormonal regulation in women with PCOS. This review states the potential mechanisms through which myo-inositol modulates insulin resistance, a key metabolic feature of PCOS, and its impact on ovarian function, including its role in improving oocyte quality and promoting regular menstrual cycles. Furthermore, the combination of myo-inositol with D-chiro-inositol (DCI) has been studied for its synergistic effects in managing PCOS symptoms. By evaluating the current literature, this review provides insights into the clinical efficacy of myo-inositol as a safe and effective adjunct in the management of PCOS, with particular emphasis on its role in restoring metabolic balance and improving reproductive outcomes. The review also discusses the challenges and areas for future research to further elucidate the optimal dosing, treatment regimens, and long-term outcomes of myo-inositol therapy for PCOS.

Keywords: Myoinositol, PCOS, Insulin Resistance, Hirsutism, Fertility management

BACKGROUND

Polycystic Ovary Syndrome (PCOS) is the most common metabolic disorder among women of reproductive age. It is influenced by various factors, with genetic predisposition being a significant contributor, along with lifestyle and environmental factor [1] PCOS is also the most prevalent endocrine disorder affecting women of reproductive age. Depending on the population studied and the definitions used, the prevalence of this heterogeneous familial disorder ranges from 8–13% in women and 6% in adolescent girls [2]

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XII Issue IV April 2025

Characteristics and Signs of PCOS

PCOS is characterized by signs and symptoms of androgen excess, irregular menses, chronic anovulation, and infertility. Women with PCOS are at increased risk for diabetes mellitus, obesity, dyslipidemia, hypertension, anxiety, and depression [3]. The condition influences women's health throughout their lifespan, starting prior to conception and extending through post-menopausal years. The disorder can manifest physiologically as polycystic ovaries or biochemically as hyperandrogenemia. Hyperandrogenism, a hallmark of PCOS, disrupts follicular development, leads to ovarian cysts, anovulation, and menstrual irregularities. Environmental factors, such as obesity, poor dietary habits, and physical inactivity, exacerbate PCOS. Infectious agents and toxins may also play a role [4]

Insulin Resistance in PCOS

The pathophysiology of PCOS involves defects in the hypothalamic-pituitary axis, insulin secretion, and ovarian function. Insulin resistance and obesity are closely linked to the condition, with follicular maturation arrest being a key indicator of ovarian abnormalities [5]. Insulin resistance disrupts glucose homeostasis, impacting tissues such as adipose tissue, skeletal muscle, liver, and heart. It also suppresses hepatic glucose production and lipolysis, leading to elevated free fatty acids and worsening metabolic symptoms [5]. PCOS is often associated with chronic low-grade inflammation, characterized by elevated white blood cell counts, high levels of C-reactive protein (CRP), and inflammatory cytokines like interleukin 6 (IL-6), interleukin 18 (IL-18), and tumor necrosis factor-alpha (TNF-α). This inflammation exacerbates the metabolic and hormonal imbalances seen in PCOS [5].

Infertility and Hyperandrogenism in PCOS

Hyperandrogenism in PCOS can result from defects in ovarian theca cell steroidogenesis or elevated luteinizing hormone (LH) levels due to hypothalamic-pituitary axis dysregulation. Insulin also plays a role in stimulating androgen production. Additionally, alterations in adrenal steroidogenesis, specifically CYP17α1 hyperactivation, may contribute to hyperandrogenism [5]. This results in impaired follicular development, ovulatory dysfunction, and infertility, which are common in PCOS [4]. Myoinositol (MI) is a cyclic carbohydrate that was once considered a B vitamin (vitamin B8). It plays a vital role in ovarian physiology by supporting follicle-stimulating hormone (FSH) signaling, crucial for oocyte maturation. D-chiro-inositol (DCI), another isomer, mediates insulin-dependent testosterone synthesis [6]. In women with PCOS, systemic insulin resistance disrupts the physiological MI-to-DCI ratio. Enhanced epimerase activity favors DCI production, leading to hyperandrogenism, impaired FSH signaling, and ovulatory dysfunction. Supplementation with myoinositol restores the MI-to-DCI balance, improving insulin sensitivity, reducing hyperandrogenemia, and enhancing ovarian function. This addresses key symptoms of PCOS [6]. Clinical evidence underscores the importance of timely diagnosis and targeted management strategies for PCOS. Treatment options include lifestyle modifications, medications, and in severe cases, bariatric surgery to manage obesity. Goals of therapy focus on improving fertility, reducing hirsutism or alopecia, and protecting the endometrium to prevent endometrial cancer [4]. Early identification of high-risk patients enables preventive screening and treatment for complications such as type 2 diabetes, hypertension, and cardiovascular disease. The diversity of PCOS phenotypes highlights the need for individualized treatment plans based on a patient's unique clinical features and ethnic background.

Mechanism of Action of Myoinositol

Myo-inositol (MI) is a naturally occurring stereoisomer of a C_6 sugar alcohol, belonging to the inositol family, and plays a critical role in cellular signaling and metabolic regulation. Structurally, it is a cyclohexane hexol ($C_6H_{12}O_6$) with six hydroxyl (-OH) groups, making it highly water-soluble and essential for various physiological functions. In the context of PCOS, MI functions as a precursor for inositol triphosphate (IP3), a crucial intracellular second messenger that regulates multiple hormones, including thyroid-stimulating hormone (TSH), follicle-stimulating hormone (FSH), and insulin. Its biochemical role in glucose metabolism is mediated through phosphoinositol-3-phosphate (PIP3), which enhances GLUT4 translocation, facilitating glucose uptake into cells and improving insulin sensitivity. Additionally, its derivative, inositol phosphoglycan

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XII Issue IV April 2025

(MI-IPG), inhibits adenylate cyclase activity, preventing excessive free fatty acid (FFA) release from adipose tissues, which is linked to insulin resistance and increased triglyceride synthesis. MI and D-chiro-inositol (DCI) work together to modulate metabolic pathways; while MI regulates glucose uptake and FSH signaling, DCI influences insulin-induced androgen synthesis in the ovary. Through these mechanisms, MI contributes to glycogen synthesis, hormonal balance, and reduction of hyperinsulinemia, which are critical for managing the metabolic and reproductive dysfunctions seen in PCOS. Given its well-established insulin-sensitizing effects, MI has been widely studied for its therapeutic potential in PCOS, metabolic syndrome, and gestational diabetes, offering a natural and effective approach to mitigating insulin resistance and hormonal imbalances associated with these conditions [7] Figure 1 illustrates the same biochemical mechanisms by which Myo-inositol (MI) exerts its effects in PCOS.

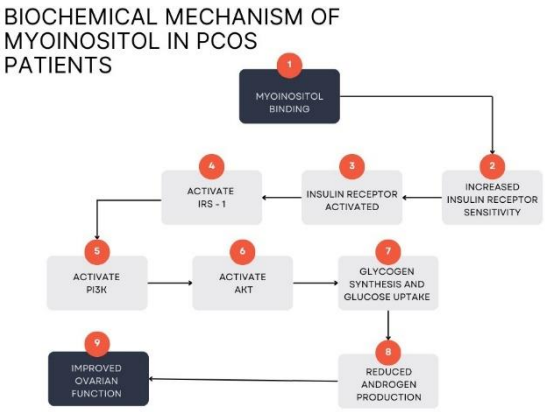

Figure 1: Biochemical mechanism of myoinositol in PCOS patients

Myo-inositol (MI) plays a crucial role in insulin signaling and ovarian function, making it a promising therapeutic option for PCOS management. As a member of the vitamin B family, MI functions as a secondary messenger in insulin signal transduction, addressing defects in the inositol glycan system observed in PCOS women. In individuals with PCOS-related insulin resistance, MI supplementation compensates for reduced tissue availability of inositol, thereby enhancing insulin sensitivity. Unlike traditional insulin signaling, which relies on tyrosine phosphorylation, MI mediates insulin action in the ovary through the IGF-1 receptor, which becomes overactive under hyperinsulinemic conditions. This mechanism allows the ovaries to maintain their insulin response, contributing to androgen excess and ovarian dysfunction. By improving insulin sensitivity, MI reduces compensatory hyperinsulinemia, thereby lowering androgen production and restoring ovulatory function. Additionally, MI promotes HDL increase, weight loss, and reductions in insulin levels, triglycerides, testosterone, and blood pressure, further aiding in metabolic regulation. D-chiro-inositol (DCI), a complementary inositol isoform, functions as an intracellular messenger, supporting ovulation and fertility, while MI primarily enhances insulin sensitivity and glucose metabolism. Studies suggest that a combination of MI and DCI in specific ratios may offer superior benefits compared to either form alone. Given its ability to correct hormonal imbalances, regulate metabolic dysfunction, and restore reproductive health, MI represents a safe and effective alternative to traditional insulin-sensitizing agents like metformin, without the gastrointestinal side effects commonly associated with such treatments [8]

Role of Myoinositol in Pcos Management

In Menstrual Cycle Regulation and Psychological Well Being

Several studies have explored the impact of Myoinositol on mood disturbances in women with PCOS. This multicenter cross-sectional study identified anxiety as a mediator between body image distress and reduced quality of life in women with PCOS, suggesting that interventions targeting anxiety could improve overall well-being [9]. A cross-sectional study reported higher levels of depression, anxiety, and stress in adolescents with PCOS, emphasizing the need for early psychological assessment and intervention [10]. A randomized controlled trial demonstrated that cognitive-behavioral therapy significantly reduced depression and anxiety in

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XII Issue IV April 2025

women with PCOS, highlighting the effectiveness of psychological interventions [11]. This study found that adolescents with PCOS exhibited higher anxiety and depression levels, correlating with increased insulin resistance and hyperandrogenism [12]. A systematic review and meta-analysis reported a higher prevalence of anxiety disorders in women with PCOS compared to controls, suggesting a need for routine psychological screening in this population [13].

The role of Myoinositol in restoring menstrual regularity has been substantiated through various studies. A randomized controlled trial found that Myoinositol supplementation led to ovulation in 70% of treated women, with 66% achieving regular menstrual cycles [14]. This study demonstrated that Myoinositol improved ovarian function and menstrual regularity in women with PCOS, with 88% of participants reporting restored ovulation [15]. A clinical trial showed that Myoinositol combined with folic acid improved menstrual regularity in women with PCOS, with 86% achieving regular cycles after six months [16]. This study reported that Myoinositol supplementation resulted in a significant reduction in menstrual irregularities, with 82% of participants experiencing cycle normalization [17]. A randomized controlled trial found that Myoinositol improved menstrual cycle regularity in 72% of women with PCOS, highlighting its efficacy as a treatment option [18].

In Insulin Sensitivity

Myo inositol has shown various benefits on insulin sensitivity. It has been shown to enhance insulin sensitivity, which is important for treating illnesses such as type 2 diabetes and gestational diabetes. It works by improving insulin signaling pathways while decreasing insulin resistance. Myo-inositol works through several mechanisms to improve insulin sensitivity and metabolic function. First, it enhances insulin signaling by increasing the expression of insulin receptor substrates and glucose transporter 4 (GLUT4), which are essential for the absorption of glucose into cells. This boosts insulin sensitivity, making it more effective at regulating blood sugar levels. Additionally, myo-inositol has beneficial effects on adipose tissue. It helps to reduce the accumulation of white adipose tissue by decreasing adipose cell volume, which further improves insulin sensitivity. Interestingly, this reduction in adipose tissue is linked to lower lipogenesis (fat creation) rather than enhanced lipolysis (fat breakdown). Finally, myo-inositol may also act as a second messenger, mimicking the effects of insulin and contributing to its overall beneficial effects on metabolism. Insulin resistance in PCOS women is often linked to excessive serine phosphorylation of the insulin receptor, potentially causing both insulin resistance and hyperandrogenism [19].

The association between insulin resistance, reproductive issues, and clinical hyperandrogenism was first observed in the "diabetes of bearded women." Subsequent studies confirmed insulin resistance in both obese and lean PCOS patients. While insulin resistance, hyperinsulinemia, and beta-cell dysfunction are common in PCOS, they are not required for diagnosis. Research has shown that insulin resistance plays a central role in PCOS, influencing treatment options such as the use of insulin sensitizers to manage cycle abnormalities and improve fertility in obese women. Understanding insulin resistance has helped uncover various metabolic issues associated with PCOS, and today, the condition is recognized as having broader health implications than previously thought [20]. Insulin resistance in PCOS is linked to intrinsic abnormalities in insulin signaling, including increased serine phosphorylation of IRS-1 (Ser312) and altered insulin receptor substrate (IRS)-1 and IRS-2 signaling pathways in skeletal muscle cells. In cultured myotubes from women with PCOS, basal and insulin-stimulated glucose transport, as well as GLUT1 abundance, were elevated. While insulin receptor (IR) abundance and tyrosine autophosphorylation remained unchanged, IRS-1 protein levels were increased, leading to reduced PI 3-kinase activity when normalized for IRS-1. These intrinsic defects, combined with increased IRS-1 Ser312 phosphorylation, may predispose women with PCOS to insulin resistance . The findings of a study suggest that PCOS has unique genetic and molecular characteristics that differentiate it from other insulin-resistant states and contribute to an elevated risk of type 2 diabetes [21]. Myo-inositol supplementation may help reduce insulin resistance (IR) in women with polycystic ovary syndrome (PCOS) with minimal serious side effects. In a PCOS-IR rat model, myo-inositol supplementation improved insulin resistance, as indicated by a decreased HOMA-IR index. It also reduced serum levels of luteinizing hormone (LH), the LH/follicle-stimulating hormone ratio, and testosterone, while increasing estradiol levels. The treatment led to a downregulation of interleukin 6 (IL-6), phospho-STAT3 (p-STAT3), and miR-21/miR-155, while increasing PPAR-γ and GLUT4 expression. These molecular changes suggest that myo-inositol

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XII Issue IV April 2025

supplementation may alleviate insulin resistance by modulating the IL-6/p-STAT3/miR-155/miR-21/PPAR-γ/GLUT4 pathway, offering potential therapeutic benefits for PCOS patients [22].

In an animal trial conducted by Marine L. Croze published in the The Journal of nutritional biochemistry (February 2013) suggested that ,chronic treatment with myo-inositol improves insulin sensitivity and reduces white adipose tissue accretion in female mice, suggesting potential as a nutritional strategy for preventing or treating insulin resistance and type 2 diabetes. Research indicates that myo-inositol treatment in women with polycystic ovary syndrome (PCOS) improves metabolic factors, reduces circulating insulin, and increases insulin sensitivity and the results showed significant improvements in the Myo-inositol group, including decreased serum testosterone, improved insulin sensitivity, lower triglycerides, and reduced blood pressure. Ovulation rates also increased, with 16 out of 23 women ovulating compared to 4 out of 19 in the placebo group. In summary, Myo-inositol effectively improves hormonal balance, insulin sensitivity, and ovulation in women with PCOS [23].

A randomized trial investigated whether myo-inositol supplementation reduces the incidence of gestational diabetes mellitus (GDM) and improves insulin resistance in obese pregnant women. From weeks 12–13 of gestation until delivery, 220 women received either myo-inositol (2g plus 200µg folic acid twice daily) or a placebo (200µg folic acid twice daily). The GDM rate was significantly lower in the myo-inositol group (14.0%) compared to the placebo group (33.6%) (P=.001). Insulin resistance, measured via the homeostasis model assessment, also improved significantly in the myo-inositol group (−1.0±3.1 vs. 0.1±1.8, P=.048). In conclusion, myo-inositol supplementation from the first trimester reduces GDM incidence and improves insulin resistance in obese pregnant women.Myo-inositol supplementation in obese pregnant women reduces the incidence of gestational diabetes mellitus by reducing insulin resistance [24]. Phytic acid (myo-inositol hexaphosphate) and myo-inositol improve insulin sensitivity in adipocytes by enhancing lipid storage, increasing glucose uptake, and reducing lipolysis. In a study using 3T3-L1 adipocytes, both compounds increased lipid accumulation, upregulated key transcription factors (PPARγ and SREBP-1c), and boosted insulin signaling pathways, including IRS1 activation and GLUT4 expression. These findings suggest that the antidiabetic effects of phytic acid and myo-inositol are mediated directly through adipocytes.In conclusion ,Phytic acid and myo-inositol improve insulin sensitivity in adipocytes by increasing lipid storage capacity, improving glucose uptake, and inhibiting lipolysis [25].

Inositol therapy shows potential benefits in reducing insulin resistance and improving metabolic impairments in PCOS patients, but it also suggests that more research is needed for a comprehensive meta-analysis [26] . In another research study wherein Metformin and myo-inositol were both compared to check its role on insulin sensitivity showed that , Metformin and myo-inositol both improve insulin sensitivity, lower BMI, and improve menstrual cycle in PCOS women, with no significant differences between the two treatments [27]. Similarly another study compares the effectiveness of four oral insulin sensitizers—metformin, thiazolidinediones, inositols, and berberine—in managing endocrine and metabolic abnormalities in women with PCOS. A network meta-analysis of 22 trials (1,079 patients) found that Myo-inositol combined with D-chiro-inositol significantly improved menstrual frequency and reduced total testosterone levels, outperforming metformin alone. Combination therapies, such as metformin + thiazolidinediones and Myo-inositol + D-chiro-inositol, were more effective in reducing insulin resistance (HOMA-IR). Thiazolidinediones showed better results than metformin in improving lipid metabolism and glucose levels. Overall, combination therapies offer superior outcomes compared to monotherapies, with Myo-inositol + D-chiro-inositol being particularly effective for menstrual recovery [28]. A review of seven randomized controlled trials involving 1,319 pregnant women found that antenatal myo-inositol supplementation may reduce the risk of gestational diabetes, hypertensive disorders of pregnancy, and preterm birth. However, the evidence was rated as low to very low certainty due to small sample sizes, variability in dosing, and limited generalizability beyond Italy and Ireland. Myo-inositol showed no clear effect on neonatal outcomes such as large-for-gestational-age infants or neonatal hypoglycemia. Further large-scale, diverse studies are needed to establish optimal dosing, timing, and long-term effects of myo-inositol supplementation during pregnancy [29].

Myo-inositol (MYO), an insulin-sensitizer, improves insulin action in endometrial cells through the SMIT-1 transporter and AMPK activation. In an in-vitro PCOS model, MYO restored reduced p-AMPK and GLUT-4 levels, improving glucose uptake in endometrial cells, similar to metformin's effects. These findings suggest

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XII Issue IV April 2025

that MYO enhances insulin sensitivity in insulin-resistant endometrial tissue via SMIT-1 and AMPK pathways, positioning it as a potential therapeutic option for managing PCOS-related insulin resistance [30].

Myo Inositol supplementation may be a safe and effective medication for lowering the prevalence of gestational diabetes in high-risk groups without reported side effects [31]. Research indicates that ,Myo-inositol (MI) and D-chiro-inositol (DCI) , two stereoisomers with insulin-sensitizing properties and distinct roles in managing PCOS. MI acts as a second messenger for follicle-stimulating hormone (FSH), while DCI functions as an aromatase inhibitor. Research supports administering MI and DCI in a 40:1 ratio, reflecting their natural balance in the blood, for optimal therapeutic effects. Additionally, alpha-lactalbumin enhances inositol absorption, improving treatment outcomes. MI also boosts the efficacy of metformin and clomiphene in improving fertility outcomes for women with PCOS. These findings highlight the importance of precise dosing, timing, and combined supplementation of MI and DCI in PCOS treatment [32]

In Hirsutism

Hirsutism, a common symptom in polycystic ovary syndrome (PCOS), is primarily caused by an excess of androgens, resulting in male-pattern hair growth in women. The main contributors to hirsutism in PCOS include: Hyperandrogenism: Elevated testosterone and other male hormones are responsible for excessive facial and body hair growth [33], [34]. Insulin Resistance: Impaired insulin sensitivity in women with PCOS can exacerbate hyperandrogenism by stimulating the ovaries to produce more androgens [35], [36]. Hormonal Imbalances: Disrupted ratios of luteinizing hormone (LH) to follicle-stimulating hormone (FSH) contribute to ovarian dysfunction and increased androgen production, further worsening hirsutism [27], [34] These factors are interconnected, and insulin resistance significantly worsens hyperandrogenism, which in turn leads to hirsutism and menstrual irregularities.

Myo-Inositol as an Insulin Sensitizer is known for improving insulin sensitivity, which is vital for managing the hormonal imbalances associated with PCOS. Research has shown that Myo-Inositol and Insulin Sensitivity: Supplementation with myo-inositol improves insulin sensitivity, reducing hyperandrogenism and hirsutism in PCOS women [34], [35] Clinical trials show that myo-inositol supplementation significantly reduces hirsutism severity, often to levels comparable to traditional treatments like metformin [27], [37] Myo-inositol also plays a role in restoring hormone balance in PCOS by having an effect on Androgen levels, Myo-inositol has been shown to lower elevated testosterone and other androgens, directly alleviating hirsutism [33], [38] Regulation of LH/FSH Ratios: It helps in restoring a more favorable LH/FSH ratio, which is typically d disrupted in PCOS, further reducing hyperandrogenism and its related symptoms [34] Efficacy in Combination with Other Compounds. Recent studies have explored combining myo-inositol with other compounds to enhance its effects:combination with Folic Acid and Vitamin D3: Studies have found that when myo-inositol is combined with folic acid and vitamin D3, it enhances its ability to reduce both hirsutism and other metabolic issues [39], [40]. Myo-Inositol and Monacolin K: Some research suggests that adding monacolin K to myo-inositol may improve its effects on hyperandrogenism and lipid metabolism in women with PCOS [41] Research indicates that myo-inositol not only reduces hirsutism but also improves metabolic parameters in PCOS patients, with a favorable safety profile: Improvement in Metabolic Profile: Myo-inositol has been shown to improve lipid profiles and reduce insulin resistance without significant adverse effects [33], [34]

Safety Profile: It is generally considered safe and well-tolerated, with minimal side effects, making it an attractive option for long-term use in managing PCOS [35], [37] Another ongoing debate is the comparative effectiveness of myo-inositol relative to other established treatments for hirsutism, such as metformin or oral contraceptives: Myo-Inositol vs. Metformin: While some studies suggest similar efficacy between myo-inositol and metformin in improving insulin sensitivity and reducing hirsutism, others recommend metformin as the first-line treatment for PCOS [37] As research advances, there is a growing focus on personalized treatment strategies for PCOS: Tailored Therapies: Future research should focus on identifying specific PCOS subtypes that may benefit most from myo-inositol supplementation, especially considering individual metabolic and hormonal profiles [36] Molecular Mechanisms: Investigating the molecular mechanisms of myo-inositol's effects on androgen production and insulin sensitivity could lead to more effective treatments and better patient outcomes [34]

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XII Issue IV April 2025

There is a need for more extensive, high-quality clinical trials to establish the efficacy and safety of myo-inositol in treating hirsutism.

In Improving Lipid Profile

Myo-inositol is a naturally occurring carbohydrate and is often used as a supplement for managing symptoms of polycystic ovary syndrome (PCOS). Research indicates that myo-inositol can have beneficial effects on the lipid profile in women with PCOS. in which effects include:

- It has been shown that to lower the total cholesterol levels,This is important for reducing cardiovascular risks associated with PCOS.(Dorina Greff et all)
- Studies indicate myo-inositol can reduce levels of low-density lipoprotein (LDL) cholesterol, often referred to as "bad cholesterol." Lower LDL levels can help mitigate the risk of atherosclerosis and heart disease.
- Myo-inositol may also support an increase in high-density lipoprotein (HDL) cholesterol, known as "good cholesterol." Higher HDL levels are protective against cardiovascular diseases.

Mechanism in this includes hormonal regulation By helping to balance hormonal levels, myo-inositol may influence lipid metabolism positively, leading to healthier lipid levels.

The weight management is also done which in turn can have favorable effects on lipid profiles(by improved insulin production)Several studies shows evaluated the effect of myoinositol supplementation with metabolic diseases with controlled trials according to the results Overall, 14 RCTs were included into meta-analysis. Pooled results showed that inositol supplementation among patients with metabolic diseases significantly decreased triglycerides (SMD − 1.24; 95% CI, − 1.84, − 0.64; $P < 0.001$), total- (SMD − 1.09; 95% CI, − 1.83, − 0.55; $P < 0.001$), and LDL-cholesterol levels (SMD − 1.31; 95% CI, − 2.23, − 0.39; $P = 0.005$). There was no effect of inositol supplementation on HDL-cholesterol levels (SMD 0.20; 95% CI, − 0.27, 0.67; $P = 0.40$) [42].

Myo-inositol has emerged as a promising intervention for managing polycystic ovary syndrome (PCOS), particularly due to its beneficial effects on metabolic parameters, including lipid profiles. PCOS is a common endocrine disorder characterized by hormonal imbalances, insulin resistance, and various metabolic disturbances, which can lead to long-term health complications such as obesity, type 2 diabetes, and cardiovascular disease. Among the metabolic issues faced by women with PCOS, dyslipidemia—marked by elevated levels of total cholesterol, low-density lipoprotein (LDL) cholesterol, and triglycerides, along with decreased high-density lipoprotein (HDL) cholesterol—is prevalent [43].

Myo-inositol is a naturally occurring carbohydrate that plays a crucial role in cellular signaling and insulin sensitivity. Research has demonstrated that myo-inositol supplementation can significantly improve insulin sensitivity, which is vital for lipid metabolism. In women with PCOS, enhancing insulin sensitivity can lead to a cascade of metabolic improvements, resulting in favorable changes to lipid profiles.

The mechanism through which myo-inositol exerts its effects involves modulation of insulin signaling pathways. By enhancing insulin sensitivity, myo-inositol facilitates better uptake and utilization of glucose by cells, thereby reducing hyperinsulinemia, a common feature in PCOS. Lower insulin levels can lead to reduced lipogenesis (fat production) and enhanced lipolysis (fat breakdown), contributing to improved lipid levels.

Moreover, the combination of myo-inositol with D-chiro inositol—a stereoisomer of inositol—has been explored in some studies, suggesting that this combination may yield even more significant benefits in metabolic health and lipid profiles. The synergy between these two forms of inositol could enhance insulin sensitivity and lipid metabolism more effectively than either compound alone [44]

Long-term supplementation with myo-inositol has shown promise not only in improving lipid profiles but also in supporting weight management and restoring menstrual regularity, further contributing to overall metabolic

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XII Issue IV April 2025

health in women with PCOS. Given the chronic nature of PCOS and its associated health risks, myo-inositol represents a valuable adjunctive treatment in the holistic management of this conditions [45].

Myo-inositol is a beneficial supplement for women with PCOS, particularly regarding its positive impact on lipid profiles. By improving insulin sensitivity and promoting favorable changes in cholesterol and triglyceride levels, myo-inositol addresses critical aspects of the metabolic syndrome commonly associated with PCOS. As research continues to explore its effects, myo-inositol holds promise as a safe and effective option for improving both the metabolic and reproductive outcomes in women facing the challenges of pcos.

In Reducing Inflammation

Polycystic ovary syndrome is a prevalent endocrinal disorder affecting about 1 in 10 post pubertal women globally. It is characterized by hormonal dysregulation, insulin resistance, hyperandrogenism, obesity, and is influenced by genetics, epigenetics, and environmental factors. PCOS is also associated with low grade systemic and local inflammation, with rise in levels of C – reactive protein, cytokines (TNF-α, IL-6, IL-7, IL-8), and leukocytes. Additionally, markers such as the neutrophils to lymphocyte ratio, platelet to lymphocyte ratio, and CRP/albumin ratio indicating a pro inflammatory environment [46]. There are several factors that contribute to the rise in inflammatory markers in PCOS, like elevated levels of androgens seen in PCOS suggest increased inflammation, studies have suggested positive correlation between hyperandrogenism and chronic low grade inflammation in women with PCOS [47]. Additionally, many women experience insulin resistance, which leads to higher insulin levels. This insulinemia can cause chronic low grade inflammation in the ovaries by decreasing stress, disrupting follicular development [48]. Obesity, often present in PCOS, further exacerbates inflammation through hypertrophied adipocytes and immune cells in adipose tissue, which contributes to the pro inflammatory environment, only worsening insulin resistance and hyperandrogenism[47]. Lastly, limited genetic evidence suggests that certain proinflammatory genotypes, including those encoded with TNF-α, type 2 TNF receptor, and IL-6, may also contribute to chronic inflammation in women with PCOS [47].

Mechanism of myoinositol(MI) in reducing inflammation: Myoinositol (MI) is a polyalcohol that plays a key role in mediating insulin's post receptor effects, alongside D chiro inositol (DCI). These inositols interact with inositolphosphoglycans, which act as second messengers to regulate intracellular metabolism. MI has higher affinity by sodium inositol cotransporter. In the ovary, MI supports the action of follicle stimulating function, while DCI is associated with excessive insulin dependent testosterone production. In conditions like PCOS, reduced MI concentrations and dysregulated MI/DCI ratio (normally 100:1 but often 0.2:1 in PCOS) contribute to insulin resistance and hormonal imbalance by promoting a more favorable MI/DCI ratio of 40:1, which aids in improving ovulation, progesterone levels, and reducing insulin and testosterone levels. MI also improves ovarian health, antioxidant defense, and lipid synthesis, leading to indirect reductions in inflammation[49]. Myoinositol may reduce inflammation by improving insulin sensitivity, by improving insulin sensitivity, which lowers hyperinsulinemia, a key driver of inflammatory cytokine production and oxidative stress. MI acts as a precursor for second messengers like inositol triphosphate, which regulates hormones such as insulin, TSH, FSH, restoring hormonal balance and reducing androgen levels. This helps improve glucose uptake, reduce oxidatie stress, and create a less inflamed environment, especially in ovarian tissues, thus enhancing oocyte quality and overall metabolic health. Through these mechanisms, MI reduces both systemic and local inflammation in PCOS [50]. MI and DCI also play a significant role in improving insulin sensitivity, by enhancing the oxidative and non oxidative stress of glucose and glucose uptake through GLUT4, these inositols help reduce insulin resistance and compensatory hyperinsulinemia, lowering inflammation. Also, MI and DCI reduce insulin induced androgen production by decreasing LH sensitivity in ovarian cells. Lower androgen levels alleviate the pro inflammatory effects of hyperandrogenism. Furthermore, DCI has been shown to improve lipid metabolism by lowering triglyceride levels and reducing blood pressure, contributing to reduced systemic inflammation [51].

Clinical evidence of myoinositol's effectiveness in reducing inflammation : A 2017 randamized control trial study has demonstrated myoinositol's effectiveness in reducing inflammation in women with PCOS, myo inositol was associated with a significant decrease in serum high sensitivity C reactive protein levels, a marker of ystemic inflammation, showing a reduction of minus -2.6±mg/L after 12 weeks of treatment. In contrast,

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XII Issue IV April 2025

metformin showed a slight increase of +0.2±1.5 mg/L. additionally, myoinositol was found to downregulate the gene expression of interleukin-1(IL-1) in peripheral blood mononuclear cells, further suggesting a reduction in the inflammatory response at the cellular level. These findings indicate that myoinositol may be particularly effective in reducing inflammation [52]. In another study where they compared metformin and myoinositol in obsese women with PCOS, showed both treatments to improve insulin sensitivity. However, metformin showed more pronounced effects on the clinical and hormonal features of PCOS, such as a decrease in body weight, improved menstrual cycles, and a reduction in hirsutism. Although myoinositol did not significantly impact these clinical symptoms, it showed improvements in metabolic parameters, indirectly reducing low grade inflammation associated with insulin resistance [53]. In a 2017 randomised trial published in Gynecological Endocrinology, researchers compared the effects of metformin and myoinositol on the clinical and metabolic features in PCOS, all 50 women included in the study showed improvements in insulin sensitivity and a decrease in body mass index (BMI). Although neither treatment had significant effect on acne or hirsutism, the sensitivity likely reduced chronic inflammation [54]. In a further investigation investigating which is more effective between metformin and myoinositol on hormonal, clinical, and metabolic parameters in obese women with PCOS. 34 women randomly received metformin (840mg twice daily) or myoinositol (1000mg twice daily), both after a wash out period of 3 months showed significant improvement in glycoinsulinanemic features, indirectly reducing inflammation [53]. In 2020 study published in the American Journal of Physiology – Endocrinology and Metabolism, researchers studied insulin sensitizing mechanism of myoinositol in human endometrial cells, conclusion was that myoinositol is a potential insulin sensitizing agent that could be effective in improving metablic parameters as well as their reproductive status [55]. These all suggest myoinositol acting as an anti inflammatory in women with PCOS.

Safety of Myoinositol in Pcos Management

Myoinositol has proven to be a new treatment option for women with PCOS with no moderate to severe side effects with dosage upto 4000mg per day and only minute gastrointestinal symptomns by increasing the dosage upto 12000mg per day [56].Overall, myoinositol appears to be safe and well tolerated by most individuals, with minimal reported side effects, including mild gastrointestinal issues (nausea, flatulence, diarrhea) and occasional dizziness, tiredness, and headache. These side effects occur at a higher dose than that generally recommended. Patients with bipolar disorder are advised to avoid myoinositol supplementation until further research can confirm its safety in these cases. As with any supplementation, individuals with pre existing medical conditions should consult a healthcare professional before starting myoinositol [57].

CONCLUSION

Our review found a positive correlation between myo-inositol (MI) supplementation and improvements in key PCOS-related abnormalities. MI effectively reduces androgen levels (testosterone and androstenedione), corrects the LH/FSH ratio, and improves insulin sensitivity, leading to a restoration of ovulatory menstrual cycles. By counteracting hyperinsulinism and lowering LH levels, MI helps prevent follicular arrest, a major cause of anovulation in PCOS. Additionally, MI's role in enhancing FSH response and reducing multifollicular development risk supports its potential in spontaneous ovulation and pregnancy. These findings reinforce MI as a promising natural alternative for managing PCOS-related metabolic and reproductive dysfunctions, especially in women with insulin resistance [7] . Furthermore, MI exerts its therapeutic effects in PCOS by acting as a secondary messenger in insulin signaling, addressing defects in the inositol glycan system that contribute to insulin resistance. By enhancing insulin sensitivity, MI reduces compensatory hyperinsulinemia, which in turn lowers androgen production and supports ovulatory function. Its role in modulating the IGF-1 receptor pathway in the ovaries further helps regulate hormonal balance, while additional metabolic benefits, including improved lipid profiles, weight regulation, and reduced triglyceride levels, make MI a comprehensive treatment approach. Given its ability to restore both metabolic and reproductive health in PCOS without the side effects associated with traditional insulin sensitizers, MI presents a safe and effective alternative for managing this condition [8]. Myoinositol offers a safe and effective approach through its mechanisms of improving insulin sensitivity, regulating androgen levels, managing hirsutism, reducing oxidative stress, and mitigating inflammation, contributing to the overall management of PCOS related symptomns. The clinical evidence supports its role as a valuable therapeutic agent in addressing PCOS [57].

ACKNOWLEGMENT

The authors extend their sincere gratitude to Dr. Mamta Saraf for her invaluable contributions as an author and supervisor, providing guidance and expertise throughout the development of this review article. Special appreciation goes to Zoya Sadaf for conceptualizing the idea for this review and laying the foundation for its framework. We also acknowledge Malak Shariff for initiating the manuscript draft and Valanka Melicia Fernandes for meticulously managing the references.

Furthermore, we recognize and appreciate the collective contributions of all authors—Zoya Sadaf, Malak Shariff, Valanka Melicia Fernandes, Bhalavikashini D R, Sai Krishna Mohana Kondra, Rohan K, and Samuel Bilgates Brettle—whose collaborative efforts in writing, reviewing, and revising the manuscript have been instrumental in shaping this work.

Conflict Of Interest

The authors declare no conflict of interest

REFERENCES

1. N. Salari et al., “Global prevalence of polycystic ovary syndrome in women worldwide: a comprehensive systematic review and meta-analysis,” Arch Gynecol Obstet, vol. 310, no. 3, pp. 1303–1314, Sep. 2024, doi: 10.1007/S00404-024-07607-X,.
2. S. F. Witchel, H. J. Teede, and A. S. Peña, “Curtailing PCOS,” Pediatr Res, vol. 87, no. 2, pp. 353–361, Jan. 2020, doi: 10.1038/S41390-019-0615-1,.
3. B. Zehra and C. Bintey Zehra, “Polycystic ovarian syndrome: Symptoms, treatment and diagnosis: A review,” J Pharmacogn Phytochem, vol. 7, no. 6, pp. 875–880, 2018, Accessed: Jan. 25, 2025. [Online]. Available: https://www.phytojournal.com/ archives/ 2018.v7.i6.6290/polycystic-ovarian-syndrome-symptoms-treatment-and-diagnosis-a-review
4. Y. V. Louwers and J. S. E. Laven, “Characteristics of polycystic ovary syndrome throughout life,” https://doi.org/10.1177/2633494120911038, vol. 14, p. 263349412091103, Mar. 2020, doi: 10.1177/2633494120911038.
5. D. Armanini, M. Boscaro, L. Bordin, and C. Sabbadin, “Controversies in the Pathogenesis, Diagnosis and Treatment of PCOS: Focus on Insulin Resistance, Inflammation, and Hyperandrogenism,” Int J Mol Sci, vol. 23, no. 8, p. 4110, Apr. 2022, doi: 10.3390/IJMS23084110.
6. G. Martinez, D. Armanini, M. Boscaro, L. Bordin, and C. Sabbadin, “Controversies in the Pathogenesis, Diagnosis and Treatment of PCOS: Focus on Insulin Resistance, Inflammation, and Hyperandrogenism,” 2022, doi: 10.3390/ijms23084110.
7. V. Unfer, F. Facchinetti, B. Orrù, B. Giordani, and J. Nestler, “Myo-inositol effects in women with PCOS: a meta-analysis of randomized controlled trials,” Endocr Connect, vol. 6, no. 8, pp. 647–658, Nov. 2017, doi: 10.1530/EC-17-0243.
8. R. Qamar, “Role of myo - inositol in treatment of young females affected by polycystic ovarian syndrome: Quasi experimental study.” Accessed: Feb. 16, 2025. [Online]. Available: https://applications.emro.who.int/imemrf/666/J-Bahria-Univ-Med-Dent-Coll-2020-10-2-142-146-eng.pdf
9. M. Sun and Q. Yi, “Mediating role of anxiety between body image distress and quality of life among women with polycystic ovary syndrome: a multicentre cross-sectional study,” BMC Womens Health, vol. 24, no. 1, Dec. 2024, doi: 10.1186/S12905-024-03490-5.
10. F. N. Amiri, F. R. Tehrani, M. Simbar, A. Montazeri, and R. A. M. Thamtan, “The experience of women affected by polycystic ovary syndrome: a qualitative study from iran,” Int J Endocrinol Metab, vol. 12, no. 2, 2014, doi: 10.5812/IJEM.13612.

11. F. Shishehgar, F. Ramezani Tehrani, P. Mirmiran, S. Hajian, and A. R. Baghestani, "Comparison of the Association of Excess Weight on Health Related Quality of Life of Women with Polycystic Ovary Syndrome: An Age- and BMI-Matched Case Control Study," PLoS One, vol. 11, no. 10, Oct. 2016, doi: 10.1371/JOURNAL.PONE.0162911.
12. F. Nasiri-Amiri, F. R. Tehrani, M. Simbar, A. Montazeri, and R. A. Mohammadpour, "The Polycystic Ovary Syndrome Health-Related Quality-of-Life Questionnaire: Confirmatory Factor Analysis," Int J Endocrinol Metab, vol. 16, no. 2, Apr. 2018, doi: 10.5812/IJEM.12400.
13. M. Amiri, R. Bidhendi Yarandi, F. Nahidi, M. Tohidi, and F. Ramezani Tehrani, "The relationship between clinical and biochemical characteristics and quality of life in patients with polycystic ovary syndrome," Clin Endocrinol (Oxf), vol. 90, no. 1, pp. 129–137, Jan. 2019, doi: 10.1111/CEN.13858.
14. V. Unfer, G. Carlomagno, G. Dante, and F. Facchinetti, "Effects of myo-inositol in women with PCOS: a systematic review of randomized controlled trials," Gynecol Endocrinol, vol. 28, no. 7, pp. 509–515, Jul. 2012, doi: 10.3109/09513590.2011.650660.
15. V. Unfer, G. Carlomagno, G. Dante, and F. Facchinetti, "Effects of myo-inositol in women with PCOS: a systematic review of randomized controlled trials," Gynecological Endocrinology, vol. 28, no. 7, pp. 509–515, Jul. 2012, doi: 10.3109/09513590.2011.650660.
16. P. A. Regidor and A. E. Schindler, "Myoinositol as a Safe and Alternative Approach in the Treatment of Infertile PCOS Women: A German Observational Study," Int J Endocrinol, vol. 2016, 2016, doi: 10.1155/2016/9537632.
17. P. A. Regidor, A. E. Schindler, B. Lesoine, and R. Druckman, "Management of women with PCOS using myo-inositol and folic acid. New clinical data and review of the literature," Horm Mol Biol Clin Investig, vol. 34, no. 2, May 2018, doi: 10.1515/HMBCI-2017-0067.
18. E. Raffone, P. Rizzo, and V. Benedetto, "Insulin sensitiser agents alone and in co-treatment with r-FSH for ovulation induction in PCOS women," Gynecological Endocrinology, vol. 26, no. 4, pp. 275–280, Apr. 2010, doi: 10.3109/09513590903366996.
19. A. Dunaif, "Insulin Resistance and the Polycystic Ovary Syndrome: Mechanism and Implications for Pathogenesis," Endocr Rev, vol. 18, no. 6, pp. 774–800, Dec. 1997, doi: 10.1210/EDRV.18.6.0318.
20. E. Diamanti-Kandarakis, "Insulin resistance in PCOS," Endocrine, vol. 30, no. 1, pp. 13–17, 2006, doi: 10.1385/ENDO:30:1:13/METRICS.
21. A. Corbould et al., "Insulin resistance in the skeletal muscle of women with PCOS involves intrinsic and acquired defects in insulin signaling," Am J Physiol Endocrinol Metab, vol. 288, no. 5 51-5, pp. 1047–1054, May 2005, doi: 10.1152/AJPENDO.00361.2004/ASSET/IMAGES/LARGE/ZH10050520890006.JPEG.
22. Y. Zhang, C. Li, W. Zhang, X. Zheng, and X. Chen, "Decreased Insulin Resistance by Myo-Inositol Is Associated with Suppressed Interleukin 6/Phospho-STAT3 Signaling in a Rat Polycystic Ovary Syndrome Model," https://home.liebertpub.com/jmf, vol. 23, no. 4, pp. 375–387, Apr. 2020, doi: 10.1089/JMF.2019.4580.
23. M. L. Croze et al., "Chronic treatment with myo-inositol reduces white adipose tissue accretion and improves insulin sensitivity in female mice," J Nutr Biochem, vol. 24, no. 2, pp. 457–466, Feb. 2013, doi: 10.1016/J.JNUTBIO.2012.01.008.
24. R. D'Anna et al., "Myo-inositol Supplementation for Prevention of Gestational Diabetes in Obese Pregnant Women: A Randomized Controlled Trial," Obstetrics and Gynecology, vol. 126, no. 2, pp. 310–315, Aug. 2015, doi: 10.1097/AOG.0000000000000958.

25. J. N. Kim, S. N. Han, and H. K. Kim, "Phytic acid and myo-inositol support adipocyte differentiation and improve insulin sensitivity in 3T3-L1 cells," Nutrition Research, vol. 34, no. 8, pp. 723–731, Aug. 2014, doi: 10.1016/J.NUTRES.2014.07.015.
26. A. D. Genazzani, "Inositol as putative integrative treatment for PCOS," Reprod Biomed Online, vol. 33, no. 6, pp. 770–780, Dec. 2016, doi: 10.1016/J.RBMO.2016.08.024/ASSET/5D6EFDEC-47EC-4400-8170-D5CB307385FF/MAIN.ASSETS/RBMO1610-FIG-5001.JPG.
27. F. Fruzzetti, D. Perini, M. Russo, F. Bucci, and A. Gadducci, "Comparison of two insulin sensitizers, metformin and myo-inositol, in women with polycystic ovary syndrome (PCOS)," Gynecological Endocrinology, vol. 33, no. 1, pp. 39–42, Jan. 2017, doi: 10.1080/09513590.2016.1236078.
28. H. Zhao, C. Xing, J. Zhang, and B. He, "Comparative efficacy of oral insulin sensitizers metformin, thiazolidinediones, inositol, and berberine in improving endocrine and metabolic profiles in women with PCOS: a network meta-analysis," Reprod Health, vol. 18, no. 1, pp. 1–12, Dec. 2021, doi: 10.1186/S12978-021-01207-7/TABLES/2.
29. S. K. Motuhifonua, L. Lin, J. Alsweiler, T. J. Crawford, and C. A. Crowther, "Antenatal dietary supplementation with myo-inositol for preventing gestational diabetes," Cochrane Database of Systematic Reviews, vol. 2023, no. 2, Feb. 2023, doi: 10.1002/14651858.CD011507.PUB3/MEDIA/CDSR/CD011507/IMAGE_N/NCD011507-CMP-001.19.SVG.
30. H. Cabrera-Cruz, L. Oróstica, F. Plaza-Parrochia, I. Torres-Pinto, C. Romero, and M. Vega, "The insulin-sensitizing mechanism of myo-inositol is associated with AMPK activation and GLUT-4 expression in human endometrial cells exposed to a PCOS environment," Am J Physiol Endocrinol Metab, vol. 318, no. 2, pp. E237–E248, Feb. 2020, doi: 10.1152/AJPENDO.00162.2019/ASSET/IMAGES/LARGE/ZH10022082810008.JPEG.
31. F. Corrado and A. Santamaria, "Myoinositol Supplementation on Insulin Resistance in Gestational Diabetes," Glucose Intake and Utilization in Pre-Diabetes and Diabetes: Implications for Cardiovascular Disease, pp. 229–234, Jan. 2015, doi: 10.1016/B978-0-12-800093-9.00019-3.
32. F. Facchinetti et al., "Inositols in Polycystic Ovary Syndrome: An Overview on the Advances," Trends in Endocrinology and Metabolism, vol. 31, no. 6, pp. 435–447, Jun. 2020, doi: 10.1016/J.TEM.2020.02.002/ATTACHMENT/9F289A6E-31CE-40ED-8CF5-9192E8BDE2A1/MMC1.DOCX.
33. M. Minozzi, G. D'Andrea, and V. Unfer, "Treatment of hirsutism with myo-inositol: a prospective clinical study," Reprod Biomed Online, vol. 17, no. 4, pp. 579–582, 2008, doi: 10.1016/S1472-6483(10)60248-9.
34. M. M. Zacchè, L. Caputo, S. Filippis, G. Zacchè, M. Dindelli, and A. Ferrari, "Efficacy of myo-inositol in the treatment of cutaneous disorders in young women with polycystic ovary syndrome," Gynecological Endocrinology, vol. 25, no. 8, pp. 508–513, 2009, doi: 10.1080/09513590903015544.
35. E. A. Ramanan, S. Ravi, K. R. R. Anbu, and M. Michael, "Efficacy and Safety of Tracnil™ Administration in Patients with Dermatological Manifestations of PCOS: An Open-Label Single-Arm Study," Dermatol Res Pract, vol. 2020, 2020, doi: 10.1155/2020/7019126.
36. "Management of polycystic ovary syndrome among Indian women using myo-inositol and D-chiro-inositol." Accessed: Jan. 26, 2025. [Online]. Available: https://www.bioinformation.net/018/97320630018103.htm
37. A. Biswas and A. Biswas, "Assessment of role of myoinositol in the management of PCOS and Obesity," International Journal of Life Sciences, vol. 13, no. 8, 2024, doi: 10.69605/ijlbpr_13.8.2024.75.

38. H. Qamar and R. Mustafa, "Role of Myo-Inositol in Treatment of Young Females Affected By Polycystic Ovarian Syndrome: Quasi Experimental Study," Journal of Bahria University Medical and Dental College, vol. 10, no. 02, pp. 142–146, Mar. 2021, doi: 10.51985/JBUMDC2019092.
39. S. J. Wood, A. Kelsey, B. Brennan, J. Bruce, and R. J. Craigie, "Granular hemostat deposits mimicking disseminated malignancy," J Pediatr Surg, vol. 48, no. 3, Mar. 2013, doi: 10.1016/J.JPEDSURG.2012.12.044.
40. M. L. Okun and A. Lac, "Postpartum Insomnia and Poor Sleep Quality Are Longitudinally Predictive of Postpartum Mood Symptoms," Psychosom Med, vol. 85, no. 8, pp. 736–743, Oct. 2023, doi: 10.1097/PSY.0000000000001234.
41. S. A. Sands et al., "Group-Based Trajectory Modeling of Distress and Well-Being Among Caregivers of Children Undergoing Hematopoetic Stem Cell Transplant," J Pediatr Psychol, vol. 42, no. 3, pp. 283–295, Apr. 2017, doi: 10.1093/JPEPSY/JSW064.
42. D. Greff et al., "Inositol is an effective and safe treatment in polycystic ovary syndrome: a systematic review and meta-analysis of randomized controlled trials," Reprod Biol Endocrinol, vol. 21, no. 1, Dec. 2023, doi: 10.1186/S12958-023-01055-Z.
43. A. Gateva, V. Unfer, and Z. Kamenov, "The use of inositol(s) isomers in the management of polycystic ovary syndrome: a comprehensive review," Gynecological Endocrinology, vol. 34, no. 7, pp. 545–550, Jul. 2018, doi: 10.1080/09513590.2017.1421632.
44. V. Fitz et al., "Inositol for Polycystic Ovary Syndrome: A Systematic Review and Meta-analysis to Inform the 2023 Update of the International Evidence-based PCOS Guidelines," J Clin Endocrinol Metab, vol. 109, no. 6, pp. 1630–1655, Jun. 2024, doi: 10.1210/CLINEM/DGAD762.
45. N. Mendoza et al., "Comparison of the effect of two combinations of myo-inositol and D-chiro-inositol in women with polycystic ovary syndrome undergoing ICSI: a randomized controlled trial," Gynecological Endocrinology, vol. 35, no. 8, pp. 695–700, Aug. 2019, doi: 10.1080/09513590.2019.1576620.
46. R. Dey et al., "Inflammatory perspectives of polycystic ovary syndrome: role of specific mediators and markers," Middle East Fertility Society Journal 2023 28:1, vol. 28, no. 1, pp. 1–12, Dec. 2023, doi: 10.1186/S43043-023-00158-2.
47. S. Aboeldalyl, C. James, E. Seyam, E. M. Ibrahim, H. E. D. Shawki, and S. Amer, "The Role of Chronic Inflammation in Polycystic Ovarian Syndrome—A Systematic Review and Meta-Analysis," Int J Mol Sci, vol. 22, no. 5, p. 2734, Mar. 2021, doi: 10.3390/IJMS22052734.
48. M. Orisaka et al., "Chronic low-grade inflammation and ovarian dysfunction in women with polycystic ovarian syndrome, endometriosis, and aging," Front Endocrinol (Lausanne), vol. 14, p. 1324429, Dec. 2023, doi: 10.3389/FENDO.2023.1324429/BIBTEX.
49. P. Merviel et al., "Impact of myo-inositol treatment in women with polycystic ovary syndrome in assisted reproductive technologies," Reprod Health, vol. 18, no. 1, pp. 1–8, Dec. 2021, doi: 10.1186/S12978-021-01073-3/TABLES/1.
50. Z. Kamenov and A. Gateva, "Inositols in PCOS," Molecules 2020, Vol. 25, Page 5566, vol. 25, no. 23, p. 5566, Nov. 2020, doi: 10.3390/MOLECULES25235566.
51. "Inositol: history of an effective therapy for Polycystic Ovary Syndrome." Accessed: Jan. 26, 2025. [Online]. Available: https://www.europeanreview.org/article/7565?utm_source=chatgpt.com
52. M. Jamilian et al., "Comparison of myo-inositol and metformin on clinical, metabolic and genetic parameters in polycystic ovary syndrome: A randomized controlled clinical trial," Clin Endocrinol (Oxf), vol. 87, no. 2, pp. 194–200, Aug. 2017, doi: 10.1111/CEN.13366.
53. V. Tagliaferri et al., "Metformin vs myoinositol: which is better in obese polycystic ovary syndrome patients? A randomized controlled crossover study," Clin Endocrinol (Oxf), vol. 86, no. 5, pp. 725–730, May 2017, doi: 10.1111/CEN.13304.

54. F. Fruzzetti, D. Perini, M. Russo, F. Bucci, and A. Gadducci, "Comparison of two insulin sensitizers, metformin and myo-inositol, in women with polycystic ovary syndrome (PCOS)," Gynecol Endocrinol, vol. 33, no. 1, pp. 39–42, Jan. 2017, doi: 10.1080/09513590.2016.1236078.
55. H. Cabrera-Cruz, L. Oróstica, F. Plaza-Parrochia, I. Torres-Pinto, C. Romero, and M. Vega, "The insulin-sensitizing mechanism of myo-inositol is associated with AMPK activation and GLUT-4 expression in human endometrial cells exposed to a PCOS environment," Am J Physiol Endocrinol Metab, vol. 318, no. 2, pp. E237–E248, Feb. 2020, doi: 10.1152/AJPENDO.00162.2019.
56. P. A. Regidor, A. E. Schindler, B. Lesoine, and R. Druckman, "Management of women with PCOS using myo-inositol and folic acid. New clinical data and review of the literature," Horm Mol Biol Clin Investig, vol. 34, no. 2, May 2018, doi: 10.1515/HMBCI-2017-0067/MACHINEREADABLECITATION/RIS.
57. "Benefits of Myo-Inositol for Polycystic Ovary Syndrome (PCOS) | Nutri Advanced." Accessed: Feb. 16, 2025. [Online]. Available: https://www.nutriadvanced.co.uk/news/benefits-of-myo-inositol-for-polycystic-ovary-syndrome-pcos/?