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Therapeutic potential of Vitamin B8 for polyendocrine metabolic ovarian syndrome (PMOS): A novel perspective in endocrinology

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Abstract
Polyendocrine Metabolic Ovarian Syndrome (PMOS) has emerged as a broader and metabolically aggravated form of Polycystic Ovary Syndrome (PCOS), characterized by endocrine disruption, insulin resistance, chronic inflammation, oxidative stress, obesity, reproductive dysfunction, and metabolic abnormalities. Increasing evidence suggests that micronutrient deficiencies and impaired metabolic signaling play critical roles in the progression of PMOS. Among various nutritional therapeutics, Vitamin B8, commonly referred to as inositol, has gained considerable attention due to its insulin-sensitizing, hormonal balancing, antioxidant, and reproductive health-promoting properties. Myo-inositol and D-chiro-inositol, the two biologically important isoforms, participate in intracellular signaling pathways, glucose metabolism, ovarian follicular maturation, and endocrine regulation. Clinical and experimental studies demonstrate that Vitamin B8 supplementation improves ovulatory function, reduces hyperandrogenism, enhances insulin sensitivity, regulates menstrual irregularities, and decreases metabolic complications associated with PMOS. Furthermore, Vitamin B8 exhibits anti-inflammatory and antioxidant actions that may prevent the transition from reproductive dysfunction to systemic metabolic syndrome. This review explores the pathophysiology of PMOS, the biochemical significance of Vitamin B8, its molecular mechanisms, therapeutic efficacy, clinical evidence, and future perspectives in endocrine and metabolic medicine.

Keywords: Vitamin B8, Inositol, PMOS, PCOS, insulin resistance, endocrinology, metabolic syndrome, reproductive health, oxidative stress

Introduction

Polycystic Ovary Syndrome (PCOS) is one of the most prevalent endocrine disorders affecting women of reproductive age (Stener-Victorin *et al*., 2024) [20]. Traditionally, PCOS has been considered a reproductive disorder characterized by anovulation, hyperandrogenism, and polycystic ovarian morphology (Joham *et al*., 2022) [13]. However, recent evidence demonstrates that the disorder extends beyond ovarian dysfunction and involves profound metabolic and endocrine abnormalities including obesity, insulin resistance, dyslipidemia, chronic inflammation, cardiovascular risk, and altered glucose metabolism (Tewari *et al*., 2026b). This expanded metabolic phenotype has led researchers to propose the term Polyendocrine Metabolic Ovarian Syndrome (PMOS).

PMOS reflects the multifactorial nature of the disorder where reproductive, endocrine, metabolic, and inflammatory pathways interact simultaneously (Tewari *et al*., 2026a) [25]. One of the central pathogenic mechanisms in PMOS is insulin resistance, which contributes to hyperinsulinemia, ovarian androgen excess, impaired follicular development, and systemic metabolic disturbances. Oxidative stress and chronic low-grade inflammation further aggravate endocrine dysfunction (Teede *et al*., 2026) [32].

Nutritional interventions are increasingly being explored as complementary therapeutic approaches for PMOS management. Among these, Vitamin B8 (inositol) has emerged as a promising therapeutic agent. Inositol functions as a precursor of phosphoinositides and secondary messengers involved in insulin signaling, glucose uptake, and ovarian function. Myo-inositol (MI) and D-chiro-inositol (DCI) are the most important isoforms in human physiology and exhibit insulin-mimetic properties (Gashi, 2024) [11].

Recent clinical studies suggest that Vitamin B8 supplementation improves insulin sensitivity, restores ovulation, reduces androgen levels, improves oocyte quality, and enhances fertility outcomes. Due to its safety profile and metabolic benefits, Vitamin B8 is increasingly recognized as a potential endocrine therapeutic agent for PMOS (Natarajan and Nataraj, 2026) [19].

Understanding Polyendocrine Metabolic Ovarian Syndrome (PMOS)

1. Concept of PMOS

PMOS is considered an advanced metabolic and endocrine manifestation of PCOS involving multiple hormonal axes and metabolic pathways.

Table 1: Components of PMOS (Sengupta and Dutta, 2026) [25]

Component	Clinical Significance
Polyendocrine	Multiple endocrine pathways are disrupted
Metabolic	Insulin resistance, obesity, dyslipidemia
Ovarian	Ovulatory dysfunction and infertility
Inflammatory	Chronic low-grade inflammation
Oxidative	Increased oxidative stress and mitochondrial dysfunction

2. Pathophysiology of PMOS

Major Mechanisms

The pathogenesis of Polyendocrine Metabolic Ovarian Syndrome (PMOS) involves several interconnected mechanisms that collectively contribute to endocrine, metabolic, and reproductive dysfunction. Insulin resistance

is considered the central abnormality, leading to impaired glucose utilization and compensatory hyperinsulinemia, which further stimulates ovarian androgen production. Hyperandrogenism disrupts follicular maturation, resulting in anovulation, menstrual irregularities, acne, and hirsutism. Simultaneously, excessive production of reactive oxygen species promotes oxidative stress, causing cellular and mitochondrial damage within ovarian and metabolic tissues. Chronic low-grade inflammation characterized by elevated inflammatory cytokines such as TNF-α, IL-6, and CRP further aggravates insulin resistance and endocrine disturbances. Mitochondrial dysfunction impairs cellular energy metabolism and enhances oxidative injury, contributing to poor oocyte quality and metabolic imbalance. In addition, alterations in gut microbiota composition may influence hormonal regulation, systemic inflammation, intestinal permeability, and insulin signaling through the gut–brain–ovarian axis. Together, these mechanisms create a complex pathological network that drives the progression of PMOS from a reproductive disorder to a multisystem metabolic syndrome (Teede *et al*., 2026; Tewari *et al*., 2026a) [25].

Insulin Resistance Pathway

"Insulin Resistance"→"Hyperinsulinemia"→↑"Androgen Production"→"Ovulatory Dysfunction"

Insulin resistance stimulates excessive insulin secretion, which promotes ovarian androgen synthesis. Elevated androgen levels impair follicular maturation, leading to menstrual irregularities and infertility (Ding *et al*., 2021) [9].

Vitamin B8 (Inositol): Biochemistry and Physiological Functions

Vitamin B8, commonly known as inositol, is a naturally occurring carbocyclic sugar alcohol involved in cell signaling, lipid metabolism, insulin signaling, and neurotransmitter regulation (Awuchi and Echeta, 2019) [3].

Table 2: Major Isoforms of Inositol (Barker *et al*., 2009) [4]

Isoform	Physiological Role
Myo-inositol (MI)	Glucose uptake and ovarian signaling
D-chiro-inositol (DCI)	Glycogen synthesis and insulin action
Scyllo-inositol	Neurological function
Neo-inositol	Cellular signaling

Myo-inositol and D-chiro-inositol are the primary therapeutic forms used in PMOS management (Biskup *et al*., 2026).

Table 3: Dietary Sources of Vitamin B8 (Rébeillé *et al*., 2007)

Food Source	Inositol Content
Citrus fruits	High
Whole grains	Moderate
Beans and legumes	High
Nuts and seeds	Moderate
Cantaloupe	Rich source
Brown rice	Moderate

Mechanism of Action of Vitamin B8 in PMOS

1. Improvement of Insulin Sensitivity

Vitamin B8 acts as an insulin sensitizer by enhancing insulin receptor signaling pathways and improving glucose uptake in peripheral tissues (Tardy *et al*., 2020) [31].

Insulin Signaling

"Glucose Uptake"∝"Insulin Sensitivity"

Myo-inositol serves as a secondary messenger in insulin signaling and restores impaired insulin pathways commonly observed in PMOS patients (Bevilacqua and Bizzarri, 2018) [5].

2. Reduction of Hyperandrogenism

Hyperinsulinemia stimulates ovarian theca cells to produce excessive androgens. Vitamin B8 reduces insulin levels, thereby decreasing testosterone synthesis and improving hormonal balance (Jin *et al*., 2025) [36].

Table 4: Hormonal Improvement (Shpakov, 2021) [26]

Hormone	Effect of Vitamin B8
Testosterone	Reduced
LH/FSH ratio	Normalized
Insulin	Reduced
SHBG	Increased

3. Restoration of Ovulation

Vitamin B8 improves follicular maturation and ovarian function, promoting regular ovulation and menstrual cycles (Michels *et al*., 2017) [17].

Follicular Development

Antioxidant and Anti-inflammatory Effects

Oxidative stress is significantly elevated in PMOS. Vitamin B8 improves antioxidant defense mechanisms and reduces inflammatory cytokines (Tewari *et al*., 2026a).

Table 5: Important Biomarkers

Biomarker	Function
Superoxide dismutase (SOD)	Antioxidant defense
Glutathione peroxidase (GPx)	ROS detoxification
Catalase	Hydrogen peroxide metabolism
Malondialdehyde (MDA)	Lipid peroxidation marker

Therapeutic Benefits of Vitamin B8 in PMOS

1. Regulation of Menstrual Cycles

Vitamin B8, particularly myo-inositol, plays an important role in restoring menstrual regularity in women with Polyendocrine Metabolic Ovarian Syndrome (PMOS) by improving insulin sensitivity and correcting hormonal imbalance. Insulin resistance and elevated androgen levels are major contributors to irregular menstrual cycles and anovulation in PMOS (Tewari *et al*., 2026b). Myo-inositol acts as a secondary messenger in insulin signaling pathways, helping to reduce circulating insulin levels and subsequently lowering ovarian androgen production. This hormonal normalization supports proper follicular maturation, ovulation, and endocrine stability, leading to more regular menstrual cycles. Clinical studies have demonstrated that women receiving Vitamin B8 supplementation experience improved cycle frequency, reduced amenorrhea, and enhanced ovarian function without significant adverse effects (Sigue and Decena, 2022) [22].

2. Fertility Enhancement

Vitamin B8 supplementation has shown significant therapeutic potential in improving fertility outcomes among women with PMOS. Myo-inositol enhances ovarian responsiveness, promotes healthy follicular development, and improves oocyte maturation by regulating intracellular calcium signaling and glucose metabolism within ovarian tissues (Bevilacqua *et al*., 2015) [7]. Several clinical trials

have reported increased ovulation rates, improved embryo quality, and higher pregnancy success in women receiving myo-inositol therapy, particularly during assisted reproductive treatments. Additionally, Vitamin B8 helps reduce hyperandrogenism and oxidative stress, both of which negatively affect reproductive performance. The combination of myo-inositol and D-chiro-inositol in physiological ratios has also been associated with improved endocrine function and better fertility outcomes, making Vitamin B8 a promising nutritional therapeutic agent in reproductive endocrinology (Wdowiak *et al*., 2025) [36].

3. Weight Management

Vitamin B8 may contribute to effective weight management in women with PMOS by improving insulin sensitivity, regulating glucose metabolism, and enhancing lipid utilization. Insulin resistance commonly leads to increased fat accumulation, abdominal obesity, and difficulty in maintaining healthy body weight in PMOS patients. By acting as an insulin sensitizer, myo-inositol reduces hyperinsulinemia and promotes better cellular glucose uptake, thereby decreasing excessive fat storage and improving metabolic efficiency. Furthermore, Vitamin B8 supports lipid metabolism and may help lower triglyceride levels and visceral adiposity. Clinical studies have demonstrated reductions in body mass index (BMI), waist circumference, and overall metabolic risk following inositol supplementation, highlighting its beneficial role in obesity management and metabolic health improvement in PMOS (Stener-Victorin *et al*., 2026) [29].

Metabolic Relationship

$$BMI = \frac{\text{Weight (kg)}}{\text{Height (m)}^2}$$

Reduction of Metabolic Syndrome Risk

Vitamin B8 demonstrates significant potential in reducing the risk of metabolic syndrome (Andersen and Fernandez, 2013) [2] in women with Polyendocrine Metabolic Ovarian Syndrome (PMOS) through its beneficial effects on glucose and lipid metabolism. Myo-inositol and D-chiro-inositol improve insulin signaling pathways, thereby reducing insulin resistance and lowering circulating insulin levels, which are central contributors to metabolic dysfunction (Bevilacqua and Bizzarri, 2018) [5]. Supplementation with Vitamin B8 has been associated with decreased fasting blood glucose levels, improved glycemic control, and enhanced cellular glucose utilization. In addition, Vitamin B8 positively influences lipid metabolism by reducing triglycerides and low-density lipoprotein (LDL) cholesterol levels while improving overall metabolic homeostasis (Aguilera-Méndez *et al*., 2022) [1]. These metabolic improvements may decrease the long-term risk of obesity, type 2 diabetes mellitus, cardiovascular disease, and other complications associated with metabolic syndrome, making Vitamin B8 an important nutritional therapeutic agent in PMOS management (Tewari *et al*., 2026a) [22].

Mental Health Improvement

Women with PMOS often experience anxiety, depression, and mood disorders. Inositol participates in neurotransmitter signaling pathways and may improve psychological well-being (Qi *et al*., 2025).

Clinical Evidence Supporting Vitamin B8 Therapy

Several randomized clinical trials demonstrate improved insulin sensitivity and ovulatory function following myo-inositol supplementation (Unfer *et al*., 2012) [35].

Table 6: Myo-Inositol Supplementation

Clinical Outcome	Observed Effect
Ovulation rate	Increased
Menstrual regularity	Improved
Insulin resistance	Reduced
Testosterone levels	Decreased
Pregnancy rate	Increased

1. Combination Therapy

Combination therapy using myo-inositol and D-chiro-inositol in physiological ratios (40:1) appears more effective than monotherapy (Dinicola *et al*., 2014) [10].

Physiological Ratio

"MI:DCI Ratio"=40:1

This ratio mimics physiological plasma concentrations and optimizes ovarian and metabolic responses.

Molecular Mechanisms Linking Vitamin B8 and PMOS

1. PI3K/Akt Pathway

Vitamin B8 plays a crucial role in regulating the phosphatidylinositol 3-kinase/protein kinase B (PI3K/Akt) signaling pathway, which is one of the major intracellular pathways involved in insulin action and glucose metabolism. In women with Polyendocrine Metabolic Ovarian Syndrome (PMOS), impaired PI3K/Akt signaling contributes to insulin resistance, hyperglycemia, and metabolic imbalance. Myo-inositol acts as a precursor for phosphoinositides that function as secondary messengers in insulin receptor activation. By enhancing PI3K/Akt pathway activity, Vitamin B8 promotes glucose transporter translocation, increases cellular glucose uptake, and improves insulin sensitivity. This mechanism helps restore metabolic homeostasis, reduce hyperinsulinemia, and minimize androgen overproduction associated with PMOS (Ran *et al*., 2026) [22].

2. AMPK Activation

Vitamin B8 may contribute to the activation of AMP-activated protein kinase (AMPK), a key cellular energy sensor involved in regulating glucose and lipid metabolism. Activation of AMPK enhances fatty acid oxidation, stimulates glucose uptake, and inhibits lipid synthesis, thereby improving overall metabolic efficiency in PMOS patients. Since women with PMOS frequently exhibit obesity, dyslipidemia, and excessive lipid accumulation, AMPK activation plays an important therapeutic role in reducing adiposity and improving metabolic health. Furthermore, AMPK helps decrease inflammatory signaling and improves insulin responsiveness in peripheral tissues. Through these metabolic effects, Vitamin B8 may aid in controlling body weight, reducing triglyceride accumulation, and lowering the risk of metabolic syndrome in PMOS (Teede *et al*., 2026; Sid *et al*., 2015) [25, 27].

3. Mitochondrial Function

Vitamin B8 supports mitochondrial function by enhancing cellular energy metabolism and protecting cells against oxidative stress-induced damage (Mukherjee *et al*., 2023) [18]. Mitochondria are essential for ATP production, steroid

hormone synthesis, and ovarian follicular development, but mitochondrial dysfunction is commonly observed in PMOS due to chronic oxidative stress and metabolic disturbances. Inositol helps maintain mitochondrial membrane stability, improves energy production, and reduces the generation of reactive oxygen species (ROS). By strengthening antioxidant defense systems, Vitamin B8 minimizes oxidative injury to ovarian tissues and metabolic organs, thereby improving oocyte quality, endocrine balance, and overall cellular function. This protective role of Vitamin B8 against mitochondrial dysfunction may contribute significantly to improved reproductive and metabolic outcomes in PMOS patients (Tewari *et al*., 2026b) [25].

Table 7: Comparison of Vitamin B8 with Conventional Therapies

Therapy	Advantages	Limitations
Metformin	Effective insulin sensitizer	Gastrointestinal side effects
Oral contraceptives	Hormonal regulation	Does not address insulin resistance
Vitamin B8	Safe, improves fertility and metabolism	Requires long-term supplementation
Anti-androgens	Reduces hirsutism	Hormonal adverse effects

Vitamin B8 demonstrates fewer adverse effects and better tolerability compared to many pharmacological interventions.

Recommended Dosage and Safety

1. Dosage

Vitamin B8 supplementation, particularly in the forms of myo-inositol and D-chiro-inositol, has been widely used in the management of Polyendocrine Metabolic Ovarian Syndrome (PMOS) due to its beneficial effects on insulin sensitivity, hormonal regulation, and reproductive function (Khandelwal, 2025) [14]. Common therapeutic dosages recommended in clinical studies include 2–4 g/day of myo-inositol and 50–100 mg/day of D-chiro-inositol, often administered in a physiological ratio of 40:1 to mimic normal plasma concentrations. These doses have shown positive outcomes in improving ovulation, menstrual regularity, glucose metabolism, and fertility parameters in women with endocrine and metabolic disorders. The dosage may vary depending on the severity of insulin resistance, obesity, reproductive dysfunction, and individual metabolic status. In many cases, Vitamin B8 is administered alongside folic acid or other nutritional supplements to enhance therapeutic efficacy and reproductive health outcomes (Paduch-Jakubczyk and Dubińska, 2024) [20].

2. Safety Profile

Vitamin B8 is generally considered a safe and well-tolerated nutritional therapeutic agent with minimal adverse effects, even during long-term supplementation (Rogovik *et al*., 2010) [24]. Unlike several pharmacological insulin sensitizers, inositol therapy exhibits a favorable safety profile and rarely causes severe complications. Most clinical studies report only mild and temporary side effects, including nausea, gastrointestinal discomfort, bloating, or occasional headache (Max and Sherer, 2000) [16]. These symptoms are usually dose-dependent and tend to diminish with continued use or dosage adjustment. Due to its natural occurrence in human physiology and food sources, Vitamin B8 is regarded as a low-risk therapeutic option for women with PMOS, especially for those seeking non-pharmacological or adjunctive treatment approaches. Nevertheless, appropriate medical supervision and individualized dosage recommendations are important to ensure optimal therapeutic outcomes and safety (Halloran *et al*., 2014) [10].

Possible Side Effects

Although Vitamin B8 (inositol) is generally considered safe and well tolerated, some individuals may experience mild side effects during supplementation, particularly at higher doses. The most commonly reported adverse effects include mild nausea and gastrointestinal discomfort such as bloating, stomach upset, flatulence, or diarrhea, which are usually temporary and improve as the body adapts to the supplement. In rare cases, individuals may also experience headache or dizziness. These side effects are typically non-serious and dose-dependent, and they can often be minimized by dividing the daily dosage or taking the supplement with meals. Overall, Vitamin B8 demonstrates a favorable safety profile compared to many conventional pharmacological therapies used in metabolic and endocrine disorders (Lukaski, 2004) [15].

Future Perspectives

Future research on the therapeutic role of Vitamin B8 in Polyendocrine Metabolic Ovarian Syndrome (PMOS) should focus on developing standardized diagnostic criteria to clearly differentiate PMOS from conventional PCOS and related metabolic disorders. Greater emphasis is needed on personalized nutritional therapeutics, where treatment strategies are tailored according to genetic background, metabolic profile, hormonal status, and gut microbiota composition of individual patients. Long-term clinical trials involving larger populations are essential to evaluate the sustained efficacy, safety, and reproductive outcomes of Vitamin B8 supplementation over extended periods. In addition, the identification of molecular biomarkers for treatment monitoring may help clinicians assess therapeutic response, disease progression, and metabolic improvement more accurately. Future studies should also explore synergistic combination therapies involving Vitamin B8 with probiotics, antioxidants, omega-3 fatty acids, and other nutraceuticals to enhance endocrine and metabolic benefits. Furthermore, investigation into the epigenetic effects of Vitamin B8 may provide deeper insights into how inositol influences gene expression, insulin signaling, inflammation, and ovarian function at the molecular level. Advancements in nutrigenomics, metabolomics, and precision endocrinology may ultimately establish Vitamin B8 as a cornerstone therapeutic approach for managing metabolic reproductive disorders such as PMOS.

Conclusion

Polyendocrine Metabolic Ovarian Syndrome represents a complex endocrine-metabolic disorder extending beyond conventional PCOS pathology. Insulin resistance, oxidative stress, chronic inflammation, and hormonal dysregulation are central contributors to disease progression. Vitamin B8, particularly myo-inositol and D-chiro-inositol, offers a promising therapeutic strategy due to its insulin-sensitizing, antioxidant, anti-inflammatory, and reproductive health-enhancing properties. Clinical evidence supports its efficacy

in improving ovulation, menstrual regularity, hormonal balance, fertility outcomes, and metabolic health. Its excellent safety profile and multifaceted mechanism of action make Vitamin B8 an attractive adjunctive or alternative therapy in PMOS management. Future endocrine and nutritional research may further establish Vitamin B8 as a novel therapeutic cornerstone in reproductive metabolic medicine.

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