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THE POTENTIAL ROLE OF L-CARNITINE SUPPLEMENTATION IN MANAGEMENT OF POLYENDOCRINE METABOLIC OVARIAN SYNDROME

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ABSTRACT

Polyendocrine Metabolic Ovarian Syndrome (PMOS), formerly known as polycystic ovary syndrome, is a common endocrine and metabolic disorder affecting women of reproductive age, characterized by hyperandrogenism, ovulatory dysfunction, and insulin resistance. Despite its high prevalence, its pathophysiology remains incompletely understood, and current therapies are largely symptomatic. Increasing evidence implicates mitochondrial dysfunction, oxidative stress, and chronic low-grade inflammation in disease development. In this context, L-carnitine, a key regulator of mitochondrial fatty acid transport and energy metabolism, has emerged as a potential adjunctive therapeutic agent.

This narrative review summarizes current evidence on the role of L-carnitine and its derivatives in PMOS, integrating findings from randomized controlled trials, observational studies, systematic reviews, and preclinical models. Available data suggest that L-carnitine supplementation may improve metabolic parameters, including insulin resistance and lipid profiles, while exerting antioxidant and anti-inflammatory effects in ovarian tissue. However, evidence regarding endocrine and fertility outcomes remains inconsistent.

Although preclinical studies strongly support biological plausibility, clinical evidence is limited by heterogeneity in study design, small sample sizes, and reliance on surrogate endpoints. L-carnitine should therefore be considered a promising adjunct rather than a standard treatment for PMOS. Further large-scale randomized controlled trials are required to define optimal dosing, formulation, and patient subgroups most likely to benefit.

KEYWORDS

PMOS, PCOS, L-Carnitine, Nutrition, Oxidative Stress, Insulin Resistance

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1. Introduction

Polyendocrine Metabolic Ovarian Syndrome (PMOS), previously known as Polycystic Ovary Syndrome (Teede et al., 2026), is one of the most common endocrine, metabolic and gynecological disorders worldwide that affects roughly 5-20% of women of reproductive age (Escobar-Morreale, 2018; Teede et al., 2026). Although it has been investigated since 1935, when Irving F. Stein and Michael L. Leventhal first published a research paper describing the syndrome and presenting seven cases (Stein & Leventhal, 1935), PMOS remains incompletely understood. In 2003, the 'Rotterdam Criteria' were proposed as a universal diagnostic tool (Fauser et al., 2004) (Fig. 1). They have been widely adopted among physicians, despite ongoing controversies related to the heterogeneity, progression, and consequences of this syndrome (Baracat et al., 2022). PMOS is associated not only with fertility issues but also with hormonal imbalance that may manifest in weight gain, obesity, insulin resistance (IR), type 2 diabetes mellitus (T2DM), and increased cardiovascular risk. Moreover, affected patients frequently experience increased anxiety, depression, and fear of long-term complications (Tauqir et al., 2021), making PMOS a significant interdisciplinary health issue. Its etiology and pathogenesis remain poorly understood as different theories are being explored, thus limiting therapeutic strategies (Di Emidio et al., 2020). Due to the variety of phenotypes, every case has to be approached individually. In order to handle the symptoms, different drugs (e.g., oral contraceptive pills, antiandrogens, insulin sensitizers, aromatase inhibitors) and supplements (e.g., vitamin D, inositol, berberine, magnesium) may be useful (Alesi et al., 2022; Bashir et al., 2026; Escobar-Morreale, 2018). Recently, carnitine has emerged as a potential agent in the management of PMOS with seven different clinical studies registered in the ClinicalTrials.gov database (search performed in May 2026). In this narrative review, we focus on the molecular mechanisms underlying PMOS and the potential beneficial effects of L-carnitine (LC) supplementation.

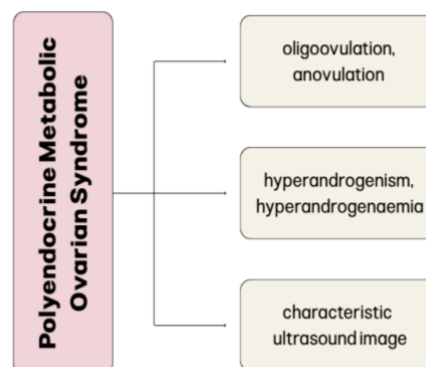


Fig. 1. Rotterdam Criteria include 3 main characteristics of PMOS, including ovarian dysfunction, androgen excess and polycystic ovarian morphology. To establish the diagnosis at least two out of three features must be present in a patient (Fauser et al., 2004).

2. Methodology

This narrative review summarizes current evidence on the role of L-carnitine and its derivatives in Polyendocrine Metabolic Ovarian Syndrome. A literature search was conducted in PubMed, Scopus, and Google Scholar for studies published up to May 2026 using keywords related to “L-carnitine”, “PMOS/PCOS”, “insulin resistance”, “oxidative stress”, and “hyperandrogenism”. Given the recent adoption of the term PMOS, studies referring to PCOS were also included and considered equivalent for the purpose of this review. No time restrictions were applied; however, preference was given to studies published within the last decade. Only English-language full-text articles were included. Eligible studies comprised randomized controlled trials, observational studies, systematic reviews, meta-analyses, and relevant experimental research (in vitro and animal models). Given the heterogeneity of the available literature, a narrative synthesis was performed, with findings organized into thematic domains including oxidative stress, metabolic effects, endocrine regulation, and reproductive outcomes. No meta-analysis was conducted.

3. Biological role of carnitine

3.1. Chemical structure and synthesis of carnitine

Carnitine (3-hydroxy-4-N,N,N-trimethylaminobutyrate) has been extensively investigated for over 100 years because of its crucial role in several metabolic and biochemical pathways (Alhasaniah, 2023). In 1905, it was identified in high concentrations in skeletal muscle, from which its name derives (Latin: *carnis*) (Harmeyer, 2002). Carnitine occurs in two isomeric forms; however, only L-carnitine (Fig. 2) has beneficial effects on human body (Pękala et al., 2011). Therefore, this review focuses exclusively on the L-enantiomer.

L-carnitine is synthesized endogenously in humans in the brain, liver, and kidneys. These organs possess the complete set of enzymes required for carnitine biosynthesis, whereas other tissues depend on uptake from the circulation via active transport mechanisms. This five-step pathway involves crucial amino acids - methionine and lysin. More than 90% of the total body carnitine is stored in skeletal muscle and the myocardium due to their high metabolic demand (Harmeyer, 2002; Pękala et al., 2011). Healthy humans, even when following vegetarian diet, produce sufficient amounts of this compound (Alhasaniah, 2023; K.-G. Seline & Johein, 2007). Dietary carnitine is obtained primarily from animal-derived foods. Red meat (e.g., horse meat, beef, and pork) contains the highest concentrations, while dairy products provide moderate amounts. In contrast, vegetables, fruits, and mushrooms usually contain only trace levels of carnitine (K.-G. Seline & Johein, 2007).

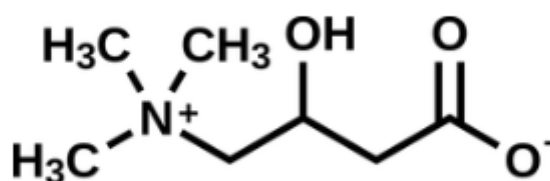


Fig. 2. Chemical structure of L-carnitine.

3.2. Physiological functions of L-carnitine

L-carnitine plays a crucial role in cellular energy metabolism. Its primary physiological function is the transport of activated long-chain fatty acids across the inner mitochondrial membrane, enabling their subsequent β -oxidation and ATP production. This process, known as the carnitine shuttle, is essential because the mitochondrial membrane is impermeable to acyl-CoA molecules (Harmeyer, 2002). By transferring acyl groups between coenzyme A and carnitine, LC facilitates the utilization of fatty acids as an energy source, particularly in highly oxidative tissues such as myocardium (Pękala et al., 2011).

Beyond its role in fatty acid oxidation, LC acts as a regulator of intracellular acyl-CoA/free CoA balance, thereby maintaining optimal activity of several mitochondrial enzymes. Through the reversible formation of acylcarnitines, especially acetyl-L-carnitine (ALC), it serves as a buffer for excess acyl residues and contributes to metabolic flexibility during conditions such as fasting, intense exercise, and hypoxia (Harmeyer, 2002). Moreover, LC participates in glucose metabolism by shuttling acetyl groups across the mitochondrial membrane and preventing the accumulation of acetyl-CoA and other intermediates implicated in insulin resistance. Increasing evidence also indicates that L-carnitine possesses antioxidant and anti-inflammatory properties, protects mitochondrial function, stabilizes cellular membranes, and reduces reactive oxygen species production (Almannai et al., 2019; Di Emidio et al., 2020; Fenkci et al., 2008).

3.3. L-carnitine levels in women with PMOS

It has been reported that circulating concentrations of total and free L-carnitine are reduced in women with PMOS compared with healthy controls, with this finding being observed in both obese and non-obese individuals (Celik et al., 2017; Fenkci et al., 2008; Tauqir et al., 2021). Interestingly, lower serum LC levels were associated with markers of hyperandrogenism, as well as with indices of hyperinsulinaemia and IR (Salehpour et al., 2019). Although it remains unclear whether reduced carnitine availability represents a primary pathogenic factor or a secondary consequence of metabolic disturbances, these observations provide a potential rationale for investigating carnitine supplementation in this population. Similar reductions (up to 25%) in circulating L-carnitine concentrations have been described in several other metabolic and chronic disease states, including obesity, T2DM, chronic kidney disease requiring dialysis and severe hepatic dysfunction, suggesting that carnitine depletion may represent a common feature of conditions characterized by impaired metabolic homeostasis and increased energetic demands (Alhasanah, 2023; Pękala et al., 2011).

4. Molecular rationale for L-carnitine use in PMOS

4.1. Antioxidant properties

Oxidative stress is considered one of the key mechanisms involved in the pathogenesis of PMOS and is present at systemic, ovarian and intrafollicular levels (Placidi et al., 2023). Increased production of reactive oxygen species (ROS), accompanied by reduced total antioxidant capacity, contributes to mitochondrial dysfunction, insulin resistance, chronic low-grade inflammation and hyperandrogenism, thereby creating a cycle that further exacerbates metabolic and reproductive abnormalities (De Rubeis et al., 2024). Within the ovary, excessive ROS generation impairs folliculogenesis, disrupts steroidogenesis and reduces oocyte quality, maturation and fertilization potential (Palmerini et al., 2023; Placidi et al., 2022, 2023). Moreover, oxidative stress promotes the formation of advanced glycation end-products (AGEs), which further amplify inflammatory signalling and oxidative damage, contributing to ovarian dysfunction and anovulation (Palmerini et al., 2023).

Carnitines may exert antioxidant effects through several complementary mechanisms involving both direct modulation of ROS and improvement of mitochondrial function. Experimental and clinical evidence suggests that L-carnitine (LC) and its derivatives, particularly ALC and propionyl-L-carnitine (PLC), reduce oxidative stress by scavenging free radicals, limiting their formation, and preserving the integrity of the mitochondrial electron transport chain, thereby decreasing mitochondrial ROS generation under stress conditions (Maleki et al., 2019; Petrillo et al., 2021). Carnitines have also been shown to increase the activity of endogenous antioxidant enzymes, including superoxide dismutase (SOD) and catalase, while modulating redox-sensitive signalling pathways such as NF- κ B, resulting in reduced production of pro-inflammatory cytokines including TNF- α , IL-6 and IFN- γ (Kalhori et al., 2019; Petrillo et al., 2021; Zhang et al., 2025). In addition, carnitines protect cellular structures from oxidative injury by maintaining membrane stability through acetylation of membrane phospholipids and by preventing free radical-induced DNA damage (Petrillo et al., 2022).

In murine ovarian tissue, carnitine supplementation has been associated with increased expression of mitochondrial regulators such as mitochondrial transcription factor A (mtTFA), SIRT1, SIRT3 and SOD2, indicating enhancement of mitochondrial biogenesis and antioxidant defence systems (Placidi et al., 2022). Animal studies further demonstrated that carnitines alleviate oxidative and glycative damage within the ovarian microenvironment, reduce lipid peroxidation and malondialdehyde concentrations, and improve mitochondrial activity and oocyte competence under conditions of redox imbalance (Placidi et al., 2022). Importantly, the addition of PLC to LC-ALC formulations appears to provide superior protection against oxidative and glycative stress, with greater efficacy in preserving mitochondrial function and tissue architecture (Hu et al., 2023). Collectively, these findings suggest that the antioxidant activity of carnitines extends beyond simple free radical scavenging and involves broader regulation of mitochondrial function, inflammatory signalling and cellular redox balance.

4.2. Insulin-sensitizing and metabolic effects

Beyond its antioxidant activity, L-carnitine plays an important role in metabolic homeostasis. By facilitating the translocation of long-chain fatty acids into the mitochondrial matrix, carnitines enhance lipid utilization and reduce intracellular lipid accumulation, which is a key contributor to insulin resistance (Fenkci et al., 2008; Mazza et al., 2024). This mechanism is particularly relevant in PMOS, where IR is a central feature linking metabolic dysfunction with reproductive abnormalities.

Several clinical studies have demonstrated favorable effects of L-carnitine supplementation on metabolic parameters associated with PMOS, especially when combined with other supplements (e.g. chromium, myo-inositol, L-arginine, L-cysteine) (Genazzani et al., 2025; Jamilian et al., 2020). Improvements in fasting insulin concentrations, HOMA-IR values and insulin sensitivity indices have been reported following treatment with both LC and ALC formulations (Hafezi et al., 2024; Salehpour et al., 2019; Tauqir et al., 2021). These effects appear to be particularly pronounced in overweight, obese and hyperinsulinaemic patients, suggesting that carnitines may be most beneficial in metabolically impaired phenotypes (Genazzani et al., 2020, 2025).

In addition to improving insulin sensitivity, carnitine supplementation has been associated with reductions in body weight, body mass index and waist circumference, although the magnitude of these effects varies considerably between studies (Liao et al., 2022; Maleki et al., 2019; Zhao et al., 2025). The influence of carnitines on lipid metabolism remains less consistent; while several clinical trials and meta-analyses demonstrated reductions in triglycerides, total cholesterol and LDL cholesterol accompanied by increases in HDL cholesterol, other studies failed to observe significant changes in lipid profiles (Liao et al., 2022; Salehpour et al., 2019; Sangouni et al., 2022).

Studies assessing the impact of lipid and carbohydrate metabolism also yield inconsistent results. Sangouni et al. suggest no improvement in liver fat content or cardiometabolic outcomes, whereas Talari et al. report a significant decrease in carotid intima-media thickness and an increase in plasma NO concentration in patients with PMOS (Sangouni et al., 2021; Talari et al., 2019). These findings combined show that fully understanding and accurately assessing the effects of LC is difficult and poses a significant challenge in the scientific community.

4.3. Effects on steroidogenesis and androgen metabolism

Different observations suggest that carnitines may influence endocrine abnormalities associated with PMOS by modulating androgen homeostasis. Clinical studies in women with PMOS have reported associations between reduced circulating L-carnitine concentrations and markers of hyperandrogenism, including increased free androgen index (FAI) and lower sex hormone-binding globulin (SHBG) concentrations (Fenkci et al., 2008). Moreover, some clinical studies and meta-analyses reported reductions in serum testosterone concentrations following L-carnitine supplementation, although the magnitude and consistency of these effects varied between studies (Shukri et al., 2022). Experimental data from animal models additionally demonstrated improvements in ovarian endocrine function, menstrual cycle regularity, and pregnancy rates. Interestingly, formulations containing PLC appear to exert more pronounced anti-androgenic effects than LC or ALC alone, with superior efficacy in maintaining testosterone concentrations close to physiological values in DHEA-induced PMOS models (Di Emidio et al., 2020).

Various authors have proposed that these effects may involve modulation of hypothalamic-pituitary-gonadal axis activity and subsequent alterations in gonadotropin secretion (Di Emidio et al., 2020). Improvements in LH concentrations and menstrual regularity have been reported in some clinical studies employing carnitine-containing formulations, although the results are not consistent (Genazzani et al., 2020, 2025; Placidi et al., 2022). In addition, experimental evidence suggests that carnitines may indirectly support physiological steroidogenesis by preserving granulosa and theca cell function and limiting pathological alterations within the ovarian microenvironment known to promote excessive androgen production (Kalhori et al., 2019; Palmerini et al., 2023). The available data remain heterogeneous and it is currently unclear whether the endocrine benefits observed in clinical studies result from direct modulation of steroidogenic pathways or represent secondary consequences of broader improvements in ovarian physiology.

4.4. Reproductive and fertility outcomes

Evidence regarding the effects of carnitine supplementation on menstrual cyclicity, reproductive hormones and fertility outcomes in women with PMOS remains limited and inconclusive. While several studies and systematic reviews have reported improvements in menstrual regularity, ovulation rates and pregnancy outcomes following carnitine administration (Pandey et al., 2025; Petrillo et al., 2021; Placidi et al., 2023), randomized controlled trials evaluating assisted reproductive technology outcomes failed to demonstrate significant benefits (Abu-Zaid et al., 2025; Hafezi et al., 2024; Sheida et al., 2021). Moreover, interpretation of the available literature is further complicated by the retraction of three influential studies investigating the effects of L-carnitine in clomiphene-resistant PMOS patients, which substantially limits the strength of evidence in this area and precludes firm conclusions regarding the reproductive efficacy of carnitine supplementation (I. A. El Sharkwy & Abd El Aziz, 2019; I. A. El Sharkwy & Sharaf El-Din, 2019; Ismail et al., 2014). Figure 3. represents different proposed mechanisms of action and potential benefits from L-carnitine supplementation in patients with PMOS (Fig. 3).

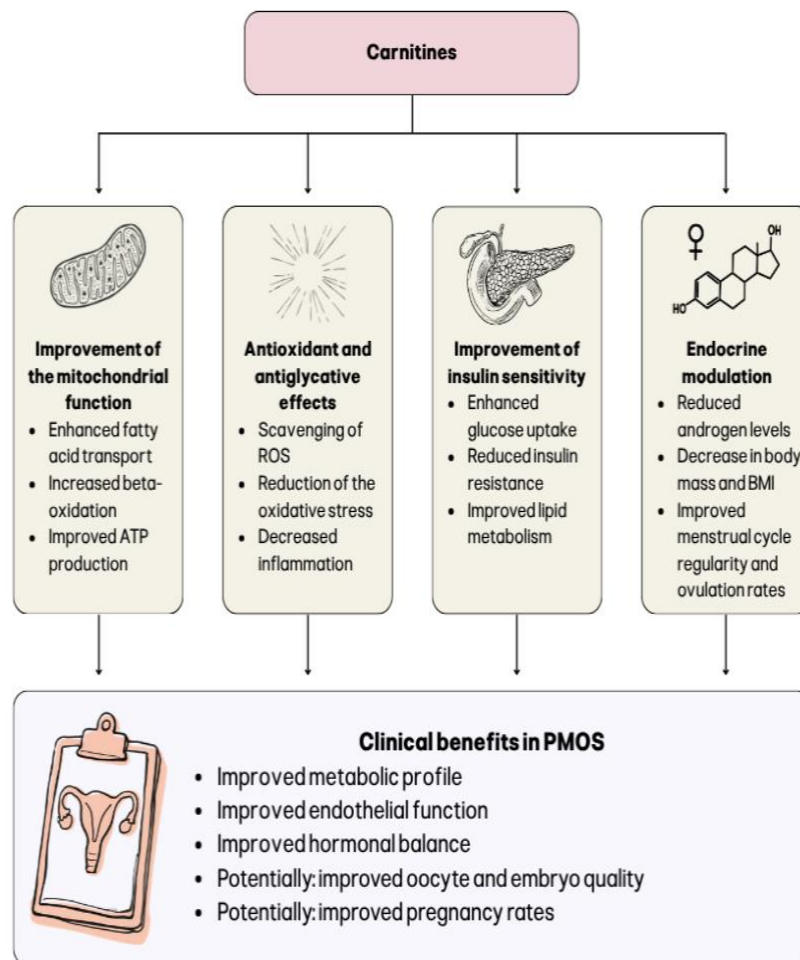


Fig. 3. Overview of potential mechanisms of action and beneficial influence of L-carnitine and its derivatives on women affected by PMOS.

5. Current challenges and future prospects

5.1. Effective dosage and drug safety

Due to the large number of clinical studies investigating carnitine supplementation in women with PMOS, as well as the considerable heterogeneity of intervention protocols with respect to administered dosage, the relative proportions of ALC and PLC, and treatment duration, it remains difficult to define a single optimal or universally effective daily dose. The majority of randomized controlled trials evaluated oral L-carnitine at doses ranging from 250 to 3000 mg/day, with treatment periods typically lasting 12–24 weeks (Genazzani et al., 2020; Maleki et al., 2019; Sangouni et al., 2022). Machine learning-based modelling proposed that daily doses of at least 250 mg administered for approximately 14 weeks may be required to achieve clinically meaningful reductions in body weight (D.-D. Wang et al., 2022). Other analyses suggested that doses around 2000 mg/day may provide maximal therapeutic effects, although a clear dose-response relationship has not been consistently demonstrated (Gong et al., 2023).

The available evidence further indicates that treatment response may differ according to baseline metabolic status. Improvements in insulin sensitivity and glucose homeostasis appear to be more pronounced in overweight, obese and hyperinsulinaemic women, whereas metabolically healthy or normoinsulinaemic individuals often derive less measurable benefit (Genazzani et al., 2020, 2025).

Carnitine supplementation has generally demonstrated an excellent safety profile in clinical studies involving women with PMOS. No serious adverse events attributable to treatment were reported in randomized controlled trials or meta-analyses, and supplementation was generally well tolerated even during prolonged administration. The most commonly described adverse effects in studies conducted in other populations include mild gastrointestinal symptoms such as nausea, abdominal discomfort and diarrhea, which are typically dose-dependent and self-limiting (Liao et al., 2022; Shukri et al., 2022).

5.2. Supplement formulation

Some studies suggest differential effects among individual carnitine derivatives, with ALC and PLC potentially exhibiting higher effectiveness than LC and distinct tissue-specific activities, possibly due to their pharmacokinetics (Di Emidio et al., 2020; Palmerini et al., 2023).

It should be emphasized that a proportion of the available evidence derives from studies evaluating L-carnitine as part of combination nutraceutical regimens rather than as monotherapy. Among these, co-administration of LC and chromium was associated with significant reductions in body weight, improved glycaemic control and favorable effects on psychological health in women with PMOS, including relieving depression symptoms (Jamilian et al., 2019, 2020).

Similarly, integrative formulations combining LC and ALC with compounds such as L-arginine, N-acetyl-cysteine, L-cysteine and myo-inositol demonstrated beneficial effects on several metabolic parameters, including fasting insulin concentrations, HOMA-IR, triglycerides and total cholesterol levels, while increasing HDL concentrations (Genazzani et al., 2020, 2025). Several authors have proposed that this differential response may be partially explained by impaired hepatic insulin extraction, which is increasingly recognized as an important contributor to compensatory hyperinsulinaemia in obese women with PMOS (Genazzani et al., 2020; Placidi et al., 2022).

Moreover, treatment with pioglitazone was associated with significant increases in circulating free carnitine, propionyl-carnitine and total carnitine concentrations after 16 weeks of therapy (Vigerust et al., 2012). Additional evidence comes from studies evaluating ALC as part of combination insulin-sensitizing regimens. In women with PMOS treated with metformin and pioglitazone, the addition of ALC for 3 months was associated with a significant increase in circulating adiponectin concentrations, a hormone typically reduced in PMOS and linked to metabolic syndrome risk (Tauqir et al., 2021). However, given the concomitant administration of multiple insulin-sensitizing agents, the specific contribution of LC to the observed effects remains difficult to determine.

5.3. Limitations of current evidence

The current evidence regarding the use of carnitines in PMOS is limited by several important methodological shortcomings. Most randomized clinical trials enrolled relatively small study populations, frequently comprising fewer than 100 participants, which substantially limits statistical power and generalizability of the findings (Gong et al., 2023; Sangouni et al., 2022; Sheida et al., 2021). Considerable heterogeneity exists across studies with respect to patient characteristics, including BMI, degree of insulin resistance, hyperandrogenic phenotype and infertility status, making direct comparisons difficult (Liao et al., 2022).

Additional variability arises from differences in intervention protocols, including the type of carnitine formulation administered (LC, ALC or PLC), dosage, treatment duration and the frequent use of combination nutraceutical regimens involving chromium, myo-inositol, N-acetyl-cysteine or L-arginine (Genazzani et al., 2020, 2025; Jamilian et al., 2019, 2020). Consequently, the independent contribution of carnitines to the observed clinical effects often cannot be reliably determined. Furthermore, several studies combined carnitine supplementation with pharmacological agents such as metformin or pioglitazone, introducing additional confounding factors (Tauqir et al., 2021; Vigerust et al., 2012).

Finally, a substantial proportion of the mechanistic evidence supporting the use of carnitines originates from animal experiments and in vitro studies, particularly those investigating oxidative stress, glycativ pathways and mitochondrial function within the ovarian microenvironment (De Rubeis et al., 2024; Kalhori et al., 2019; Palmerini et al., 2023). While these findings provide important biological plausibility, their translation into clinically meaningful outcomes in women with PMOS remains insufficiently established.

6. Discussion

The growing interest in L-carnitine supplementation in PMOS reflects the increasing recognition of the multifactorial nature of this syndrome and the need for therapeutic strategies targeting not only reproductive abnormalities but also metabolic dysfunction and chronic low-grade inflammation. Unlike conventional pharmacological approaches that predominantly address single aspects of the disease, carnitines appear to act at multiple levels simultaneously, including mitochondrial bioenergetics, oxidative stress, insulin sensitivity and endocrine regulation (Liao et al., 2022; Zhang et al., 2025).

The available evidence suggests that the most clinically relevant effects of carnitines may occur in metabolically impaired phenotypes, particularly in overweight, obese and hyperinsulinaemic women. This observation is biologically plausible given the close relationship between mitochondrial dysfunction, impaired fatty acid oxidation and insulin resistance in PMOS. Improvements in glucose homeostasis and insulin sensitivity may subsequently contribute to partial normalization of ovarian function and androgen excess, although the extent to which these endocrine effects result directly from carnitine activity remains uncertain (Maleki et al., 2019; Shukri et al., 2022).

An important emerging concept is that the therapeutic efficacy of carnitines may depend not only on dosage but also on the specific formulation used. Increasing evidence suggests that ALC and PLC possess distinct pharmacokinetic properties and tissue-specific activities that may translate into different clinical outcomes (Di Emidio et al., 2020). Similarly, several studies indicate that carnitines may exert synergistic effects when administered alongside other nutraceuticals or insulin-sensitizing agents. However, the widespread use of combination regimens considerably complicates interpretation of the available data and limits the ability to identify the independent contribution of individual compounds (Genazzani et al., 2020, 2025).

7. Conclusions

L-carnitine and its derivatives represent promising adjunctive agents in the management of PMOS due to their pleiotropic effects on mitochondrial function, oxidative stress, insulin sensitivity and metabolic homeostasis. Despite encouraging mechanistic and clinical findings, current evidence remains insufficient to support routine recommendation of carnitine supplementation as a standard component of PMOS management. Therefore, at present, carnitines should be considered a promising adjunctive strategy rather than a replacement for established lifestyle and pharmacological interventions.

Future research should focus on large, adequately powered randomized trials using standardized carnitine formulations, clearly defined dosages and clinically relevant endpoints. Particular attention should be paid to identifying patient subgroups most likely to benefit from supplementation. Improved understanding of these issues may facilitate the integration of carnitines into personalized therapeutic approaches for women with PMOS.

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