Chapter

Optimizing Nutrition for PCOS Management: A Comprehensive Guide

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Abstract

This chapter aims to provide a comprehensive guide to optimizing nutrition for the management of polycystic ovary syndrome (PCOS), a hormonal disorder affecting reproductive-aged women that are associated with various metabolic and reproductive complications. It explores the critical role of nutrition in PCOS management, focusing on evidence-based dietary strategies to alleviate symptoms, promote hormonal balance, and enhance overall health outcomes. Beginning with the pathophysiology of PCOS, the chapter highlights the impact of insulin resistance, inflammation, and hormonal imbalances on the condition. The chapter provides practical guidelines for optimizing macronutrient intake, including recommendations for carbohydrate quality, protein sources, and fat composition. Additionally, it explores the potential benefits of dietary supplements and herbal remedies in PCOS management. It addresses key lifestyle factors—physical activity, stress management, and adequate sleep—which synergistically enhance nutrition in optimizing PCOS management. This valuable resource is tailored for healthcare professionals, nutritionists, and individuals with PCOS seeking evidence-based guidance on effectively managing this complex condition through optimized nutrition.

Keywords: polycystic ovary syndrome, endocrine-metabolic disorder, nutrition in PCOS, dietary therapy, dietary supplements

1. Introduction

Polycystic ovary syndrome (PCOS) is an endocrine-metabolic disorder affecting women of reproductive age [1]. It is a heterogeneous endocrine condition characterized by elevated androgen levels and endocrine variation, menstrual irregularities, and anovulation and/or small cysts on one or both ovaries that severely impact the life of a woman [2–4]. PCOS, marked by enlarged ovaries and amenorrhea, was characterized in 1935 by Stein and Leventhal. Extensive research since then aims to understand its molecular mechanisms and improve management. PCOS involves a complex interplay of genetic and environmental factors [5]. PCOS, known for reproductive issues, also poses metabolic risks like obesity, diabetes, and cardiovascular diseases. It adversely affects mental health, reducing quality of life. Weight reduction through lifestyle changes is crucial for managing and improving the reproductive, metabolic,

and psychological aspects of PCOS. Thus, lifestyle changes should be the primary management approach for PCOS [6].

2. Polycystic ovarian (PCO) physiology

The ovarian follicles are functional units of the mammalian ovary, which are roughly spheroid cellular aggregations consisting of an oocyte (germ cell) surrounded by granulosa cells forming intercellular connections and further surrounded by theca cells [7, 8]. There are approximately 295,000 primordial follicles in the ovarian reserve per ovary of a female human child at birth [9, 10]. Follicular growth is coordinated, usually resulting in the selection of a single follicle for maturation and ovulation sequentially. Over time, the continual recruitment of more primordial follicles from this pool is a dynamic process. The regulation of the rate at which primordial follicles enter the growing pool has a crucial role in maintaining the ovarian reserve and safeguarding fertility. However, during PCOS, due to a potential dysregulation in the recruitment mechanism of primordial follicles for growth, a greater number of small antral follicles (2–9 mm in diameter) are formed than in the normal ovary. During a normal menstrual cycle, the luteinizing hormone (LH) response is limited to the dominant follicle, usually when it attains a diameter of around 10 mm. However, in individuals with PCOS, the LH response occurs unusually in smaller follicles. Consequently, a significant proportion of antral follicles undergo terminal differentiation before the appropriate time. As the antral follicles produce steroids (estrogen) and inhibin B, the presence of a large number of these follicles results in an increased production of a higher amount of steroids (estrogen) and inhibin B. They have negative feedback on the production of follicle-stimulating hormone (FSH). As FSH has a role in the maturation of the follicles and the release of the ovum, its imbalance leads to the arrest of follicular growth and the ovum is not released, creating a large number of cysts-like structures containing immature ovum [11–13]. PCOS is distinguished by an elevated count of follicles across all developmental stages, with a notable increase observed in the pre-antral and small antral follicles [14].

3. Pathophysiology of PCOS

PCOS is a complex endocrine disorder involving genetics, environment, obesity, ovarian dysfunction, and hormonal imbalances like elevated androgens and hyperinsulinemia. It disrupts the hypothalamic-pituitary-ovarian (HPO) axis and leads to symptoms of excess androgens and irregular ovulation [6, 15]. Hyperandrogenism, often characterized by elevated levels of unbound (free) testosterone in the blood, is the prevailing anomaly in this syndrome and plays a significant role in perpetuating the irregular hormonal factors contributing to the pathophysiology of PCOS. PCOS is complex, with disruptions in the menstrual cycle, hyperandrogenism, and obesity. Ovarian dysfunction is crucial to its pathophysiology, involving multiple factors and genes [16]. Here are some of the complications of PCOS:

3.1 Hyperandrogenism

Clinical and biochemical hyperandrogenism are major features of PCOS. Disruptions in hypothalamic-pituitary feedback, excessive LH secretion, premature

luteinization of granulosa cells, irregular oocyte maturation, and premature arrest of activated primary follicles are associated with persistent hyperandrogenism [15]. Excessive ovarian androgen production is the result of a combination of intrinsic ovarian factors, such as alterations in steroidogenesis, and external factors, such as hyperinsulinemia [15].

3.2 Polycystic ovaries, ovulatory dysfunction

A well-coordinated interaction of reproductive, metabolic, and intraovarian processes is necessary for ovulation. Follicle development is disrupted by ovarian hyperandrogenism, hyperinsulinemia due to insulin resistance (IR), and altered intraovarian paracrine signaling during PCOS. This disruption leads to follicular arrest, resulting in menstrual irregularities, anovulatory subfertility, and the accumulation of small antral follicles in the ovarian periphery, which imparts a polycystic morphology to the ovary [17].

3.3 Insulin resistance (IR), impaired lipid metabolism, obesity

Excessive levels of androgens influence where fat is stored in the body. The pattern of fat accumulation is altered in hyperandrogenic women with PCOS [18]. Testosterone promotes visceral fat accumulation and IR [19]. Hyperinsulinemia then further exacerbates androgen generation. The anabolic effect of hyperinsulinemia on fat metabolism via the adipogenesis process results in an elevated uptake of glucose into adipocytes and the subsequent production of triglycerides, contributing to obesity [20]. Central obesity is a distinctive feature of PCOS, as evidenced by an elevated waist-to-hip ratio in these patients compared to obese women without PCOS. Hyperinsulinemia may contribute to the development of central adiposity, further exacerbating underlying or latent IR [21].

4. Complications and symptoms

4.1 Menstrual abnormalities

Chronic anovulation often manifests as various forms of menstrual irregularities such as secondary amenorrhea, oligomenorrhea, and dysfunctional uterine bleeding [21]. In PCOS, irregular menstrual cycles begin at menarche or shortly after, often progressing to oligomenorrhea or amenorrhea. Menstrual dysfunction, marked by anovulation and unpredictable bleeding, correlates with IR severity. Longer cycles, beyond 3 months, indicate higher IR. Amenorrhea in PCOS exacerbates IR. Prolonged anovulation results in irregular bleeding resembling regular periods. Chronic anovulation, especially in obesity, leads to atypical endometrial thickening, a precursor to endometrial cancer [20].

4.2 Hirsutism, acne, and male pattern alopecia

Hirsutism, acne, and male pattern alopecia are manifestations of hyperandrogenism. Hirsutism, the growth of coarse pigmented hairs in androgen-dependent areas, including the face, chest, back, and lower abdomen, is driven by testosterone and dihydrotestosterone [20, 21].

Androgenic alopecia, a form of hair loss, is a less well-studied marker for androgen excess [16]. The balding pattern primarily affects the frontal and parietal scalp zones, with the occipital area maintaining a higher hair density [20].

In PCOS, acne is exacerbated because sebaceous glands, influenced by androgens, are sensitive structures that contribute to acne and seborrhoea intensified by sebaceous gland sensitivity [16, 20]. Androgens stimulate the proliferation of sebocytes and the secretion of sebum, which comprises lipids such as glycerides, squalene, free fatty acids (FFA), and cholesterol.

4.3 Dyslipidaemia

The majority of PCOS patients exhibit dyslipidaemia, driven by factors like insulin, estrogen, and androgens influencing lipoprotein lipid metabolism. Elevated hepatic lipase activity, stimulated by insulin, plays a role in lipid alterations. Hyperandrogenism is linked to adverse lipid profiles, particularly testosterone's negative impact on lipids. The typical lipid profile in PCOS features elevated low-density lipoprotein (LDL) cholesterol, increased very low-density lipoprotein (VLDL) cholesterol, higher triglycerides, and reduced high-density lipoprotein (HDL) cholesterol. These lipid issues worsen in PCOS women with glucose intolerance [20].

4.4 Non-alcoholic fatty liver disease (NFALD)

Common pathophysiological factors linking NAFLD and PCOS include obesity and IR. Elevated liver enzymes and IR are associated with both conditions. NAFLD worsens IR, aggravating it in PCOS. Conversely, IR leads to lipolysis, increasing hepatic fat accumulation and collagen production. Hyperandrogenism is linked to IR and affects NAFLD independently of it. Hyperandrogenic women with PCOS tend to have a higher liver fat [22].

4.5 Chronic inflammation, endothelial function, and atherosclerosis

Chronic inflammation, endothelial dysfunction, and atherosclerosis are key considerations in understanding cardiovascular implications of PCOS. Endothelial injury is an early indication of cardiovascular issues. Testosterone levels in hyperandrogenic insulin-resistant women correlate with abnormal endothelial function. Mechanisms include reduced nitric oxide synthesis, enhanced inactivation, increased vasoconstrictor synthesis, and insulin's direct effects. Obesity exacerbates endothelial dysfunction and reduced adiponectin in PCOS further contributes. PCOS, a proinflammatory state, links chronic inflammation to metabolic and ovarian dysfunction. Elevated C-reactive protein promotes atherosclerosis and endothelial cell inflammation, raising cardiovascular risk [20].

4.6 Gestational diabetes mellitus (GDM) and diabetes mellitus (DM)

In a typical pregnancy, maternal carbohydrate metabolism changes, including pancreatic β-cell hyperplasia and increased insulin sensitivity, followed by the development of insulin resistance (IR). Women with PCOS, already predisposed to IR, face a higher risk of gestational diabetes mellitus (GDM) due to these changes. The pathophysiology involves IR and abnormalities in β-cell glucose sensitivity, resulting in inadequate insulin response. Pregnancy-related IR, combined with pre-existing IR in

PCOS, heightens the risk. PCOS women with GDM also face an increased likelihood of impaired glucose tolerance post-delivery. Their heightened risk of progressing to impaired glucose metabolism and type II diabetes (T2D) is influenced by a prevalent family history of T2D. Diabetes may contribute more significantly to mortality rates in PCOS women compared to the general population [20].

4.7 Infertility and recurrent pregnancy loss (RPL)

PCOS often leads to anovulatory infertility, but some women with PCOS can conceive, though with longer conception times. In cases of infertility, overweight is common among PCOS-affected women. RPL occurs in PCOS, with uncertain reasons like uterine dysfunction, disrupted cell-embryo interaction, or insulin-related factors. PCOS mainly affects fertility through oligo-ovulation or anovulation. High LH concentrations during the follicular phase can reduce conception rates and cause early pregnancy loss. LH hypersecretion in PCOS may trigger premature oocyte maturation and impact folliculogenesis, leading to endometrial receptivity issues. Hyperinsulinemia in PCOS might hinder preimplantation conditions and affect embryo-endometrial interaction, contributing to pregnancy loss [20, 21].

5. Etiology, causes and associated factors

PCOS is a complex polygenic disorder resulting from the interplay of various genetic, environmental, and intrauterine influences, with an estimated heritability of about 70% [13, 23]. Several susceptible genes have been identified as contributors to the pathophysiology of the. Additionally, the environment plays a major role in the expression of these genes and the development and progression of the disease. The most common environmental factors include obesity and IR [24–27]. Some factors that can lead to PCOS are:

5.1 Heredity and genetic linkages

PCOS often runs in families, showing a dominant trait inheritance pattern. Twin studies highlight family factors in PCOS. Maternal PCOS, PCOM (polycystic ovarian morphology), hyperandrogenaemia, and metabolic syndrome are heritable risk factors. Daughters of PCOS women exhibit elevated AMH in infancy, larger ovaries, and increased insulin responses in childhood. Post-menarche, they may have higher testosterone. PCOM tends to follow an inherited pattern, with sisters having a higher risk of PCOM, hirsutism, and irregular periods. Parental factors and defective insulin secretion contribute, leading to increased adiposity, abnormal glucose tolerance, and diabetes in relatives. Gene variants are associated with PCOS [28].

5.2 Intrauterine environment

There is growing evidence that developmental exposure to a distorted environment can induce enduring alterations in the epigenome. These modifications subsequently contribute to altered gene expression and an elevated susceptibility to adult-onset diseases. Factors such as congenital virilization and intrauterine nutrition have been recognized as potential contributors to the risk of developing PCOS [28].

5.3 Postnatal environment

Postnatal environmental factors can trigger latent, congenitally programmed susceptibility traits to surface as PCOS symptoms. Key factors include:

Insulin resistance: PCOS is linked to extreme IR, with high insulin levels contributing to anovulation. Weight loss and improved insulin sensitivity enhance ovulation and menstrual cyclicity [28].

Hyperandrogenism: postnatal androgen excess, observed in some animal models and conditions like congenital adrenal virilizing disorders, contributes to ovarian hyperandrogenism [28].

Obesity: obesity, independently and by exacerbating PCOS, increases reproductive features—hyperandrogenism, hirsutism, infertility and pregnancy complications. Additionally, obesity amplifies the risk factors associated with PCOS, such as impaired glucose tolerance, T2D, and cardiovascular disease (CVD) [29].

6. Nutrition in PCOS

Some evolutionary biologists posit that numerous genetic and hormonal predispositions contributing to PCOS may have originated during the transition from a pre-agrarian age diet to a contemporary diet. This hypothesis is substantiated by the concurrent increase in rates of diabetes, heart disease, and PCOS, aligning with the swift changes in the modern human diet. For all women diagnosed with PCOS, the inclusion of dietary therapy and regular exercise offers noteworthy benefits. Indeed, dietary and lifestyle interventions are regarded as primary strategies for managing PCOS. While there is not a specific "PCOS diet" that can completely reverse the syndrome, several dietary principles should be followed to ameliorate its symptoms [30].

A growing body of evidence indicates that various dietary strategies might yield positive effects on PCOS features, even without resulting in weight loss. Here, the impact of different nutrients and other dietary modifications according to diet strategies will be discussed.

6.1 Different nutrients in PCOS

6.1.1 Dietary carbohydrates

There is no optimum amount of carbohydrate intake for women with PCOS, and, therefore, any range (about 40–55%) of dietary carbohydrates can be adopted, according to the individuals' dietary assessment, metabolic goals, dietary habits and preferences. However, a beneficial strategy might involve consuming a larger portion of carbohydrates during lunchtime. Another appropriate approach would be to evenly spread carbohydrates across meals throughout the day. It would be better to avoid having a high-carbohydrate breakfast. While limited, studies have been done incorporating low-glycaemic index (GI) foods that might offer slight additional benefits for certain PCOS outcomes [31].

6.1.2 Protein

Studies have found a diet higher in protein may yield several positive health outcomes, including increased weight loss, preservation of lean mass during weight

loss and maintenance, improved glycaemic control, and mitigation of other CVD risk factors such as blood pressure. However, it remains unclear whether these effects are primarily attributable to the higher protein intake or a reduction in carbohydrate intake. Some factors like increased thermogenesis and enhanced satiety have been proposed. Adding 7–15 g of dietary protein to meals and snacks might offer health benefits for women with PCOS, particularly regarding insulin sensitivity and post-prandial glucose levels [31].

6.1.3 Fat

It has been found that low-fat hypocaloric diets can help reduce body weight and composition compared to high-fat hypocaloric diets. Moderately low-carbohydrate, high-fat diets can help to decrease fasting insulin, increase insulin sensitivity, and improve metabolic parameters in women with PCOS. Furthermore, a diet moderately low in carbohydrates (43%) but rich in unsaturated fatty acids may lead to a significant decline in fasting insulin levels A diet rich in fat and moderately limited in carbohydrates (~41% carbohydrate, 19% protein, 40% fat) may significantly reduce in basal β-cell response, fasting insulin, fasting glucose, and IR and decrease testosterone levels, in conjunction with declines in blood lipid levels and adipose tissue mass [31].

6.1.4 Micronutrients

Women with PCOS often have imbalanced diets with deficiencies in essential nutrients such as fiber, Ω-3 fatty acids, calcium, magnesium, zinc, and vitamins (folic acid, vitamin C, vitamin B12, and vitamin D). There is also an excess intake of certain nutrients like sucrose, sodium, total fats, saturated fatty acids, and cholesterol. Balancing deficiencies with a calorie-reduced diet with a low GI can positively influence water-soluble vitamins [32]. While most B vitamins respond well to increased dietary supply, a study has shown that such an effect may not be observed for vitamins B_3, B_2 and thiamine [33]. Women with PCOS are treated with metformin, but its chronic intake may lead to deficiencies in thiamine and cobalamin [34]. So, these vitamin supplementations may be necessary.

Micronutrients like selenium, chromium, zinc, carotenoids, and vitamin E can have potential benefits in the metabolic condition of PCOS patients and deficiency in these nutrients might contribute to the exacerbation of metabolic disturbances in PCOS patients with metabolic syndromes [35]. Supplementation of micronutrients like zinc, selenium, chromium, and folate may positively impact fasting glucose, insulin, IR, blood lipid levels, and inflammatory and oxidative stress biomarkers in PCOS individuals. Despite potential benefits, recommending micronutrient supplements for PCOS management is considered premature based on current evidence [31, 36]. Thus, the consumption of micronutrient-rich foods on a daily basis becomes important.

6.2 Dietary strategies

6.2.1 Negative energy balance and weight reduction

Calorie restriction diets (1000–1500 kcal/day) can help in weight loss and improvements in hirsutism, IR, and androgen levels [37]. Modest weight loss (5–10%) in PCOS shows positive impacts on cardiovascular and diabetes risk, hormone levels, and PCOS outcomes. Weight reduction yields improved insulin sensitivity and lipid

profiles, alleviating hyperandrogenism, increased Sex hormone Binding Globulin (SHBG), reduced Free Androgen Index (FAI) and testosterone, and normalizing menstrual cycles. Weight loss benefits overweight PCOS women by reducing IR and hyperandrogenism and enhancing ovarian health, menstrual function, and ovulation. Effects on LH vary, while hirsutism may improve. The extent of the caloric deficit should be tailored to individual needs, including dietary preferences, habits, cultural factors, metabolic objectives, and physical activity levels [31].

6.2.2 Glycaemic index and glycaemic load

From different studies, it has been found that low-GI diets are helpful for successful weight loss, increase insulin sensitivity, and reduce IR, fasting insulin, LDL cholesterol, triglycerides, waist circumference, total testosterone and maintaining menstrual regularity when compared to high GI diets. A low to medium glycaemic load (GL) diet containing high-protein, moderately low-carb can also be helpful for improvement in IR, and inflammation markers. Low-GI foods, however, have similar effects as conventional diets on fasting glucose, HDL cholesterol, free androgen, inflammation, and quality of life [31, 32].

6.2.3 Meal frequency

Meal frequency and timing are important considerations in lifestyle changes for PCOS management, although there is limited specific data for women with PCOS. There are contrasting viewpoints on the effects of meal frequency on body composition and glycaemic control. Some argue that frequent meals might lead to weight gain due to increased fat deposition after meals or higher energy intake. Others suggest that increased meal frequency could spread nutrient load, leading to lower postprandial insulin levels, reduced hunger, and improved glucose clearance. In a study, a six-meal pattern showed improved post-oral glucose tolerance test insulin sensitivity and reduced subjective hunger in women with PCOS compared to a three-meal pattern. Another study showed that consuming a high-energy breakfast instead of a high-energy dinner improved insulin sensitivity and reproductive markers in lean women with PCOS. Meal timing has also gained attention. Eating late in the day has been linked to decreased energy expenditure, impaired glucose tolerance, and disrupted circadian rhythms. People with prediabetes who prefer evening meals might have a higher risk of developing T2D. The American Heart Association suggests that meal frequency and timing could be crucial in managing chronic diseases and reducing cardiometabolic risk factors [31].

6.2.4 Dietary modification

Multiple dietary compositions show promise in treating obesity and its associated conditions in PCOS [29]. Implementing low-GI diets, exercise, and omega-3 supplementation leads to increased HDL, SHBG synthesis, and reduced body fat. Studies support the efficacy and safety of the low-GI diet in relieving IR, and proper professional dietary advice should be provided for PCOS patients [32].

The DASH diet, which is low-GI and high in complex carbohydrates, demonstrated positive effects on weight loss, insulin metabolism, and inflammation markers in women with PCOS. Adherence to the DASH diet led to significant reductions in body weight, insulin levels, IR, high-sensitivity C-reactive protein, and triglycerides,

encouraging healthy dietary patterns like DASH or Mediterranean-style diets, rich in fiber, antioxidants, and anti-inflammatory nutrients, could be beneficial for women with PCOS due to their satiety, anti-hyperlipidaemic, antihypertensive, and anti-diabetic properties [31].

Low-carbohydrate diets (<30% of energy) contribute to weight loss and metabolic enhancements. Specifically, long-term low-carb diets, including low-fat/low-carb variations, are recommended to reduce BMI, address PCOS with IR, prevent high LDL-C, increase FSH and SHBG levels, and decrease total testosterone. Controlled carbohydrate intake positively affects PCOS aspects, presenting a significant intervention for symptom improvement [37, 38]. Studies suggest that a high-protein, low-carb diet may aid weight loss and improve metabolic and reproductive parameters in PCOS. Carbohydrate restriction, especially with a low glycaemic index (GI), is proposed for satiety and cardiovascular health, though sustaining long-term adherence proves challenging (**Table 1**) [29].

6.3 Dietary supplements in PCOS management

6.3.1 Omega-3 fatty acids

Omega-3 fatty acids, often lacking in PCOS diets, enhance reproductive performance by affecting hormone secretion and ovarian functions [32]. Omega-3 fatty acids, specifically EPA and DHA, offer various positive effects, such as antioxidant, anti-inflammatory, anti-obesity, and insulin-sensitizing properties. They enhance insulin sensitivity by reducing inflammatory cytokines and boosting anti-inflammatory adiponectin secretion in PCOS women, which is evident through decreased

1. Adjust according to standard levels for sex, age, and activity. Implement a 500–1000 kcal/day reduction for effective weight loss (7–10% over 6–12 months).
2. For nutritionally complete dietary patterns include:
   - Low-fat dairy (two to three servings/day)
   - Whole-grain/low-GI bread and cereals (at least three servings/day)
   - Fruit (at least two servings/day)
   - Vegetables (at least two cups/day)
   - Lean meat, chicken, fish (one to two serves/day)
   - Low-saturated fat fats/oils (three to four teaspoons or nuts/seeds)
3. Maintain <10% of calories from saturated fat.
4. Increase consumption of fiber, whole-grain bread, cereals, and fruits/vegetables.
5. Increasing dietary protein or unrefined carbohydrates equally improves reproductive and metabolic parameters.
6. Reduce refined carbohydrates, favoring complex carbohydrates.
7. Include low glycaemic index foods in the diet.
8. Increase fiber Intake to enhance glucose regulation.
9. Emphasize high-protein foods, particularly at breakfast, for greater fullness, increased satiety, and reduced ghrelin concentrations.
10. Maintain a regular eating pattern for optimal results.

Table 1.
Dietary recommendations for PCOS [39].

high-sensitivity C-reactive protein and increased adiponectin levels. However, the impact of omega-3 supplementation on PCOS remains debated, with mixed study results on waist circumference, lipid profiles, and menstrual regularity. Studies indicate that n-3 PUFA supplementation may reduce total testosterone levels, while further research is required to explore the potential antiandrogenic effects of long-chain n-3 PUFAs, including EPA and DHA [31].

6.3.2 Vitamin D

The complex interplay between vitamin D and Polycystic Ovary Syndrome (PCOS) reveals significant implications. Vitamin D deficiency, prevalent in PCOS, is closely tied to symptoms such as central obesity, IR, infertility, and hirsutism. Functioning as a steroid hormone with progesterone-like activity, vitamin D is pivotal in insulin synthesis, receptor expression, and glucose transport, normalizing calcium and parathyroid levels [31, 32, 40–42].

Supplementation studies suggest potential relief for PCOS symptoms, with observed reductions in total testosterone levels. Combining calcium and vitamin D enhances insulin levels, reduces resistance, and improves lipid profiles. A combination of metformin, calcium, and vitamin D exhibits positive impacts on weight loss, menstrual regularity, and hyperandrogenism in PCOS-associated infertility, with a noteworthy dose of 20,000 IU cholecalciferol weekly showcasing improvements in carbohydrate metabolism and menstrual frequency [31, 32, 41–43].

6.3.3 Zinc

Zinc is crucial for corpus luteum formation, supporting progesterone production essential for implantation [44]. Studies link zinc supplementation to elevated progesterone, while deficiency inhibits LH and estrogen, impacting luteal function [45–48]. Zinc supplementation is linked to enhanced lipid and glucose metabolism [32]. In an 8-week trial among PCOS women, zinc supplementation (50 mg elemental zinc/day) increased serum zinc and reduced IR, total cholesterol, LDL-C, triglycerides, testosterone, and TG/HDL-C ratio [49]. A study among PCOS subjects revealed that twice-daily co-supplementation of 250 mg magnesium oxide and 220 mg zinc sulphate (50 mg elemental zinc) notably decreased inflammation and oxidative stress markers [50]. These findings suggest potential benefits of at least 50 mg zinc/day for 8 weeks in PCOS management.

6.3.4 Selenium

As an antioxidant, selenium intake in PCOS may offer benefits by reducing oxidative stress along with IR, and hyperandrogenism, with its levels correlating with estrogen changes during the menstrual cycle [32, 51–57].

A rat model suggests that combined selenium nanoparticles and metformin therapy improve insulin sensitivity, lipid profile, inflammation, oxidative stress, and mitochondrial functions [51]. In different randomized trials, 200 μg daily selenium supplementation for 8–12 weeks in PCOS women showed improved pregnancy rates, reduced alopecia, acne, and lowered inflammatory markers [52–54]. Hence, a daily dose of 200 μg selenium for at least 8 weeks may benefit individuals with PCOS, suggesting potential advantages for hormonal and metabolic aspects, but it warrants further exploration.

6.3.5 Vitamin C

Vitamin C exhibits antioxidant properties and is involved in ovarian regulation and endometrial health. Vitamin C levels modulate throughout the menstrual cycle, affecting ovulation and progesterone production. Vitamin C levels decline immediately before ovulation and increase again after post-ovulation temperature rises. Ascorbic acid stimulates progesterone and oxytocin production. Vitamin C may play a role in regulating menstrual cycle irregularities in PCOS women, but further research is needed [40].

6.3.6 Vitamin E

Vitamin E, a crucial antioxidant, shows potential in counteracting reproductive system oxidative stress, impacting oocyte quality and countering pregnancy-related diseases [58]. It might positively affect endometrial thickness and overall ovarian function. Vitamin E supplementation, combined with coenzyme Q10, can increase SHBG levels and reduce free plasma testosterone concentrations in PCOS patients [40].

In a clinical trial with PCOS women, a 100 mg/day short-term vitamin E supplementation demonstrated the potential to diminish oxidative stress, resulting in reduced markers. Vitamin E can reduce oxidative stress, consequently reducing the exogenous human menopausal gonadotropin (HMG) dosage. The study revealed improved endometrial thickness and estrogen levels. However, this supplementation had no significant impact on pregnancy rates, regardless of initiation in the follicular or luteal phase [40, 58].

6.3.7 Inositol

Inositol represents a cyclic carbohydrate with six hydroxyl groups, one on each of the ring carbons. Nine stereoisomers of inositol exist, with myo-inositol (MI) and D-chiro-inositol (DCI) being the two primary stereoisomers found in the human body [40, 59, 60].

In the ovary, DCI plays a role in insulin-driven testosterone production, whereas MI is involved in FSH signaling. The insulin-dependent epimerase activity controls the ratio of MI to DCI, and it is noteworthy that ovaries do not develop IR, unlike muscles and the liver. This suggests that in PCOS, there could be an increased conversion of MI to DCI within the ovary due to insulin overproduction, resulting in excessive DCI levels and MI deficiency, disrupting hormonal balance [61].

6.3.8 Berberine

Berberine is a quaternary ammonium salt found in various medicinal plants like *Berberis and Hydrastis canadensis.* It belongs to the protoberberine group of isoquinoline alkaloids [62, 63]. Among PCOS patients, berberine positively impacts lipid profile, enhances insulin sensitivity, and increases ovulation rates, promoting fertility. It is considered safe for premenopausal women with minimal side effects [64]. It is efficient against IR and obesity, particularly targeting visceral adipose tissue [64], and if associated with a healthy lifestyle, improves women's body composition and causes androgen reduction [65]. Berberine may benefit PCOS management by improving metabolic, hormonal, and anthropometric parameters.

6.3.9 Polyphenols

Polyphenols, diverse secondary plant metabolites, are polyhydroxyphenols with multiple phenolic rings, often conjugated with sugars lacking nitrogen-based functional groups. Derived from shikimate and acetate pathways, they include phenolic acids, stilbenes, flavonoids, and lignans [66–68].

Resveratrol, a polyphenol found in grapes and berries, has anti-inflammatory and antioxidant properties. Initially considered for infertility treatment, caution is urged during pregnancy and the luteal phase due to potential adverse effects. Despite limitations, resveratrol inhibits proinflammatory cytokines, emphasizing the need for further PCOS research [40]. Various clinical trials using 800–1500 mg/day of resveratrol at least 40 days to 3 months have demonstrated positive effects on ovarian morphology, dominant follicle incidence, and androgen levels, anti-inflammatory effects and ER stress modulation, improved menstrual cyclicity and reduced hair loss in PCOS women [69–72]. Thus, resveratrol supplementation among PCOS women at doses up to 1500 mg/day for at least 40 days can be beneficial.

Naringenin, a key flavonoid in human diets, imparts color and a bitter-sour taste to foods. Found in grapefruit, sour orange, cherries, tomatoes, citrus fruits, and Greek oregano, it is also present in smaller amounts in bergamot, beans, fenugreek, milk thistle, tea, coffee, cocoa, and red wine naringenin's potential in PCOS treatment involves the AKT pathway, steroidogenesis, and gut microbiota modulation [73–75]. This indicates the supplementation of naringenin among PCOS women may be beneficial, but further study is required.

Quercetin, a flavonoid in fruits and vegetables, demonstrated therapeutic effects in PCOS treatment [76]. Administered at varying doses (15–150 mg/kg) for 3–10 weeks in rat models, it alleviated obesity, diabetes, and infertility. Quercetin enhanced antioxidants, reduced weight gain, normalized hormone levels, and inhibited PI3 kinase, showcasing multifaceted benefits in PCOS management [77–79]. A 40-day study with 500 mg quercetin supplementation among women daily reduced LH, TNF-alpha, and IL-6 levels, improved oocyte and embryo grades and increased pregnancy rates [80]. Thus, at least 500 mg/day supplementation of quercetin can be beneficial.

Individualized approach: supplementation needs vary among individuals, requiring consultation and active participation for optimal outcomes. A balanced diet and healthy lifestyle remain fundamental in PCOS therapy.

6.4 Herbs supporting treatment for PCOS

A balanced diet is vital in managing PCOS, and herbal extracts like Aloe vera, cinnamon, green tea, chamomile, and white mulberry complement this therapy. Certain herbs can influence lipid profiles, blood glucose, and IR, benefiting all PCOS phenotypes. Some herbs, such as green tea and marjoram, possess endocrine properties, improving hormonal levels, ovarian health, insulin sensitivity, and reducing inflammation. Green mint and liquorice root are recommended for women with elevated androgen levels. They have antiandrogen effects and reduce excess testosterone. Flaxseed lignans, turmeric, nettle, milk thistle, artichoke, dandelion, and black cumin offer various therapeutic benefits for PCOS, including antioxidant, anti-inflammatory, and hepatoprotective properties [32].

6.4.1 Flaxseed

Flaxseed, a nutrient-rich seed encompasses omega-3 fatty acids, lignans, fiber, niacin, vitamin E (39.5–50 mg/100 g), minerals, proteins, and peptides. With 37–45% lipid content, it is a prime omega-3 source. Rich in lignans and phenolic compounds, it offers diverse health benefits, including cardiovascular and anti-inflammatory effects [81, 82]. Flaxseed lignans stand out as well-studied dietary phytoestrogens. They can influence key enzymes involved in estrogen synthesis, shaping sex hormone levels [32]. A 4-month study on PCOS, patients taking 30 g/day of flaxseed exhibited reduced BMI, testosterone, insulin levels, and hirsutism [83]. In a 12-week study on women with PCOS, twice-daily supplementation of flaxseed oil omega-3 fatty acids (1000 mg capsule) significantly improved insulin levels, IR, hirsutism, triglycerides, VLDL-cholesterol, and CRP levels, demonstrating positive effects on insulin metabolism and specific metabolic markers [84]. Thus flaxseed (at least 20 g/day) or flaxseed oil flaxseed oil omega-3 fatty acids (1000 mg) for a minimum of 3 months can be beneficial for PCOS women.

6.4.2 Curcumin

Curcumin, found in turmeric, possesses strong antioxidant properties, reducing oxidative stress in PCOS patients. It also modulates proangiogenic and proinflammatory factors, suggesting potential pharmacologic benefits for PCOS [32, 85]. Turmeric extract exhibits promising effects in treating PCOS in albino rats, showing improvements in hormone and lipid profiles, antioxidant and glycaemic status, and ovarian morphology compared to metformin [85]. Additionally, in a mouse model, curcumin protects granulosa cells from apoptosis in PCOS rats by inhibiting the ER stress-related IRE1α-XBP1 pathway and activating the PI3K/AKT signaling pathway, suggesting its potential as a beneficial supplement for PCOS patients [86].

In a 12-week double-blind trial, curcumin intake (500 mg thrice daily) by women with PCOS demonstrated significant reductions in blood sugar and dehydroepiandrosterone, along with a potential increase in oestradiol [87]. Similarly, another study for 12 weeks found intake of 500 mg of curcumin per day can have beneficial effects on body weight, glycaemic control, and serum lipids except triglycerides and VLDL-cholesterol levels [88]. Most of the clinical trials using curcumin extract have used about 500–1500 mg of curcumin per day for 6–12 weeks has shown beneficial effects on PCOS patients [87–89].

6.4.3 Cinnamon

Cinnamon, valued for its fragrance, has diverse uses. Its essential oil, containing cinnamaldehyde, and the bark, with antioxidants like procyanidins, provide various biological benefits. The bark, rich in cinnamaldehyde, eugenol, and linalool, plays a significant role in its effects. With an abundance of phytochemicals, cinnamon exhibits potential health benefits, including anti-inflammatory, antimicrobial, antioxidant, and cardioprotective effects [90, 91].

A study done in mice found cinnamon (10 mg/100 g body weight) could restore oestrous cyclicity, normalize hormone levels, and improve ovarian morphology [92]. A 12-week study among women with PCOS using cinnamon powder capsules (1.5 g/day in three doses) showed significant reductions in fasting insulin and IR, with a decrease in low-density lipoprotein levels [93]. Thus, about 1.5 g of cinnamon powder consumption can be beneficial for PCOS women.

7. Lifestyle in PCOS management

7.1 Exercise and physical activity in PCOS management

Exercise offers metabolic benefits beyond weight management, particularly relevant to PCOS-related risk factors like hypertension, IR, elevated blood glucose, and endothelial dysfunction. Research demonstrates that increased physical activity and fitness, regardless of weight loss, can ameliorate these factors. Endurance training has been shown to reduce IR and improve metabolic profiles in overweight PCOS women. Combining aerobic and resistance training proves effective in reducing IR and body fat, and resistance training maintains basal metabolic rate and enhances muscle strength, facilitating regular physical activity [29].

Exercise reduces IR by two mechanisms as below [30]:

- Induces a reduction in visceral fat even if there is moderate weight loss and BMI reduction.

- Increases muscle cell metabolism: Exercise modulates the expression or the activity of proteins mediating insulin signaling in the skeletal muscles.

It has been shown that exercise improves menstrual abnormalities and restores ovulation in obese patients with PCOS, and its benefit on reproductive function is greater than the benefit of a low-calorie diet only. Exercise exerts its beneficial effects on body composition with greater reduction in fat mass and better preservation of fat-free mass [30]. Collectively, the evidence underscores the health advantages of exercise, both for weight management and metabolic well-being in PCOS and beyond [29].

Exercise is increasingly recognized as a vital element in managing PCOS, enhancing insulin sensitivity through optimized glucose transport and metabolism. Recent research emphasizes the importance of exercise intensity for health improvements. Meta-analysis and systematic reviews highlight the significant impact of vigorous intensity exercise on factors like cardiorespiratory fitness, IR, and body composition. Studies using metrics like HOMA-IR and BMI show substantial decreases in IR, supporting the benefits of physical activity. Engaging in a minimum of 120 minutes of aerobic activity per week is recommended for optimal results in managing PCOS-related concerns [32].

Public health recommendations advise overweight and obese individuals, including those with PCOS, to gradually increase physical activity to 200–300 minutes per week of moderate exercise, like brisk walking, to prevent unhealthy weight regain and promote long-term weight maintenance. This evidence highlights the importance of incorporating adequate physical activity into PCOS weight management programmes [29]. At the moment, there are no guidelines for the type, intensity, frequency, and duration of exercise in patients with PCOS, but physical activities as of a normal adult should performed regularly as below [30]:

- *Moderate-intensity aerobic physical activity* (e.g., brisk walking) for at least 30 min and for at least 5 days per week should be recommended in all PCOS patients.

- *Vigorous-intensity aerobic activity* (e.g., jogging) for at least 20 min and for at least 3 days per week or combinations of moderate- and vigorous-intensity exercise can also be recommended.

- *Resistance training* for at least two non-consecutive days per week.

- *Endurance exercise* for patients who cannot manage high-intensity exercise, prolonged lower-level activity is an appropriate way to gain fitness and increase energy expenditure (**Table 2**).

7.2 Lifestyle modification

Lifestyle intervention (diet and physical activity) leading to a 5–10% weight loss has shown significant improvements in IR, ovulation, menstrual regularity, and other PCOS symptoms. Women with PCOS adopt both healthy and non-healthy practices for weight management. Despite its benefits, many PCOS patients do not receive lifestyle advice from healthcare providers. Lifestyle programmes combine diet, exercise, and cognitive strategies. They have been effective in preventing diabetes and improving PCOS-related factors like weight, hormones, and metabolic issues. Studies support their impact on BMI, blood glucose, and hormonal balance. While positive effects are seen, clinical reproductive outcomes and quality of life need further study. Combining lifestyle changes with treatments like metformin can enhance results. In overweight PCOS women, lifestyle changes led to better menstrual regularity and insulin sensitivity. Lifestyle interventions should be the primary approach for PCOS management, but maintaining healthy habits long-term remains a challenge. A team-based approach could offer better results for comprehensive PCOS care [31].

1. Support from health professional, family, spouse, peers is necessary for lifestyle modification.
2. Prioritize smoking cessation and reduce alcohol consumption.
3. Weight loss/maintenance and lifestyle modification programmes should be well structured and individualized according to health professionals' advice.
4. Summary of the main components of exercise prescription based on *FITT*:
   - *Frequency*: engage in physical activity 3–5 days per week, emphasizing the establishment of a consistent exercise routine before advancing frequency.
   - *Intensity*: initiate with low to moderate intensity, gradually increasing over weeks, prioritizing duration for optimal energy expenditure, emphasizing prolonged activity over intensity.
   - *Time*: 30–60 min, using a gradual progression (can be accumulated in multiple short bouts of at least 10 min that may promote greater adherence).
   - *Type*: choose low-impact activities such as walking, cycling, or low-impact aerobics, ensuring convenience and enjoyment.
5. *Resistance training*: should be performed two to three times per week, with one set of 8–15 repetitions at a moderate intensity, using 8–10 different exercises that work each of the major muscle groups.
6. *Warm-up and cool-down*: emphasize appropriate warm-up and cool-down periods to enhance safety and flexibility.
7. *Daily lifestyle activities*: emphasize reducing sedentary behaviors and time spent being physically inactive. Increase participation in daily lifestyle activities such as stair climbing, walking during breaks, climbing stairs whenever possible, and house cleaning.

Adapted from: Refs. [30, 39].

Table 2.
Exercise and lifestyle modification guidelines.

Exercise is a vital component of successful lifestyle modifications for weight management in PCOS. Studies show that physical activity is associated with sustained weight loss and that combining exercise with diet enhances weight reduction compared to diet alone. Research suggests that highly active individuals have the greatest success in maintaining weight loss [29].

Lifestyle adjustments play a crucial role in managing PCOS in women, complementing medical treatments. This encompasses regular behavioral adjustments, social support, and psychological adaptations. Essential modifications include maintaining regular physical activity and exercise, long-term weight management strategy, adhering to a balanced diet, behavior therapies, and avoiding tobacco—a comprehensive approach aligned with clinical guidelines to prevent and treat metabolic issues. Prioritizing overall well-being and mental health is a personal choice, offering valuable steps toward a more fulfilling life [29, 32].

8. Conclusion

Polycystic Ovary Syndrome (PCOS) is a complex endocrine disorder affecting women, marked by hormonal imbalances, menstrual irregularities, and ovarian cysts. Its pathophysiology involves genetic, environmental, and hormonal factors, disrupting the HPO axis and contributing to reproductive and metabolic complexities. Hyperandrogenism, ovarian dysfunction, insulin resistance, and obesity amplify PCOS's intricacy, elevating the risk of metabolic syndrome and cardiovascular diseases. The interplay of genetic predisposition and an "obesogenic" environment remains to be fully elucidated. PCOS complications encompass menstrual irregularities, hirsutism, acne, alopecia, acanthosis nigricans, dyslipidaemia, fatty liver disease, inflammation, obstructive sleep apnoea, gestational diabetes, type II diabetes, infertility, and recurrent pregnancy loss.

PCOS management includes supplementation with vitamin D, zinc, selenium, omega-3 fatty acids, vitamin C, vitamin E, chromium, inositol, and berberine. These supplements address deficiencies, reduce inflammation, improve hormonal balance, enhance insulin sensitivity, and mitigate metabolic abnormalities in PCOS patients. An individualized approach, considering diverse needs and factors, is essential for optimal outcomes, emphasizing the importance of a balanced diet and a healthy lifestyle in PCOS therapy. Further research is needed to establish precise dosages and guidelines for supplementation in PCOS management.

Polyphenols like resveratrol, naringenin, and rutin show antioxidant benefits. Herbs such as flaxseed, turmeric, nettle, and traditional remedies offer diverse therapeutic support for PCOS management. Exercise, particularly aerobic and resistance training, plays a crucial role in managing PCOS. It improves insulin sensitivity, reproductive function, and overall health, promoting lasting lifestyle changes.

Personalized, sustainable lifestyle adjustments, including 5–10% weight loss, significantly improve PCOS symptoms, enhancing IR, ovulation, and menstrual regularity. A team-based approach could offer better results for comprehensive PCOS care. A holistic approach to PCOS management involves medical treatments complemented by lifestyle modification, which integrates exercise, dietary adjustments, and prioritizing psychological well-being for comprehensive women's health.

DOI: http://dx.doi.org/10.5772/intechopen.114149

Conflict of interest

The authors declare no conflict of interest.

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