

***Parquetina nigrescens* in the Management of Polyendocrine Metabolic Ovarian Syndrome: Therapeutic Potential, Mechanistic Insights, and Future Perspectives**

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Abstract

Polyendocrine Metabolic Ovarian Syndrome (PEMOS), traditionally known as Polycystic Ovary Syndrome (PCOS), is one of the most prevalent endocrine-metabolic disorders affecting women of reproductive age and a leading cause of anovulatory infertility worldwide. The syndrome is characterized by hyperandrogenism, ovulatory dysfunction, polycystic ovarian morphology, insulin resistance, oxidative stress, chronic low-grade inflammation, menstrual irregularities, and metabolic disturbances that collectively impair reproductive and overall health. Although current management strategies—including lifestyle modification, metformin, letrozole, clomiphene citrate, gonadotrophins, and assisted reproductive technologies—have improved clinical outcomes, their use is often limited by adverse effects, treatment resistance, high costs, restricted accessibility, and the need for specialized monitoring. These challenges are particularly evident in low- and middle-income countries, where traditional medicinal plants continue to play an important role in reproductive healthcare. *Parquetina nigrescens*, a medicinal plant widely used in West African ethnomedicine, has attracted increasing scientific attention because of its diverse pharmacological properties. Experimental studies have demonstrated antioxidant, anti-inflammatory, antidiabetic, hepatoprotective, haematinic, and reproductive-modulating activities that may target key pathophysiological mechanisms underlying PEMOS. Emerging evidence suggests that the plant may improve ovarian function, attenuate oxidative stress, modulate endocrine disturbances, enhance insulin sensitivity, and support reproductive health. This review critically evaluates current evidence on the potential role of *Parquetina nigrescens* in the management of PEMOS. Particular emphasis is placed on its phytochemical constituents, pharmacological activities, proposed mechanisms of action, reproductive effects, safety considerations, and translational potential. By synthesizing available evidence, this review highlights *P. nigrescens* as a promising, accessible, and affordable candidate for further investigation as a complementary therapeutic approach to PEMOS management.

Keywords: *Parquetina nigrescens*; Polyendocrine Metabolic Ovarian Syndrome (PEMOS); Infertility; Phytotherapy; Oxidative Stress.

1. Introduction

Polyendocrine Metabolic Ovarian Syndrome (PEMOS), traditionally known as Polycystic Ovary Syndrome (PCOS), is a multifaceted endocrine, reproductive, and metabolic disorder

that affects millions of women of reproductive age worldwide. The term PEMOS has recently been proposed to better reflect the complex endocrine and metabolic abnormalities underlying the condition, extending beyond the ovarian morphology

implied by the traditional nomenclature [1]. PEMOS is recognized as one of the leading causes of anovulatory infertility and is characterized by hyperandrogenism, ovulatory dysfunction, polycystic ovarian morphology, menstrual irregularities, obesity, insulin resistance, oxidative stress, chronic low-grade inflammation, dyslipidaemia, and an increased risk of long-term cardiometabolic complications [2–7]. Beyond its effects on fertility, PEMOS is increasingly regarded as a lifelong metabolic condition with profound implications for reproductive health, pregnancy outcomes, cardiovascular function, psychological wellbeing, and overall quality of life [1, 2].

The clinical presentation of PEMOS is remarkably heterogeneous, reflecting the complex interplay of genetic, endocrine, metabolic, and environmental factors that contribute to its development. While some women present primarily with infertility and menstrual disturbances, others exhibit manifestations such as hirsutism, acne, obesity, insulin resistance, or features of metabolic syndrome [3, 5]. This variability contributes significantly to the challenges associated with diagnosis and management. The Rotterdam criteria, which remain the most widely accepted diagnostic framework, require the presence of at least two of the following features: oligo-ovulation or anovulation, clinical or biochemical hyperandrogenism, and polycystic ovarian morphology, after excluding other related disorders [8]. Although these criteria have improved diagnostic consistency, they do not fully capture the biological complexity and phenotypic diversity of the syndrome [3, 5].

The burden of PEMOS extends far beyond its clinical manifestations. Because the disorder affects women during their most productive reproductive years, it carries substantial personal, social, and economic consequences. Women with PEMOS frequently experience subfertility, repeated cycles of fertility treatment, emotional distress, reduced self-esteem, and diminished quality of life [2, 9]. In many African societies, where motherhood is often closely linked to social identity and family expectations, infertility can have profound psychosocial and cultural consequences. Women may face stigma, marital challenges, social isolation, and pressure from family and community members, creating an urgent need for accessible, affordable, and culturally acceptable treatment options [10].

Current management strategies for PEMOS are largely symptom-oriented and depend on the patient's primary clinical concerns. Lifestyle modification remains the cornerstone of management, particularly among overweight and obese women, where weight reduction can improve both metabolic and reproductive outcomes [1, 2, 11]. Pharmacological interventions such as metformin are commonly prescribed to address insulin resistance and associated metabolic abnormalities [12]. Combined oral contraceptives are

frequently used to regulate menstrual cycles and manage hyperandrogenic symptoms in women who are not actively seeking pregnancy [2, 13]. For women desiring conception, ovulation induction agents such as letrozole and clomiphene citrate represent the mainstay of treatment [6, 14, 15]. More advanced interventions, including gonadotrophin therapy, laparoscopic ovarian drilling, and assisted reproductive technologies, may be required when first-line treatments fail [2, 16].

Despite these advances, the management of PEMOS remains challenging. A significant proportion of women exhibit resistance to conventional ovulation-induction therapies, particularly clomiphene citrate, which remains a recognized clinical problem [17]. Gonadotrophin therapy, although effective, requires intensive monitoring because of the risks of multiple pregnancy and ovarian hyperstimulation syndrome [16]. Assisted reproductive technologies offer additional opportunities for conception but are often prohibitively expensive and inaccessible to many women, especially in low-resource settings [10, 18]. Furthermore, concerns regarding adverse effects, treatment fatigue, repeated clinical visits, and the emotional burden associated with prolonged fertility management frequently affect treatment adherence and patient satisfaction [18].

These limitations have stimulated growing interest in the exploration of medicinal plants as complementary or alternative approaches to reproductive health management. Traditional medicine continues to play a vital role in healthcare delivery across many low- and middle-income countries, where it remains culturally acceptable, readily accessible, and often more affordable than conventional medical care [19, 20]. Increasing evidence suggests that medicinal plants contain diverse bioactive compounds capable of targeting multiple pathogenic pathways involved in PEMOS, including oxidative stress, chronic inflammation, hormonal imbalance, insulin resistance, and ovarian dysfunction [21, 22]. Such multi-targeted actions are particularly attractive in a disorder as complex and multifactorial as PEMOS.

Among the medicinal plants attracting increasing scientific attention is *Parquetina nigrescens*. This plant has a long history of use in African traditional medicine for the management of a variety of conditions, including anaemia, diabetes, inflammatory disorders, infections, gastrointestinal disturbances, and reproductive ailments [23–25]. Its widespread use in female reproductive health suggests potential modulatory effects on ovarian physiology, endocrine regulation, and fertility. Emerging experimental evidence further indicates that *P. nigrescens* contains a rich array of bioactive phytochemicals with antioxidant, anti-inflammatory, hepatoprotective, antidiabetic, and reproductive-modulating activities [24–27]. These pharmacological properties directly target several of the

pathophysiological mechanisms implicated in PEMOS, making the plant an intriguing candidate for further investigation.

The relevance of *P. nigrescens* to PEMOS management is strengthened by the central role of oxidative stress, chronic inflammation, insulin resistance, and endocrine dysfunction in the pathogenesis of the syndrome. Oxidative stress contributes to ovarian dysfunction, follicular arrest, poor oocyte quality, and impaired fertility, while chronic low-grade inflammation exacerbates metabolic and reproductive abnormalities. Likewise, insulin resistance, a hallmark feature of PEMOS, contributes to hyperinsulinaemia and ovarian androgen excess, thereby perpetuating the cycle of reproductive dysfunction [3, 5, 21]. Natural products capable of simultaneously targeting these interconnected pathways may offer important therapeutic advantages over single-target interventions.

Given the increasing need for affordable, accessible, and mechanistically relevant interventions for PEMOS, a critical evaluation of the therapeutic potential of *Parquetina nigrescens* is warranted. This review therefore examines the available evidence regarding the role of *P. nigrescens* in the management of PEMOS, with particular emphasis on its ethnomedicinal relevance, phytochemical composition, pharmacological activities, reproductive effects, safety profile, and potential mechanisms of action. By integrating current knowledge on PEMOS pathophysiology with emerging data on *P. nigrescens*, this review aims to highlight its prospects as a complementary therapeutic option and identify key areas requiring further experimental and clinical investigation.

2. Polyendocrine Metabolic Ovarian Syndrome (PEMOS): Pathophysiology and Clinical Burden

2.1 Evolution from PCOS to PEMOS

Polyendocrine Metabolic Ovarian Syndrome (PEMOS), formerly known as Polycystic Ovary Syndrome (PCOS), is increasingly recognized as a complex endocrine-metabolic disorder rather than a purely ovarian disease [1]. The syndrome arises from the interaction of endocrine, metabolic, inflammatory, genetic, and environmental factors that collectively impair reproductive and metabolic homeostasis [1, 2]. Although its precise aetiology remains incompletely understood, several interrelated mechanisms have been implicated, including hyperandrogenism, insulin resistance, hypothalamic-pituitary-ovarian (HPO) axis dysfunction, oxidative stress, chronic inflammation, follicular arrest, and altered ovarian steroidogenesis [2-7].

2.2 Neuroendocrine Dysregulation and Ovarian Dysfunction

The HPO axis plays a central role in female reproductive physiology. Gonadotropin-releasing hormone (GnRH) released from the hypothalamus stimulates secretion of follicle-

stimulating hormone (FSH) and luteinizing hormone (LH) from the anterior pituitary gland. FSH promotes follicular growth and granulosa cell proliferation, whereas LH stimulates androgen production by ovarian theca cells. These androgens are subsequently aromatized to oestrogens within granulosa cells [5, 11]. In PEMOS, increased GnRH pulse frequency favours LH secretion over FSH production, resulting in excessive ovarian androgen synthesis and impaired follicular maturation [5, 11]. Consequently, follicles fail to progress to ovulation and instead accumulate within the ovary, producing the characteristic polycystic morphology.

2.3 Hyperandrogenism and Follicular Arrest

Hyperandrogenism is a defining feature of PEMOS and contributes directly to hirsutism, acne, androgenic alopecia, menstrual irregularity, and ovulatory dysfunction [3, 5]. Elevated androgen concentrations disrupt folliculogenesis, impair dominant follicle selection, and promote chronic anovulation [3, 11].

2.4 Insulin Resistance and Metabolic Dysfunction

Insulin resistance represents one of the most important metabolic abnormalities associated with PEMOS and may occur independently of obesity [12]. Hyperinsulinaemia stimulates ovarian androgen production and suppresses hepatic synthesis of sex hormone-binding globulin (SHBG), thereby increasing circulating free androgen concentrations [12, 13]. These changes perpetuate endocrine dysfunction and contribute to obesity, dyslipidaemia, impaired glucose tolerance, metabolic syndrome, and type 2 diabetes mellitus [12,13].

2.5 Oxidative Stress and Chronic Inflammation

Oxidative stress is increasingly recognized as a major contributor to PEMOS pathogenesis. Excessive production of reactive oxygen species (ROS) overwhelms endogenous antioxidant defenses, resulting in lipid peroxidation, protein oxidation, and DNA damage [9, 14]. Elevated malondialdehyde (MDA) levels and reduced antioxidant enzyme activities have consistently been reported in women with PEMOS [9,14]. Similarly, chronic low-grade inflammation contributes significantly to disease progression. Increased concentrations of tumour necrosis factor-alpha (TNF- α), interleukin-1 beta (IL-1 β), interleukin-6 (IL-6), and C-reactive protein (CRP) have been documented in affected women [8,15]. These inflammatory mediators worsen insulin resistance, impair ovarian function, and amplify oxidative stress [8,15].

Table 1. Major Pathophysiological Mechanisms Involved in PEMOS

Pathophysiological Process	Principal Mediators	Clinical Consequences
HPO Axis Dysfunction	Altered GnRH pulsatility, increased LH:FSH ratio	Anovulation, follicular arrest
Hyperandrogenism	Testosterone, androstenedione	Hirsutism, acne, infertility
Insulin Resistance	Hyperinsulinaemia	Ovarian androgen excess, metabolic syndrome
Oxidative Stress	ROS, MDA	Oocyte damage, impaired folliculogenesis
Chronic Inflammation	TNF- α , IL-1 β , IL-6, CRP	Ovarian dysfunction, metabolic abnormalities
Ovarian Remodeling	Cystic follicles, stromal hypertrophy	Infertility and chronic anovulation

3. Current Therapeutic Approaches and Unmet Clinical Needs in PEMOS

3.1 Lifestyle-Based Interventions

Lifestyle modification remains the cornerstone of PEMOS management, particularly among overweight and obese women. Weight reduction through dietary modification and physical activity improves insulin sensitivity, lowers androgen levels, restores ovulation, and enhances fertility outcomes [2,16]. However, long-term adherence remains challenging.

3.2 Pharmacological Therapies

3.2.1 Clomiphene Citrate

Clomiphene citrate acts as a selective oestrogen receptor modulator that stimulates gonadotropin release and ovulation [17]. Despite its widespread use, approximately 15–40% of women exhibit clomiphene resistance [18].

3.2.2 Letrozole

Letrozole, an aromatase inhibitor, has emerged as the preferred first-line ovulation induction agent because of superior ovulation and live-birth rates compared with clomiphene citrate [10,19].

3.2.3 Metformin

Metformin improves insulin sensitivity, menstrual cyclicity, and metabolic outcomes [20]. Nevertheless, gastrointestinal adverse effects and variable fertility outcomes may limit compliance.

3.2.4 Gonadotrophins and Assisted Reproductive Technologies

Although effective, gonadotrophin therapy and assisted reproductive technologies (ART) are costly and require specialist monitoring [21, 22].

Table 2. Current Therapeutic Options for PEMOS and Their Limitations

Intervention	Primary Target	Advantages	Major Limitations
Lifestyle Modification	Obesity, insulin resistance	Improves fertility and metabolic health	Poor long-term adherence
Clomiphene Citrate	Ovulation induction	Widely available	Resistance and anti-estrogenic effects
Letrozole	Ovulation induction	Superior live-birth rates	Cost and accessibility
Metformin	Insulin resistance	Metabolic benefits	Gastrointestinal side effects
Gonadotrophins	Ovulation induction	High efficacy	Multiple pregnancy risk
IVF/ART	Refractory infertility	High success rates	Expensive and inaccessible

4. Medicinal Plants as Emerging Therapeutics for PEMOS

4.1 Traditional Medicine and Women's Reproductive Health

Traditional medicine has served as a cornerstone of women's healthcare for centuries and continues to play a significant role in reproductive health management worldwide [28-30]. The World Health Organization estimates that approximately 80% of individuals in many developing countries rely partly or wholly on traditional medicine for their primary healthcare needs [25]. In Africa, medicinal plants remain integral to the management of menstrual disorders, infertility, pregnancy-related complications, postpartum recovery, and general reproductive wellbeing [23, 26, 30].

The sustained reliance on traditional medicine is driven by several factors, including affordability, accessibility, cultural acceptability, and longstanding empirical use. In many low- and middle-income countries, access to specialist reproductive care is often limited by economic constraints, inadequate healthcare infrastructure, and shortages of trained fertility specialists [22]. Consequently, medicinal plants continue to represent an important source of therapeutic intervention for women experiencing reproductive disorders.

Historically, many modern pharmaceutical agents have originated from medicinal plants initially used in traditional healing systems. This observation underscores the importance

of ethnomedicine as a valuable starting point for drug discovery and therapeutic innovation. In the context of reproductive disorders, traditional medicinal plants offer particular promise because they frequently contain multiple bioactive constituents capable of acting on diverse physiological pathways simultaneously [23, 24, 28-30].

As understanding of Polyendocrine Metabolic Ovarian Syndrome (PEMOS) continues to evolve, there is increasing recognition that successful management may require interventions capable of addressing the syndrome's multifaceted endocrine, metabolic, inflammatory, and oxidative components. This realization has renewed scientific interest in medicinal plants as potential complementary therapeutic agents.

4.2 Why Botanical Therapeutics Matter in PEMOS

The complexity of PEMOS presents unique therapeutic challenges. Unlike many endocrine disorders that arise from a single pathogenic defect, PEMOS involves intricate interactions among hyperandrogenism, insulin resistance, oxidative stress, chronic low-grade inflammation, altered gonadotropin secretion, and disrupted ovarian function [1-5]. Consequently, treatments directed toward a single target may not fully address the broad spectrum of abnormalities present in affected individuals.

Current therapeutic approaches, including lifestyle modification, metformin, clomiphene citrate, letrozole, gonadotropins, and assisted reproductive technologies, have significantly improved clinical outcomes [2,10, 20]. Nevertheless, these interventions are associated with important limitations, including treatment resistance, adverse effects, high costs, limited accessibility, and the need for intensive monitoring [18, 21, 22].

Botanical therapeutics may offer a unique advantage because many medicinal plants contain diverse phytochemical constituents capable of influencing several pathogenic pathways simultaneously. Rather than acting through a single molecular target, plant-derived compounds frequently exert antioxidant, anti-inflammatory, endocrine-modulating, insulin-sensitizing, hepatoprotective, and cytoprotective effects concurrently [21, 22]. Such multitarget pharmacology aligns particularly well with the multifactorial nature of PEMOS.

Furthermore, medicinal plants often possess favourable accessibility profiles, especially in resource-constrained settings where conventional fertility treatments may be financially prohibitive. Consequently, scientifically validated botanical interventions could potentially expand therapeutic options for women who otherwise have limited access to reproductive healthcare services [10, 22].

4.3 Multi-Target Pharmacology of Medicinal Plants in Reproductive Disorders

The therapeutic relevance of medicinal plants in PEMOS is rooted in their ability to target multiple interconnected biological processes. As summarized in **Table 3**, medicinal plants may influence oxidative stress, inflammation, insulin resistance, hyperandrogenism, and follicular arrest, all of which contribute significantly to PEMOS pathogenesis.

Table 3. Potential Therapeutic Targets of Medicinal Plants in PEMOS

Target	Clinical Relevance
Oxidative Stress	Improved oocyte quality
Inflammation	Reduced ovarian damage
Insulin Resistance	Improved ovulation
Hyperandrogenism	Restored endocrine balance
Follicular Arrest	Enhanced folliculogenesis

Oxidative stress has emerged as a major contributor to ovarian dysfunction in PEMOS, where excessive production of reactive oxygen species impairs granulosa cell function, damages oocytes, and disrupts follicular maturation [9, 14]. Numerous plant-derived flavonoids and phenolic compounds possess potent antioxidant properties capable of scavenging free radicals and enhancing endogenous antioxidant defenses [22, 27]. Consequently, medicinal plants rich in these compounds may help restore redox homeostasis and improve reproductive outcomes.

Similarly, chronic low-grade inflammation contributes significantly to insulin resistance and ovarian dysfunction through the actions of cytokines such as TNF- α , IL-1 β , and IL-6 [8,15, 31]. Several medicinal plants contain terpenoids, polyphenols, and alkaloids that suppress inflammatory signaling pathways including NF- κ B and cyclooxygenase activity, thereby reducing inflammatory burden and improving tissue function [27, 32].

Insulin resistance represents another critical therapeutic target. Hyperinsulinemia not only contributes to metabolic dysfunction but also stimulates ovarian androgen production and exacerbates endocrine imbalance [12,13]. Certain plant-derived compounds have demonstrated insulin-sensitizing properties capable of improving glucose metabolism and reducing insulin resistance, thereby addressing a key driver of PEMOS progression [21].

Additionally, several medicinal plants possess endocrine-modulating activities that may help restore reproductive

hormone balance. Through effects on steroidogenesis, aromatase activity, oestrogen receptor signaling, and gonadotropin regulation, these phytochemicals may promote follicular development and ovulation [31, 33]. Such multifaceted biological activities highlight the considerable therapeutic potential of medicinal plants in the management of PEMOS and provide a strong rationale for investigating species such as *Parquetina nigrescens*.

5. *Parquetina nigrescens*: Botanical, Ethnomedicinal and Pharmacological Perspectives

5.1 Botanical Description and Taxonomy

Parquetina nigrescens (Afzel.) Bullock is a perennial climbing shrub belonging to the family Apocynaceae and was previously classified under the family Asclepiadaceae [34]. The species is characterized by a slender twining stem that exudes a characteristic milky latex when injured, a feature commonly observed among members of the Apocynaceae family. The leaves are simple, opposite, ovate to elliptic in shape, and dark green in colour. Its flowers are relatively small, greenish to purplish, and occur in clusters, while the fruits consist of paired follicles containing numerous seeds [34, 35].

The plant thrives in a variety of ecological settings, including forest margins, secondary forests, fallow lands, and disturbed habitats. Its remarkable adaptability to diverse environmental conditions contributes to its widespread occurrence across tropical Africa. Traditionally, various parts of the plant, including the leaves, roots, stem bark, and latex, have been employed for medicinal purposes. Among these, the leaves are most frequently utilized because of their accessibility, ease of processing, and perceived therapeutic efficacy [36].

Taxonomically, *P. nigrescens* occupies an important position among African medicinal plants due to its extensive ethnopharmacological history and growing scientific validation. Increasing phytochemical and pharmacological investigations have begun to provide mechanistic support for many of its traditional applications, thereby bridging indigenous knowledge and contemporary biomedical research.

5.2 Geographic Distribution

Parquetina nigrescens is widely distributed throughout the tropical regions of Africa and is particularly abundant in West and Central African countries, including Nigeria, Ghana, Benin Republic, Sierra Leone, Côte d'Ivoire, Cameroon, and Togo [34, 35]. The plant is commonly found in humid and sub-humid ecological zones where rainfall and soil conditions favour its growth.

In Nigeria, the species occurs across several ecological regions and is known by different indigenous names among various ethnic groups. Its widespread distribution has facilitated its incorporation into numerous traditional medical systems and

contributed to the accumulation of extensive ethnomedicinal knowledge regarding its therapeutic uses.

The broad geographical occurrence of *P. nigrescens* has important implications for its potential development as a phytotherapeutic agent. Local availability reduces dependence on imported pharmaceutical products and may enhance the affordability and accessibility of plant-based interventions, particularly in resource-limited settings. Furthermore, the plant's adaptability suggests that large-scale cultivation could be feasible if future clinical evidence supports its therapeutic application [36, 37].

However, geographical variations may influence phytochemical composition and biological activity. Environmental factors such as climate, soil composition, altitude, harvesting season, and post-harvest processing can significantly affect the concentration of bioactive constituents [36, 37]. Consequently, future development of standardized preparations will require careful consideration of geographical and agronomic factors.

5.3 Ethnomedicinal Uses

The ethnomedicinal applications of *Parquetina nigrescens* are remarkably diverse and reflect its long-standing role in traditional African healthcare systems. For generations, the plant has been used in the management of anaemia, diabetes mellitus, inflammatory disorders, infections, jaundice, gastrointestinal disturbances, and reproductive conditions [38, 39]. Traditional preparations are commonly administered as decoctions, infusions, macerations, or ethanolic extracts, depending on local cultural practices and the condition being treated.

One of the most widely recognized traditional applications of *P. nigrescens* is its use as a haematinic or "blood-building" remedy. The plant is frequently prescribed for individuals with symptoms suggestive of anaemia, weakness, fatigue, or blood loss, and several experimental studies have subsequently provided evidence supporting its haematopoietic activity [40, 41, 42]. This traditional reputation has contributed significantly to its popularity across many West African communities.

Beyond its haematinic use, *P. nigrescens* has also been employed for the management of metabolic disorders such as diabetes mellitus. Traditional healers have long recognized its potential benefits in regulating blood sugar levels, a practice that has gained scientific support through experimental studies demonstrating hypoglycaemic and antidiabetic effects [43,44]. Of particular relevance to the present review is the plant's traditional use in female reproductive health. In several African communities, *P. nigrescens* is administered to women experiencing menstrual irregularities, infertility, delayed conception, and postpartum recovery [38]. Although the precise traditional rationale for these applications may vary across

regions, these uses suggest an empirical recognition of the plant's effects on reproductive physiology. Such observations are particularly intriguing in light of recent experimental studies demonstrating reproductive-modulating effects in animal models of Polyendocrine Metabolic Ovarian Syndrome (PEMOS) [41, 43]. The principal traditional applications of *P. nigrescens* are summarized in **Table 4**.

Table 4. Traditional Uses of *Parquetina nigrescens* in African Ethnomedicine

Condition	Plant Part Used	Traditional Application
Anaemia	Leaves	Blood tonic and haematinic remedy
Diabetes Mellitus	Leaves/Roots	Glycaemic control
Inflammatory Disorders	Leaves	Anti-inflammatory remedy
Female Infertility	Leaves	Fertility enhancement
Gastrointestinal Disorders	Whole plant	Digestive support and gastrointestinal health

The diversity of these traditional applications is noteworthy because many correspond closely with biological pathways implicated in PEMOS pathogenesis. For example, the plant's reported use in inflammatory disorders, metabolic dysfunction, and reproductive ailments aligns with contemporary understanding of the roles of inflammation, insulin resistance, and ovarian dysfunction in PEMOS [8, 12, 15]. This convergence between traditional knowledge and emerging experimental evidence strengthens the rationale for investigating *P. nigrescens* as a potential therapeutic agent for reproductive and metabolic disorders.

Furthermore, the long history of traditional use may offer an important foundation for future translational research. While traditional use alone cannot establish efficacy or safety, it provides valuable ethnopharmacological evidence that can guide scientific investigation and identify promising candidates for drug development. The growing body of experimental evidence supporting the antioxidant, anti-inflammatory, endocrine-modulating, hepatoprotective, and reproductive activities of *P. nigrescens* suggests that many of its traditional applications may indeed possess a biological basis worthy of further exploration.

6. Phytochemical Profile of *Parquetina nigrescens*

The therapeutic potential of medicinal plants is fundamentally linked to their phytochemical composition. Over the past decade, increasing attention has been directed toward the

characterization of the bioactive constituents of *Parquetina nigrescens*, driven largely by growing evidence of its antioxidant, anti-inflammatory, antidiabetic, hepatoprotective, haematinic, and reproductive-modulating activities [41–45]. Phytochemical investigations have consistently demonstrated that *P. nigrescens* contains a rich diversity of secondary metabolites capable of interacting with multiple molecular targets relevant to the pathophysiology of Polyendocrine Metabolic Ovarian Syndrome (PEMOS).

Unlike conventional pharmaceuticals that often act through a single molecular pathway, medicinal plants frequently derive their therapeutic effects from the synergistic interaction of numerous bioactive compounds. This phytochemical complexity may be particularly advantageous in PEMOS, a disorder characterized by interconnected disturbances involving oxidative stress, chronic inflammation, insulin resistance, endocrine dysfunction, and ovarian pathology [2, 8, 9]. Consequently, understanding the phytochemical profile of *P. nigrescens* is essential for elucidating its mechanisms of action and evaluating its potential as a multitarget therapeutic agent.

6.1 Major Phytochemical Classes

Phytochemical screening studies have revealed the presence of several biologically important classes of secondary metabolites in *Parquetina nigrescens*, including flavonoids, phenolic compounds, alkaloids, tannins, saponins, terpenoids, steroids, glycosides, triterpenes, reducing sugars, and fatty acid derivatives [40–42].

Among these constituents, flavonoids are particularly important because of their potent antioxidant and anti-inflammatory activities. Flavonoids exert protective effects by scavenging reactive oxygen species (ROS), inhibiting lipid peroxidation, modulating cytokine production, and enhancing endogenous antioxidant defense systems [30]. Given the significant role of oxidative stress in PEMOS-associated ovarian dysfunction, the abundance of flavonoids within *P. nigrescens* may contribute substantially to its therapeutic potential [9,14].

Phenolic compounds represent another major phytochemical group present in the plant. These compounds possess strong reducing capacity and function as effective free-radical scavengers. In addition to directly neutralizing ROS, phenolics may stimulate antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx), thereby strengthening endogenous defense mechanisms against oxidative injury [25].

Saponins identified in *P. nigrescens* may also be relevant to reproductive health. Structurally, certain saponins resemble steroid hormones and have been reported to influence steroidogenesis, endocrine regulation, lipid metabolism, and immune responses [31]. These activities are particularly

noteworthy in PEMOS, where endocrine imbalance and metabolic dysfunction represent central pathogenic features.

Terpenoids and triterpenoids constitute another important group of phytochemicals present in the plant. These compounds possess diverse biological activities including antioxidant, anti-inflammatory, hepatoprotective, antimicrobial, and metabolic regulatory effects [32]. Their presence may contribute significantly to the broad pharmacological profile attributed to *P. nigrescens*.

Collectively, the coexistence of these phytochemical classes suggests that the biological effects of *P. nigrescens* are likely mediated through multiple complementary mechanisms acting in concert rather than through a single active constituent.

6.2 Bioactive Compounds Identified by GC–MS

While preliminary phytochemical screening provides valuable information regarding the major classes of compounds present, advanced analytical techniques such as Gas Chromatography–Mass Spectrometry (GC–MS) have enabled the identification of specific bioactive constituents responsible for the pharmacological activities of *P. nigrescens*.

Recent GC–MS investigations of ethanolic leaf extracts have identified several major compounds, including friedelan-3-one, neophytadiene, n-hexadecanoic acid, tetradecanoic acid, octadecanoic acid, cis-13-octadecenoic acid, linoleic acid ethyl ester, and related fatty acid derivatives [37]. Many of these compounds possess biological activities directly relevant to the pathogenesis of PEMOS.

Among the identified constituents, friedelan-3-one has attracted considerable attention because of its documented antioxidant, anti-inflammatory, hepatoprotective, and cytoprotective properties [46]. As a pentacyclic triterpenoid, friedelan-3-one has demonstrated the capacity to suppress inflammatory mediators, reduce oxidative injury, and protect tissues from cellular damage in various experimental models.

Neophytadiene, another major constituent identified in *P. nigrescens*, is a diterpenoid known for its antioxidant, antimicrobial, anti-inflammatory, and immunomodulatory activities [47]. Its ability to attenuate oxidative stress and inflammation may be particularly relevant to ovarian protection in PEMOS.

Fatty acid derivatives identified in the extract, including palmitic acid (n-hexadecanoic acid), stearic acid (octadecanoic acid), and linoleic acid esters, may contribute to membrane stabilization, cellular signaling, inflammatory regulation, and metabolic homeostasis [48, 49]. These compounds may influence insulin sensitivity, cytokine production, and steroid hormone synthesis, all of which are relevant to the management of PEMOS.

The identification of these compounds provides a mechanistic foundation for understanding the diverse biological activities

reported for *P. nigrescens* and supports its potential development as a phytotherapeutic agent.

6.3 Pharmacological Relevance of Major Constituents

The therapeutic significance of *P. nigrescens* extends beyond the mere presence of bioactive compounds; rather, it lies in how these compounds interact with biological pathways implicated in PEMOS pathogenesis. As shown in **Table 5**, many of the major phytochemicals identified in *P. nigrescens* possess activities capable of targeting oxidative stress, inflammation, endocrine dysfunction, insulin resistance, and ovarian injury. These mechanisms closely correspond to the major pathological processes involved in PEMOS.

Table 5. Principal Phytochemicals Identified in *Parquetina nigrescens* and Their Biological Activities

Compound	Chemical Class	Reported Activities
Friedelan-3-one	Triterpenoid	Antioxidant, anti-inflammatory, hepatoprotective, cytoprotective [46]
Neophytadiene	Diterpenoid	Antioxidant, antimicrobial, anti-inflammatory [47]
n-Hexadecanoic acid	Fatty acid	Anti-inflammatory, membrane stabilization [48]
Linoleic acid ethyl ester	Fatty acid derivative	Metabolic regulation, anti-inflammatory activity [48]
Flavonoids	Polyphenols	Antioxidant, endocrine modulation, free radical scavenging [30]
Phenolic compounds	Polyphenols	Antioxidant, enhancement of endogenous antioxidant enzymes [25]
Saponins	Glycosides	Endocrine modulation, lipid regulation, immunomodulation [31]
Terpenoids	Terpenes	Anti-inflammatory, hepatoprotective, metabolic regulation [31]

The antioxidant properties of flavonoids, phenolics, friedelan-3-one, and neophytadiene may collectively reduce oxidative damage to ovarian tissues, thereby improving follicular survival, oocyte quality, and steroidogenic function [9,14]. Simultaneously, anti-inflammatory constituents may suppress pro-inflammatory cytokines such as TNF- α and IL-1 β , thereby

mitigating inflammatory damage and restoring ovarian homeostasis [8,15].

Several of these compounds may also contribute to improved metabolic function. Fatty acid derivatives and terpenoids have been associated with enhanced insulin sensitivity and improved glucose utilization, suggesting potential benefits in addressing insulin resistance—a central feature of PEMOS [12,13]. Moreover, hepatoprotective constituents may support hepatic regulation of sex hormone-binding globulin (SHBG), lipid metabolism, and hormone clearance, thereby indirectly improving reproductive endocrine function [50].

Importantly, the coexistence of multiple pharmacologically active constituents raises the possibility of synergistic interactions. Such synergy may enhance therapeutic efficacy by simultaneously targeting several pathogenic mechanisms while minimizing the limitations associated with single-target interventions. This concept of multitarget phytotherapy is increasingly recognized as a valuable approach in the management of complex disorders such as PEMOS.

Overall, the phytochemical composition of *Parquetina nigrescens* provides strong biological plausibility for its reported pharmacological activities and supports its continued investigation as a potential therapeutic agent for reproductive and metabolic disorders. The convergence of antioxidant, anti-inflammatory, endocrine-modulating, metabolic, and hepatoprotective mechanisms suggests that the plant may possess unique advantages in addressing the multifactorial pathophysiology of PEMOS

7. Therapeutic Potential of *Parquetina nigrescens* in Polyendocrine Metabolic Ovarian Syndrome (PEMOS)

The therapeutic relevance of *Parquetina nigrescens* in PEMOS derives from its ability to simultaneously target several interconnected mechanisms that contribute to disease initiation and progression. Contemporary understanding of PEMOS recognizes the syndrome as a complex interaction among oxidative stress, chronic inflammation, insulin resistance, endocrine dysregulation, ovarian dysfunction, and metabolic disturbances [2, 3, 8]. Consequently, interventions capable of modulating multiple pathological pathways may offer advantages over therapies directed at a single target.

Emerging experimental evidence indicates that *P. nigrescens* possesses antioxidant, anti-inflammatory, endocrine-modulating, hepatoprotective, haematinic, and reproductive-enhancing properties [27–30, 40–45]. These pharmacological activities are particularly relevant because they correspond closely with the major biological abnormalities implicated in PEMOS pathogenesis. Collectively, available evidence suggests that the plant may function as a multitarget phytotherapeutic agent capable of restoring reproductive and metabolic homeostasis.

7.1 Antioxidant Mechanisms

Oxidative stress has emerged as one of the most important contributors to the pathophysiology of PEMOS. Excessive production of reactive oxygen species (ROS) coupled with impaired antioxidant defense mechanisms leads to oxidative damage within ovarian tissues, disrupting follicular maturation, steroidogenesis, oocyte quality, and ovulatory function [9, 14]. Numerous studies have demonstrated elevated concentrations of malondialdehyde (MDA) and reduced activities of endogenous antioxidant enzymes in women with PEMOS, highlighting the importance of oxidative injury in disease progression [9, 14].

The antioxidant activity of *Parquetina nigrescens* represents one of its most extensively documented pharmacological properties. The plant contains flavonoids, phenolic compounds, triterpenes, and terpenoids that possess potent free-radical scavenging capabilities [30,4 1–45]. These phytochemicals can directly neutralize ROS while simultaneously enhancing endogenous antioxidant defense systems.

Experimental investigations have demonstrated significant reductions in MDA concentrations following administration of *P. nigrescens* extracts, accompanied by increases in total antioxidant capacity (TAC) and superoxide dismutase (SOD) activity [45]. These findings suggest attenuation of lipid peroxidation and restoration of redox balance. The ability to suppress oxidative stress may be particularly important in PEMOS because oxidative injury contributes directly to granulosa cell dysfunction, impaired oocyte competence, and defective folliculogenesis [17].

Beyond ovarian protection, antioxidant activity may confer broader metabolic benefits. Oxidative stress has been implicated in insulin resistance, chronic inflammation, endothelial dysfunction, and hepatic injury [9, 44, 45]. Consequently, the antioxidant effects of *P. nigrescens* may extend beyond the ovary to influence multiple aspects of PEMOS pathophysiology.

Importantly, antioxidant activity may also potentiate the effects of other pharmacological mechanisms. Because oxidative stress and inflammation are closely intertwined biological processes, reduction of oxidative injury frequently leads to attenuation of inflammatory signaling [41–45]. Thus, antioxidant activity may represent a foundational mechanism underlying many of the broader therapeutic effects of *P. nigrescens*.

7.2 Anti-inflammatory Mechanisms

Chronic low-grade inflammation is increasingly recognized as a central component of PEMOS and contributes significantly to endocrine dysfunction, insulin resistance, and reproductive impairment [8, 15]. Elevated concentrations of inflammatory mediators such as TNF- α , IL-1 β , IL-6, and CRP have consistently been reported in women with PEMOS [8,15].

These cytokines impair follicular development, promote ovarian dysfunction, exacerbate insulin resistance, and amplify oxidative stress.

Several phytochemical constituents of *P. nigrescens*, including flavonoids, phenolic compounds, terpenoids, and triterpenes, possess well-documented anti-inflammatory activities [30, 32]. These compounds may suppress inflammatory signaling pathways such as NF- κ B, cyclooxygenase (COX), and inducible nitric oxide synthase (iNOS), thereby reducing cytokine production and limiting tissue injury.

Recent experimental evidence provides support for these mechanisms. Treatment with *P. nigrescens* has been associated with reductions in pro-inflammatory cytokines, particularly TNF- α and IL-1 β , alongside increases in the anti-inflammatory cytokine IL-10 [43]. Such changes suggest a shift from a pro-inflammatory state toward a more balanced immunological environment.

The reduction of inflammatory activity may have profound implications for reproductive function. Elevated TNF- α concentrations have been linked to granulosa cell apoptosis, impaired folliculogenesis, and reduced oocyte quality [15]. Similarly, IL-1 β may interfere with ovarian steroidogenesis and follicular maturation. By suppressing these inflammatory mediators, *P. nigrescens* may help restore the ovarian microenvironment required for normal follicular development and ovulation.

The anti-inflammatory properties of the plant may also complement its antioxidant actions, creating a synergistic effect that interrupts the vicious cycle between oxidative stress and inflammation that characterizes PEMOS.

7.3 Endocrine-Modulating Effects

Endocrine dysfunction is a hallmark of PEMOS and is characterized by disturbances in gonadotropin secretion, hyperandrogenism, altered steroidogenesis, and chronic anovulation [5, 11]. Restoration of hormonal balance is therefore a major therapeutic objective.

Experimental studies have demonstrated that administration of *P. nigrescens* extracts significantly improves reproductive hormone profiles in animal models of PEMOS [41-45]. These improvements include normalization of follicle-stimulating hormone (FSH), luteinizing hormone (LH), oestradiol, and progesterone concentrations.

The increase in FSH observed following treatment is particularly important because FSH plays a critical role in follicular recruitment and maturation. Enhanced FSH activity may facilitate the progression of developing follicles beyond the stage of arrest characteristic of PEMOS. Likewise, restoration of estradiol concentrations suggests improved granulosa cell function and aromatase activity, both of which are essential for normal follicular development.

Perhaps the most significant endocrine finding is the increase in progesterone levels following treatment. Since progesterone production is dependent on corpus luteum formation after ovulation, elevated progesterone concentrations provide indirect evidence of restored ovulatory function. Although the precise molecular mechanisms remain incompletely understood, several phytochemicals present in *P. nigrescens* may contribute to endocrine regulation through effects on steroidogenic enzymes, aromatase activity, gonadotropin signaling, and ovarian responsiveness. Future molecular studies are required to determine whether these effects involve direct interactions with estrogen receptors, androgen receptors, gonadotropin receptors, or steroidogenic pathways.

7.4 Metabolic and Insulin-Sensitizing Effects

Insulin resistance represents one of the most important metabolic abnormalities associated with PEMOS and contributes significantly to hyperandrogenism, ovulatory dysfunction, obesity, dyslipidaemia, and metabolic syndrome [12, 13]. Consequently, interventions capable of improving insulin sensitivity may provide substantial therapeutic benefits. Preliminary evidence suggests that *P. nigrescens* possesses antidiabetic and metabolic regulatory properties [43, 44]. Experimental studies in diabetic animal models have demonstrated reductions in blood glucose concentrations following treatment with plant extracts, supporting its traditional use in diabetes management.

The antidiabetic activity of *P. nigrescens* may be attributable to several phytochemical constituents, including flavonoids, terpenoids, phenolic compounds, and fatty acid derivatives. These compounds have been associated with enhanced glucose utilization, improved insulin signaling, suppression of oxidative stress, and modulation of inflammatory pathways implicated in insulin resistance [30, 32].

Although direct investigations of insulin sensitivity in PEMOS models remain limited, the observed improvements in oxidative stress and inflammatory markers provide biological plausibility for metabolic benefits. Because oxidative stress and inflammation contribute significantly to insulin resistance, attenuation of these processes may indirectly enhance insulin responsiveness. Future studies should evaluate the effects of *P. nigrescens* on fasting insulin concentrations, glucose tolerance, HOMA-IR indices, adipokines, lipid profiles, and insulin receptor signaling pathways to clarify its role in metabolic regulation.

7.5 Hepatoprotective Actions

The liver occupies a central position in reproductive endocrinology through its roles in glucose metabolism, lipid regulation, hormone metabolism, and synthesis of sex hormone-binding globulin (SHBG) [50]. Hepatic dysfunction may

therefore exacerbate both metabolic and endocrine abnormalities associated with PEMOS.

Women with PEMOS are at increased risk of developing metabolic-associated fatty liver disease (MAFLD), which may further contribute to insulin resistance and hyperandrogenism [5,13]. Consequently, hepatoprotective interventions may offer indirect reproductive benefits.

Experimental studies have demonstrated that *P. nigrescens* improves liver function indices and hepatic histology [40, 51]. Treatment has been associated with reductions in serum ALT, AST, and ALP activities, suggesting protection against hepatocellular injury [51]. Histological evaluations have likewise revealed preservation of hepatic architecture and reduction of pathological alterations.

These hepatoprotective effects are likely mediated by the antioxidant and anti-inflammatory phytochemicals present in the plant, including flavonoids, phenolics, terpenoids, and triterpenes [40, 51]. By protecting hepatocytes from oxidative and inflammatory injury, *P. nigrescens* may support normal hormone metabolism and SHBG production, thereby indirectly improving reproductive endocrine function.

7.6 Haematinic and Systemic Health Benefits

One of the most widely recognized traditional applications of *P. nigrescens* is its use as a haematinic agent [42, 43]. Experimental studies have demonstrated improvements in haemoglobin concentration, packed cell volume, erythrocyte count, and other haematological parameters following administration of the plant extract [42, 43].

Although haematinic activity does not directly address the primary mechanisms of PEMOS, improved haematological status may contribute to overall reproductive health by enhancing oxygen delivery, cellular metabolism, and tissue function. Improved systemic health may be particularly beneficial in women experiencing chronic menstrual irregularities or nutritional deficiencies. Furthermore, the broad systemic benefits associated with improved antioxidant status, reduced inflammation, and enhanced haematological function may collectively support reproductive recovery and improve quality of life.

7.7 Ovarian Protective and Folliculogenic Effects

Among the various pharmacological activities attributed to *P. nigrescens*, its effects on ovarian structure and function are perhaps the most directly relevant to PEMOS management. Histopathological studies in experimental models have consistently demonstrated improvements in ovarian morphology following treatment [40, 41, 45].

Untreated PEMOS models typically exhibit ovarian enlargement, multiple cystic follicles, stromal hypertrophy, disrupted follicular organization, and reduced corpus luteum

formation. These changes reflect chronic anovulation and impaired reproductive competence [5, 36].

Treatment with *P. nigrescens* has been shown to reverse many of these pathological features. Experimental studies have reported reductions in cystic follicles, restoration of normal follicular architecture, enhanced folliculogenesis, increased corpus luteum formation, and normalization of ovarian morphology [40, 41, 45].

The increase in corpus luteum formation is particularly significant because it provides direct histological evidence of ovulation. Combined with improvements in progesterone concentrations, these findings strongly suggest restoration of reproductive function. The ovarian benefits of *P. nigrescens* are likely multifactorial and arise from the combined effects of reduced oxidative stress, suppression of inflammation, improved endocrine balance, enhanced metabolic function, and preservation of ovarian cellular integrity. This integrated mechanism aligns closely with the multifactorial pathophysiology of PEMOS and highlights the potential advantages of a multitarget phytotherapeutic approach.

Together, the available evidence suggests that *Parquetina nigrescens* possesses a unique combination of pharmacological activities that directly address several key components of PEMOS pathogenesis. While the current evidence remains predominantly preclinical, the convergence of antioxidant, anti-inflammatory, endocrine-modulating, metabolic, hepatoprotective, and ovarian-restorative effects provides strong biological plausibility for its potential therapeutic utility and justifies further investigation in translational and clinical studies.

Table 6. Alignment of *Parquetina nigrescens* Activities with PEMOS Pathophysiology

PEMOS Pathology Evidence in <i>P. nigrescens</i>	
Oxidative Stress	↓ MDA, ↑ TAC, ↑ SOD [51]
Inflammation	↓ TNF- α , ↓ IL-1 β , ↑ IL-10 [51]
Endocrine Dysfunction	Improved FSH, LH, Oestradiol, Progesterone [40, 41, 45]
Ovarian Dysfunction	Improved folliculogenesis and corpus luteum formation [4,45]
Hepatic Dysfunction	↓ ALT, AST, ALP and improved liver histology [51]
Metabolic Disturbance	Antidiabetic and metabolic regulatory activity [43, 44]

Conclusion

Polyendocrine Metabolic Ovarian Syndrome (PEMOS) remains a major cause of female infertility and reproductive dysfunction worldwide, driven by complex interactions among oxidative stress, chronic inflammation, endocrine imbalance, insulin resistance, and ovarian dysfunction. Emerging evidence indicates that *Parquetina nigrescens* possesses a unique combination of antioxidant, anti-inflammatory, hepatoprotective, metabolic-regulatory, and reproductive-modulating activities that directly target several of these pathogenic mechanisms. Experimental studies demonstrate improvements in hormonal profiles, ovarian morphology, oxidative status, inflammatory biomarkers, and folliculogenesis. Collectively, these findings provide scientific support for its traditional use and highlight *P. nigrescens* as a promising phytotherapeutic candidate for integrative PEMOS management.

Future Directions

Despite encouraging preclinical findings, substantial research is required before *Parquetina nigrescens* can be incorporated into evidence-based clinical practice. Future studies should prioritize phytochemical standardization, isolation of active constituents, and elucidation of molecular mechanisms underlying its reproductive and metabolic effects. Investigations should also evaluate its influence on insulin signaling, steroidogenic pathways, inflammatory mediators, and ovarian gene expression. Long-term toxicity, reproductive safety, herb–drug interactions, and pharmacokinetic studies are equally essential. Most importantly, well-designed randomized clinical trials are needed to establish efficacy, optimal dosing, safety, and cost-effectiveness in women with PEMOS, particularly within resource-limited settings.

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Competing interests

All authors of this paper declare that there is no conflict of interest related to the content of this manuscript.

Declaration of Generative AI and AI-Assisted Technologies in the manuscript preparation process

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