



T.C.
EGE UNIVERSITY
Faculty of Pharmacy



**AN OVERVIEW OF SPEARMINT:
THERAPEUTIC EFFECTS, IMPORTANCE IN
HERBAL MEDICINE, AND IMPACTS ON THE
ENDOCRINE SYSTEM, PARTICULARLY
REPRODUCTIVE HEALTH**

Bachelor's Degree Thesis

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İzmir
2025

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Throughout the course of this thesis, I have gained invaluable knowledge and techniques in academic research and literature review. Beyond the specific focus of my study, I have also developed a range of skills, fostered by my advisor's extensive expertise, passion for teaching, and my own curiosity and eagerness to learn.

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This thesis is lovingly dedicated to my dearest mother, who has always been my greatest supporter throughout my life.

İzmir,
28.06.2025

Adı SOYADI
Ferhat UYGUN

Abstract

Spearmint (*Mentha spicata*) has drawn increasing scientific interest due to its potential hormonal effects, particularly in reducing elevated androgen levels. Reports of improved symptoms in women with androgen-related conditions following regular spearmint consumption have prompted a closer examination of its phytochemical composition and pharmacological properties.

This thesis provides a focused review of spearmint's role in hormonal regulation, with an emphasis on its relevance to conditions such as polycystic ovary syndrome (PCOS) and hirsutism. In particular, Chapter 5.4 presents an original compound-based analysis that links specific constituents-such as rosmarinic acid, carvone, and certain flavonoids-to reported anti-androgenic activity.

While existing clinical data remain limited, this study synthesizes current findings and highlights potential mechanisms of action that warrant further research. In addition to hormonal effects, the broader pharmacological profile of spearmint-including its antioxidant and antimicrobial properties-is also discussed. The thesis aims to contribute to ongoing discussions about plant-based approaches to endocrine health and to support future investigations into the therapeutic potential of spearmint.

Keywords;

Spearmint, PCOS, Hormonal regulation, *Mentha spicata*, Anti-androgenic effect, Bioactive compounds

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Abbreviations

PCOS	: Polycystic ovary syndrome
EDCs	: Endocrine-disrupting chemicals
AFAB	: Assigned female at birth
AMAB	: Assigned male at birth
ROS	: Reactive oxygen species
DHEA	: Dehydroepiandrosterone
BPA	: Bisphenol A
LH	: Luteinizing Hormone
FSH	: Follicle-Stimulating Hormone
DHT	: Dihydrotestosterone

1. Introduction

Hormonal homeostasis, the stable balance of hormone levels in the body, plays a vital role in regulating key physiological systems such as metabolism, reproduction, immune response, and emotional health. Disruptions in this balance can lead to a range of health conditions, including thyroid disorders, diabetes, and reproductive issues (Badiu, 2019). One well-known example is polycystic ovary syndrome (PCOS), which is characterized by elevated androgen levels, insulin resistance, and menstrual irregularities. Such imbalances also affect other body systems, potentially contributing to metabolic dysfunction, mood disturbances, and cardiovascular problems (Azziz et al., 2016).

In particular, hormone-related disorders that affect women's health have gained increasing attention due to their prevalence and complex nature. Conditions such as PCOS, endometriosis, and hormonal infertility have a profound impact not only on reproductive capacity but also on psychological well-being and long-term metabolic health. PCOS alone affects an estimated 8–13% of women of reproductive age worldwide, making it one of the most common endocrine disorders among women (Teede et al., 2018). Despite its prevalence, effective and targeted treatment options remain limited, especially for those seeking alternatives to conventional hormonal therapies. This highlights the importance of exploring additional approaches that are both effective and better tolerated.

Understanding the causes of hormonal dysregulation is essential for developing such strategies. Environmental factors-such as endocrine-disrupting chemicals (EDCs) found in plastics, pesticides, and industrial waste-can interfere with hormone production and function. Compounds like bisphenol A (BPA), phthalates, and PCBs may mimic or block natural hormones, disturbing hormonal balance (Gore et al., 2015). Additionally, factors like poor diet, chronic stress, and lack of physical activity can further increase the risk of hormonal imbalances.

Alongside these influences, medicinal plants have gained attention for their potential to support hormonal health. *Mentha spicata*, commonly known as spearmint, is one such plant that has shown promise due to its potential anti-androgenic effects. Early studies suggest that spearmint may help reduce elevated testosterone levels, particularly in women with PCOS or hirsutism (Akdoğan et al., 2007). This may be attributed to its bioactive compounds, such as rosmarinic

acid, carvone, and flavonoids, which are thought to interact with hormonal pathways and modulate hormone activity (McKay & Blumberg, 2006).

This thesis presents a comprehensive review of spearmint, focusing on its chemical composition, pharmacological properties, and potential applications in hormonal disorders. A particular emphasis is placed on conditions characterized by elevated testosterone levels in women, including PCOS and hirsutism. Of special importance is Chapter 5.4, *Spearmint and Its Effects on Hormonal Balance*, which offers an original literature-based analysis of spearmint's bioactive compounds. Through a targeted keyword search focusing on hormone- and fertility-related terms, this section investigates compounds such as caffeic acid, gallic acid, and various flavonoids, and discusses their potential roles in hormonal regulation. This chapter represents the central analytical contribution of the thesis.

In addition to hormonal effects, the thesis also explores the antioxidant, anti-inflammatory, and antimicrobial properties of spearmint, providing a broader view of its therapeutic relevance. By bringing together current scientific findings, this study aims not only to summarize the existing knowledge but also to offer a foundation for future research into plant-based approaches for hormonal health. It aspires to highlight spearmint's potential role in integrative treatment strategies while acknowledging the need for further investigation into its safety, efficacy, and clinical applications.

2. Hormonal imbalances in the human organism

An excess or deficiency of hormones in the bloodstream can result in a hormonal imbalance, which may contribute to a wide array of symptoms and health disorders. These can include fatigue, weight gain, mood disturbances, infertility, and other conditions. Since hormones play a critical role in regulating key physiological functions such as growth, metabolism, reproduction, and emotional well-being, any disruption in their levels can significantly impact overall health. Hormonal imbalances may arise due to factors such as chronic stress, pharmacological interventions, underlying medical conditions like diabetes or thyroid dysfunction, as well as lifestyle factors, including dietary habits and physical activity (Cleveland Clinic, 2022).

In individuals assigned female at birth (AFAB), imbalances in the sex hormones oestrogen and progesterone, which are primarily produced by the ovaries, may occur. Additionally, elevated levels of testosterone and androgens can also contribute to hormonal dysregulation. These imbalances can result in various clinical symptoms, including acne on the face, chest, or upper back, hair loss, heavy menstrual bleeding, hirsutism (excess body hair), infertility, irregular menstrual cycles, polycystic ovary syndrome (PCOS), and reduced libido (Akdogan et al., 2004; Akdoğan et al., 2007; Cleveland Clinic, 2022). In both sexes, reduced fertility is a significant outcome of hormonal imbalances, the consequences of which particularly affect developed countries.

2.1. Polycystic ovary syndrome

Polycystic Ovary Syndrome (PCOS), also known as Stein-Leventhal syndrome, is an endocrine disorder characterized by hormonal imbalance, particularly involving hyperandrogenism and ovulatory dysfunction (Knochenhauer et al., 1998; Nagarathna et al., 2013). It is one of the most common endocrine disorders affecting women during their reproductive years. Prevalence varies according to race and ethnicity. Prevalence of PCOS varies based on both ethnic background and the diagnostic criteria applied: it is reported as 6% (95% CI: 5–8%) based on NIH criteria (18 studies), 10% (95% CI: 8–13%) according to the Rotterdam criteria (15 studies), and 10% (95% CI: 7–13%) using the AE-PCOS Society criteria (10 studies) (Bozdag et al., 2016). These variations reflect not only differences in population genetics and lifestyle but also in diagnostic methodology. PCOS is often associated with clinical features such as irregular menstrual cycles, acne, insulin resistance, anovulation, and varying degrees of obesity,

observed in 30% to 75% of cases (Gambineri et al., 2002; Ehrmann, 2005). Notably, insulin resistance may develop independently of obesity, indicating an intrinsic metabolic component in the syndrome.

The diagnosis of PCOS is established following the exclusion of other endocrine or metabolic disorders that may cause menstrual irregularities or androgen excess. According to internationally recognized criteria, a diagnosis can be made when at least two of the following three features are present: (1) oligoovulation or anovulation, typically manifesting clinically as oligomenorrhea or amenorrhea; (2) elevated levels of circulating androgens (hyperandrogenemia) or clinical signs of androgen excess (hyperandrogenism), such as hirsutism or acne; and (3) polycystic ovarian morphology as detected via ultrasonography. These criteria emphasize the functional nature of the syndrome, indicating that the presence of polycystic ovaries is not required for diagnosis, and conversely, their presence alone is insufficient to establish the diagnosis (Azziz et al., 2006; Fauser et al., 2004). Hence, understanding the interplay of metabolic, hormonal, and structural components is essential for accurate diagnosis and management of PCOS.

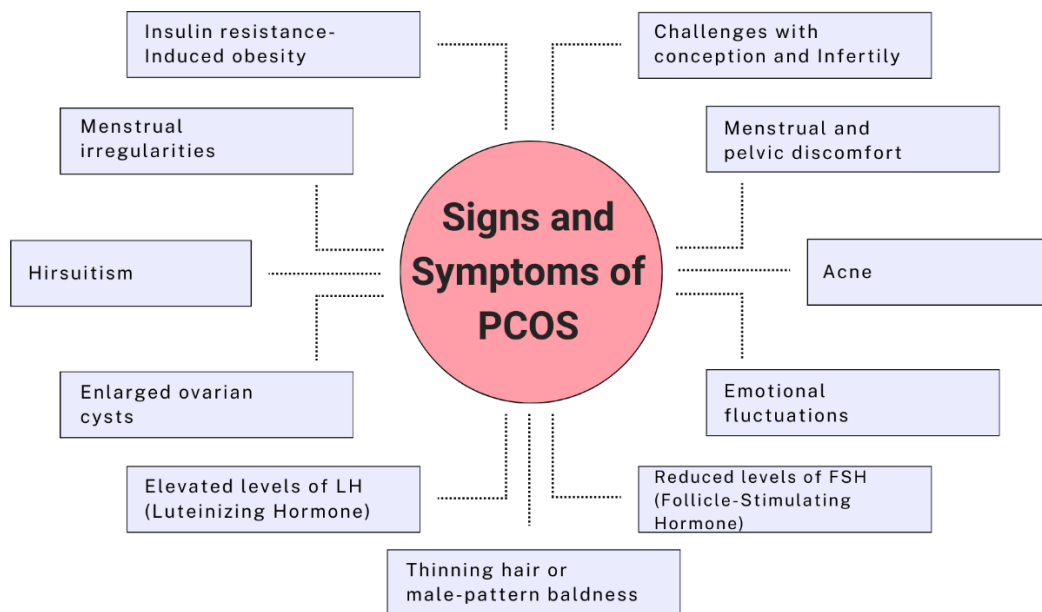


Figure 1. Sign and Symptoms of PCOS

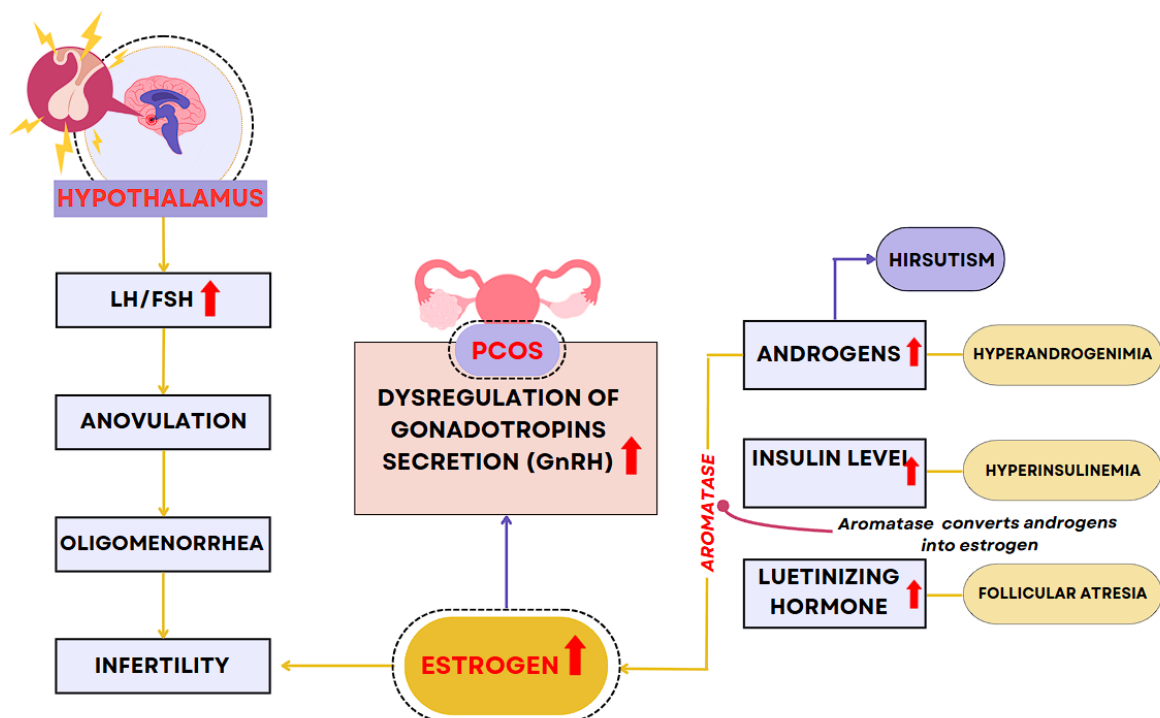


Figure 2. Hormonal imbalances related to PCOS

2.2. Male infertility

In individuals assigned male at birth (AMAB), an imbalance in testosterone, primarily produced by the testes, as well as other sex hormones, can lead to several clinical manifestations. These may include a reduction or loss of body hair, erectile dysfunction (ED), the development of gynecomastia (enlarged breast tissue), infertility, diminished libido, and a decrease in muscle mass (Cleveland Clinic, 2022).

Male infertility and diminished libido are significant issues affecting both the physical and mental health of men. Approximately 1 in 7 couples experience infertility, which is defined as the inability to conceive after having regular, unprotected sex for a year or more. Male infertility is a factor in nearly half of these cases (Anawalt, 2013). Causes of male infertility include low sperm production, impaired sperm function, or obstructions that hinder sperm delivery. Various factors such as illnesses, injuries, chronic health conditions, lifestyle choices, and other environmental influences may also play a role in male infertility.

2.3. The role of endocrine disruptors

Diet may also affect fertility both in men and women. Most attention is focused on endocrine disruptor compounds, because even in small amounts they have very marked effects on the endocrine system. These compounds are typically not natural components of our food but occur as contaminants in processed foods. The chemical similarity between many endocrine disruptors (EDs) and gonadal hormones makes the reproductive system particularly susceptible to their effects. EDs have the ability to bind to endocrine receptors, disrupting hormonal signals and posing a threat to the normal functioning of the endocrine system. For example, Bisphenol A (BPA) is a xenoestrogen, a plastic component that is currently widely used in everyday items, exposes many people in various ways. This compound is found in many plastic products, kitchen utensils, canned foods, and many other areas. It can exposure with way of ingestion, inhalation and transdermal. BPA can bind to receptors by mimicking the binding sites of oestradiol. Many EDs produce synergistic or antagonistic effects, frequently disrupting oestrogen receptors (ER) or androgen receptors (AR). Additionally, these endocrine disruptors (EDs) significantly reduce the quality of spermatogenesis in men and decrease sperm genetic quality. Moreover, they can cause epigenetic disorders that may lead to hereditary abnormalities (Lahimer et al., 2023; Silva et al., 2023).

3. Spearmint as a potential endocrine disruptor

When speaking about EDs, less attention is paid to foods that have long been widely consumed around the world, and also to plants that are used as medicinal plants and food crops. One such plant of spearmint, a medicinal plant that has been consumed traditionally as a tea for its pleasant taste in certain parts of Türkiye. A scientific article published in 2004 drew attention to the potential endocrine disrupting effects of spearmint. A survey revealed that a significant number of male patients living in Yenışarbademli sought treatment for low libido. It was discovered that these symptoms were observed in patients who drank spearmint tea regularly. Later laboratory experiments revealed that spearmint tea had spermatogenic activity in rats (Akdoğan et al., 2007). This surprising result draws attention to questions about the safety of spearmint, but this effect also raises the possibility of its possible therapeutic use through possible effects on the endocrine system.

The anti-androgenic effects of spearmint may not only lead to potential side effects but also offer therapeutic benefits. In females, these effects can be utilized in the management of PCOS-related symptoms. This thesis therefore examines the current body of research in this area, as this indication may represent one of the potential future applications of spearmint.

4. Botany of spearmint

Mentha spicata L. (Lamiaceae, synonym names: *M. crispata*, *M. viridis*, *M. chalepensis* Mill., *M. microphylla* K.Koch), commonly found in Europe and Southern Asia, stretching from France to Southern China. Typically grows between 30 and 100 cm tall, with either smooth or slightly hairy stems. Its leaves are smooth or covered with fine grey hairs, and it is a perennial herbaceous plant. The plant spreads via rhizomes, and its square-shaped stems bear leaves measuring 5-9 cm in length and 1.5-3 cm in width. Spearmint flowers are small, pink or white in colour, measuring 2.5-3 mm long, and the seeds range from 0.62 to 0.90 mm in size. The pale blue flowers are arranged in long, narrow spikes at the tips of its branches, and the plant thrives in moist environment (Joshi et al., 2022).



Figure 3. Zoomed view of spearmint

(<https://www.traditionalmedicinals.com/blogs/herb-library/spearmint>)



Figure 4. General look of spearmint

(Govindarajan et al., 2012)

Classification/Taxonomy:

Kingdom: - Plantae
Clade: - Tracheophytes
Clade: - Angiosperms
Clade: - Eudicots
Clade: - Asterids
Order: - Lamiales
Family: - Lamiaceae
Genes: - *Mentha*
Species: - *M. spicata* L.

Spearmint thrives in environments with rich, moist soils and prefers a climate that ranges from partial shade to full sun. It grows best in loam soil, a blend of sand, silt, and clay. The roots of spearmint can spread aggressively, so it is often planted in containers to prevent uncontrolled growth. Typically planted in December, the plant's first harvest is ready by the end of April, with a second harvest possible around 60-70 days later (Joshi et al., 2022).

In Türkiye, it grows on the Anamas plateau in Yenışarbademli, Isparta. This region, characterized by its rainy climate, is located at an altitude of 1800 to 2400 meters above sea level. This region, characterized by its rainy climate, is located at an altitude of 1800 to 2400 meters above sea level (Akdogan et al., 2004).

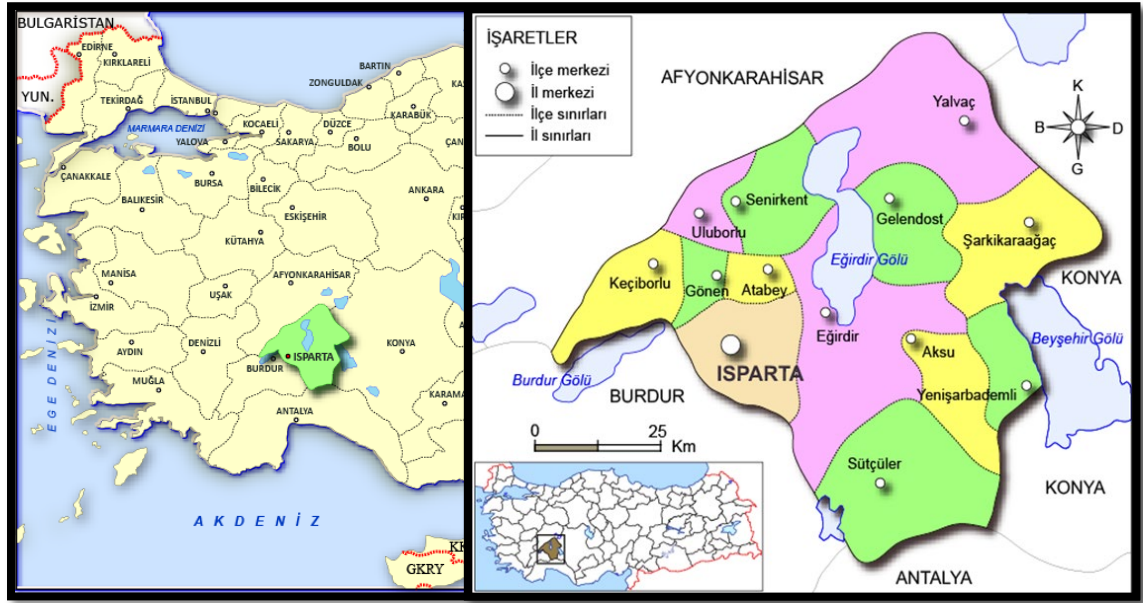


Figure 5. Isparta in map of Türkiye and location of Yenişarbademli district in Isparta

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5. Phytochemistry of Spearmint

Through various studies, numerous compounds have been identified in spearmint, including phenolic acids, flavonoids, lignans, and essential oil components. The concentrations and proportions of these compounds vary depending on the region where the plant is cultivated.

5.1. Phenolic acids

Phenolic acids are considered important active compounds in the plant (Fatih et al., 2017). These compounds are known for their antioxidant properties and play various roles in plant defence, growth, and development, as well as contributing to the colour, flavour, and potential health benefits of plant-based foods and medicines. Previous research has demonstrated that the primary metabolites are caffeic acid and rosmarinic acid. Additionally, the plant contains other compounds such as p-coumaric acid, cinnamic acid, ferulic acid, gallic acid, oleanolic acid, sinapic acid, phloretic acid, and vanillic acid, among others (Mahendran et al., 2021).

5.2. Flavonoids and lignans

Flavonoids, the major dietary polyphenols, are classified into six groups, including flavonols, flavanones, anthocyanins, flavonols, isoflavones, and flavones. Flavonoids are a type of polyphenolic compound that help plant coloration, protection from UV light and defence against pathogens. Beyond their importance for plant health, flavonoids are valuable in human diets for their potential to reduce inflammation, support heart health and protect against oxidative stress.

A total of 22 types of flavonoids have been isolated from *Mentha spicata*. Key flavonoids isolated from the plant include cirsilineol, catechin, apigenin, kaempferol, myricetin, epicatechin, and naringenin. Additionally, compounds such as naringin, 5-dimethyl sinensetin, hesperidin, didymin, linarin, luteolin-7-*O*-glucoside, 5-desmethoxynobletin, diosmin, luteolin, desmethylnobletin, thymusin, sideritoflavone, thymonin, quercetin, and rutin are present. Two novel lignan compounds have been isolated from *Mentha spicata*, named spicatolignan A and spicatolignan B (Mahendran et al., 2021; Zheng, Chen, Gao, Wu, & Wu, 2007).

5.3. Essential oil components

The plant is rich in essential oil, with the major component *R-carvone*, which gives spearmint its characteristic aroma, making it easily identifiable (Joshi et al., 2022). *M. spicata* contains between 0.04% to 2.1% volatile oils, with carvone (29% to 74%) being the most abundant component, followed by limonene (4% to 24%) and cineole (3% to 18%) (Akdogan et al., 2004; Baser, 1993). Essential oils from *Mentha spicata* have been extracted from various parts of the plant using a range of methods, most commonly hydrodistillation. The composition of these essential oils includes approximately 67.2% oxygenated monoterpenes, 7.5% sesquiterpene hydrocarbons, 20.8% monoterpene hydrocarbons, 1.2% oxygenated sesquiterpenes, and 1.7% other compounds. Among the monoterpenes, carvone (22–73%) and limonene (8–31%) are the dominant constituents. Further essential oil components identified in this plant include carvone, piperitone, limonene, menthol, myrcene, beta-pinene, linalool, and caryophyllene (Laggoune et al., 2016; Mahendran et al., 2021).

In a separate study, two novel monoterpenoid glycosides, identified as picatoside A and spicatoside B, were discovered within the non-volatile fraction (J. Zheng et al., 2003).

5.4. Compounds that may have a role in the effect of spearmint on the hormonal system

Although the existing research has not explained the endocrine effects of spearmint, there are experimental results regarding some of its components. While it would not be decisive or accurate to directly attribute these findings to spearmint, sharing them is important to provide insight. While not all constituents have been extensively studied, we will highlight examples of whose effects might directly or indirectly be associated with the endocrine effects of spearmint.

While valuable studies on spearmint exist, there is a notable absence of significant work investigating its mechanism of action. In response, the study investigates to take a pioneering step by conducting a comprehensive database search, focusing on the compounds found in spearmint. Using PubMed, we searched the keywords “*compound* and PCOS,” “*compound* and fertility,” “*compound* and infertility,” and “*compound* and hormone” for each compound present in spearmint. From this search, twenty relevant articles were identified, reviewed, and systematically incorporated into our thesis. The motivation for initiating this analysis and

including it in our thesis stemmed from recognizing the lack of studies on the topic we sought to explore.

Caffeic Acid

In women with PCOS, high levels of androgens and blood sugar can cause oxidative stress in the ovaries. This leads to an increase in harmful molecules called reactive oxygen species (ROS), which damage the ovarian tissue. Oxidative stress plays a significant role in the development of PCOS. When there is too much ROS and not enough antioxidants to balance them, it can worsen symptoms like high androgen levels and insulin resistance. Over time, this stress also causes inflammation, which further harms the ovaries and makes PCOS symptoms worse. Reducing oxidative stress by clearing out ROS may help improve PCOS symptoms. As a result of the research conducted, caffeic acid, a phenolic compound with antioxidant properties, has been shown to protect ovarian KGN cells from H₂O₂-induced oxidative stress and apoptosis. Furthermore, treatment with caffeic acid improves ovarian structure, balances steroid hormone production, and restores regular estrous cycles in rats with DHEA-induced PCOS. It also boosts insulin sensitivity, reduces glucose levels, mitigates oxidative stress-related metabolic disturbances, and aids in alleviating ER stress. These findings indicate that caffeic acid holds potential as a therapeutic approach for addressing PCOS-related complications (Chiang et al., 2023).

In another study, caffeic acid phenethyl ester (CAPE) was evaluated for its ability to mitigate cadmium (Cd)-induced damage to the male reproductive system. Mice were divided into four groups of 10: Group I (control) received distilled water, while Groups II, III, and IV were injected intraperitoneally with Cd at 3 mg/kg body weight for four consecutive days. Group III received saline, and Group IV was treated with CAPE at 3 mg/kg/day intraperitoneally for six days. The findings showed that CAPE significantly improved fertility parameters, enhanced spermatogenesis, and reduced the percentage of apoptotic cells. Additionally, levels of metalloprotease-3 (MMP-3) and vascular endothelial growth factor (VEGF) were significantly reduced. These results indicate that CAPE has a protective effect, counteracts the toxic effects of Cd, and prevents testicular damage (Abdallah & El-Refaei, 2022).

Rosmarinic acid

In a study conducted to evaluate the efficacy of rosmarinic acid (RA) on letrozole-induced polycystic ovary syndrome (PCOS) in adult female rats, the potential underlying molecular mechanisms were also explored. Forty female rats were assigned to four groups: a control

group, a RA group (50 mg/kg orally for 21 days), a PCOS group (induced by administering letrozole 1 mg/kg orally for 21 days), and a RA -PCOS group, which received RA following PCOS induction. The results revealed that PCOS caused a significant increase in serum luteinizing hormone (LH) and testosterone levels, along with an elevated LH/follicle-stimulating hormone ratio, and a notable reduction in serum oestradiol and progesterone levels. Furthermore, there was a marked upregulation in the expression of inflammatory markers such as tumour necrosis factor- α (TNF- α), interleukin-1 β , monocyte chemotactic protein-1, and vascular endothelial growth factor mRNA in the ovarian tissue. Histological analysis showed multiple cystic follicles in the ovarian cortex, with a significantly thin granulosa cell layer, vacuolated granulosa and theca cell layers, and desquamated granulosa cells. Additionally, increased immune expression of TNF- α and caspase-3 was observed in the ovarian cortex. Notably, treatment with RA alleviated both the biochemical and histopathological changes associated with PCOS. In conclusion, this study suggests that RA effectively mitigates the effects of letrozole-induced PCOS, likely through its anti-inflammatory and anti-angiogenic properties, which contribute to the improvement of biochemical and histopathological alterations related to the condition (Shalaby et al., 2024).

In another research also shows that RA has fertility stimulator effect. RA enhanced the progressive and overall motility of sperm while preserving the integrity of the acrosomal and plasma membranes (Alagawany et al., 2017; Luño et al., 2014).

Oleanolic acid

In the experiment for oleanolic acid, quite interesting results were obtained. A suspension of oleanolic acid in polyvinylpyrrolidone was administered orally to adult male Wistar rats for 30 days. Following this treatment, half of the rats underwent a 14-day drug withdrawal period. Control rats were given polyvinylpyrrolidone alone. All male rats were mated with untreated females. Males treated with oleanolic acid failed to impregnate females, while 100% pregnancy success was achieved by females mated with both control and oleanolic acid-withdrawn males. Analysis of sperm motion using the Sperm Motility Quantifier (SMQ) revealed significant differences in linearity ($P < 0.001$) and wobble ($P < 0.01$) between treated and control groups, although curvilinear velocities were not significantly affected ($P > 0.05$) across the groups. Differences in sperm motility patterns were confirmed by variations in kinematic parameters.

These findings demonstrate that a 30-day administration of oleanolic acid induces reversible sterility in male Wistar rats without impairing libido. Future research should focus on evaluating

the contraceptive potential of oleanolic acid in non-human primate models and further investigate its effects on sperm motility, with particular attention to membrane function and reproductive hormone levels (Mdhluli & Van Der Horst, 2002).

Gallic acid

A mouse model of polycystic ovary syndrome (PCOS) was established through oral gavage administration of letrozole to replicate symptoms observed in women with the condition. The study also investigated the ameliorative effects of gallic acid (GA) on PCOS using this *in vivo* model. The findings suggest that GA holds potential as a therapeutic agent for PCOS, as it demonstrated positive effects on hormonal imbalances, estrous cycle irregularities, and other reproductive abnormalities associated with reduced adiponectin levels and hyperandrogenism. Adiponectin appears to play a central role in the pathophysiology of PCOS. Furthermore, GA was found to mitigate inflammation-related comorbidities induced by letrozole treatment, while enhancing mRNA expression levels of CYP11a, CYP19a1, KITL and PTGS2. These improvements contribute to the reduction of both endocrine and metabolic disturbances associated with PCOS (Ul-Haq Shah et al., 2022).

Vanillic acid

In an experiment, polycystic ovary syndrome (PCOS) was induced in female Wistar rats through oral administration of letrozole (1 mg/kg) in carboxymethoxycellulose (1% w/v) for 21 days. Following the induction phase, the treatment groups were administered vanillic acid at doses of 25, 50, and 100 mg/kg orally for 15 days. The standard group was treated with clomiphene citrate (1 mg/kg). Rats that were not treated served as the negative control group. The parameters evaluated included body and ovary weights, blood glucose, lipid profile, hormonal levels (luteinizing hormone, follicle-stimulating hormone, and testosterone), oxidative stress markers (superoxide dismutase, reduced glutathione, catalase, and malonaldehyde), and ovarian histopathology. Statistical significance was determined at $p < 0.05$. The study revealed that vanillic acid exhibited a dose-dependent response, with the highest administered dose (100 mg/kg) demonstrating significant improvements ($p < 0.001$) in reducing body and ovary weights, restoring hormonal balance, lowering blood glucose and lipid levels ($p < 0.01$), and alleviating oxidative stress ($p < 0.001$). Histopathological analysis revealed fewer cystic follicles and the emergence of healthy follicles, effects comparable to clomiphene citrate. These findings suggest vanillic acid effectively mitigates letrozole-induced PCOS and

may be a promising alternative to treatments with significant side effects (V Gadhave et al., 2024).

Ferulic acid

DHEA-treated mice were administered low-dose ferulic acid (FA) (FA1 group: 50 mg/kg) or high-dose FA (FA2 group: 100 mg/kg) for 20 days prior to sampling for the analysis of ovarian function. Ovarian morphology, body weight, uterine and ovarian wet weights, and sex hormone levels were evaluated across the control, PCOS, FA1, and FA2 groups. Histological examination with H&E staining revealed that FA treatment reduced the number of cystic and atretic follicles while promoting the development of antral follicles and corpus lutea in PCOS ovaries. Both high- and low-dose FA treatments significantly decreased body weight as well as uterine and ovarian wet weights. Moreover, serum testosterone levels were significantly reduced in FA-treated mice compared to the PCOS group, although FA treatment had no impact on the estrous cycle. These findings demonstrate that FA alleviates ovarian dysfunction and reduces pathological damage to ovarian tissues in PCOS mice.

The regulatory effects of FA on glucose and lipid metabolism in PCOS mice were also investigated. FA treatment markedly improved glucose tolerance and significantly reduced fasting glucose, serum insulin, and HOMA-IR levels in PCOS mice. Furthermore, FA lowered BMI, Lee's index, total cholesterol (TC), and low-density lipoprotein cholesterol (LDL-C) levels. High-dose FA significantly increased high-density lipoprotein cholesterol (HDL-C) levels while decreasing triglyceride (TG) levels. In contrast, although low-dose FA reduced TG and HDL-C levels compared to the PCOS group, these changes were not statistically significant (Su et al., 2023).

Quercetin

Quercetin (QUR) is a natural flavonoid renowned for its antioxidant, anti-inflammatory, and anti-metabolic properties. It is widely present in Chinese herbal medicines, fruits, green leafy vegetables, and numerous seeds. *In vitro* studies have highlighted QUR's ability to mitigate oxidative stress and prevent apoptosis in ovarian cells. Furthermore, extensive research has shown that QUR effectively reduces serum testosterone, luteinizing hormone (LH), the LH/FSH ratio, fasting blood glucose, fasting insulin, HOMA-IR, and blood lipid levels in both PCOS patients and animal models. Animal studies have provided additional evidence, demonstrating that QUR enhances the number of preantral, antral, and preovulatory follicles

and increases corpora lutea counts, while concurrently decreasing atretic follicle numbers and preventing cyst formation in PCOS rats. The mechanisms responsible for these beneficial effects are believed to include anti-insulin resistance, anti-inflammatory activity, antioxidative stress, anti-apoptosis, and the downregulation of CNP/NPR2 expression.

Scientists have yet to develop a reliable cell model to mimic PCOS, limiting research on its development and how QUR functions in this context. While QUR is known to balance sex hormones, its role in addressing insulin resistance (IR) remains debated and needs further investigation (C. Ma et al., 2022).

Myricetin

A 3-week intervention with myricetin exhibited profound therapeutic effects in a dehydroepiandrosterone (DHEA)-induced mouse model of polycystic ovary syndrome (PCOS). The treatment significantly enhanced metabolic capacity and insulin sensitivity through the activation of brown adipose tissue (BAT). Additionally, myricetin facilitated the restoration of ovarian function, marked by an increased number of corpus lutea, a reduction in ovarian cysts, and the normalization of the estrous cycle. Hormonal homeostasis was also achieved, with luteinizing hormone (LH) levels restored to physiological norms. Collectively, these results demonstrate that myricetin effectively mitigates both reproductive and metabolic dysfunctions in PCOS, underscoring its potential as a groundbreaking therapeutic approach for managing this complex disorder (N. Zheng et al., 2024).

Quercetin, gallic acid, p-coumaric acid, ferulic acid, and cinnamic acid

High-performance liquid chromatography (HPLC) analysis of the standardized aqueous methanolic extract of bitter melon identified several bioactive phytochemicals, including quercetin, gallic acid, benzoic acid, chlorogenic acid, syringic acid, p-coumaric acid, ferulic acid, and cinnamic acid.

A total of 25 Swiss albino adult female rats (120–130 g) were procured and categorized into two groups: a control group (n = 5) and an experimental group (n = 20). Polycystic ovary syndrome (PCOS) was induced in the experimental group by administering letrozole (1 mg/kg p.o.) daily for four weeks. The successful induction of PCOS was confirmed through vaginal smear cytology analysis using microscopy, a technique that identifies the stages of the estrous cycle and helps detect hormonal imbalances characteristic of PCOS. Subsequently, the PCOS-induced rats were subdivided into four groups: one serving as the untreated PCOS control

group, while the remaining three groups received treatments of standardized bitter melon extract (500 mg/kg p.o.), a combination of bitter melon and metformin (500 mg/kg p.o.), or metformin alone for an additional four weeks. At the end of the treatment period, all rats were euthanized during the diestrus stage. Ovaries were excised, fixed in 10% buffered formalin for histopathological analysis, and blood samples were collected via direct cardiac puncture for biochemical evaluation.

Histopathological examination of ovaries revealed numerous cystic follicles (9–10) in the untreated PCOS group, while treatment groups exhibited developing and mature follicles, indicating improved ovarian health and function. Developing follicles reflect active folliculogenesis, a process critical for ovulation, while mature follicles signify readiness for ovulation and subsequent potential fertility restoration. Hormonal analysis indicated a significant ($p < 0.001$) reduction in luteinizing hormone (LH) surge, insulin, and testosterone levels, alongside an improvement in follicle-stimulating hormone (FSH) levels. Furthermore, lipid profile and antioxidant enzyme status showed marked ($p < 0.001$) improvement across the treatment groups. These findings validated the efficacy of bitter melon as an insulin sensitizer and ovulation enhancer, substantiating its potential as a therapeutic agent for managing PCOS (Hussain et al., 2022).

Apigenin

One study explored the therapeutic potential of apigenin in a rat model of polycystic ovary syndrome (PCOS). A total of 28 rats, weighing 180–250 g, were divided into four groups. Seven rats served as untreated controls, while PCOS was induced in 21 rats through a single injection of oestradiol valerate. These PCOS rats were further divided into three treatment groups: one received a vehicle, and the other two were treated with apigenin at doses of 10 mg/kg and 20 mg/kg for 14 days. Ovarian histology was assessed to evaluate follicular structures and collagen density, while immunohistochemical analysis measured endothelial and periendothelial cells. Angiogenesis-related gene expression was analysed using molecular methods. Apigenin treatment partially restored normal follicular development, reduced the number of cystic follicles, and increased the presence of corpora lutea. It also decreased collagen density in polycystic ovaries. Additionally, apigenin suppressed ovarian angiogenesis by reducing endothelial and periendothelial cell numbers and downregulating the expression of vascular endothelial growth factor (VEGF) and its receptor VEGF R2 (KDR). In conclusion, apigenin improved ovarian histological integrity and follicular dynamics in PCOS rats, primarily by

inhibiting VEGF signalling and reducing endothelial cell proliferation. These findings highlight apigenin's potential as a therapeutic agent for managing PCOS-related ovarian dysfunction (Samani et al., 2024).

Luteolin

One study examined the effects of luteolin and luteolin-7-methylether on oestrogen production and their potential roles in the treatment of polycystic ovary syndrome (PCOS). Oestrogen production in human ovarian granulosa cells was analysed using ELISA, and the signalling pathways regulating the aromatase enzyme were investigated through Western blot analysis. Transcriptomic analysis revealed that these compounds significantly influenced the MAPK signalling pathway. In granulosa cells stimulated with follicle-stimulating hormone, luteolin effectively reduced oestrogen production by suppressing aromatase expression mediated by cAMP response element-binding protein (CREB). Mechanistically, both luteolin and luteolin-7-methylether targeted TPL2 (tumour progression locus 2) to inhibit the MKK3/6-p38 MAPK-CREB signalling pathway. In animal models, these compounds effectively alleviated PCOS symptoms. This study highlights the previously unrecognized role of TPL2 in oestrogen regulation and suggests that luteolin and its derivative could be promising therapeutic agents for PCOS. These findings provide a foundation for the development of these compounds as safe and effective treatments (Shi et al., 2024).

p-Coumaric acid, gallic acid, and kaempferol

A study investigating the standardized aqueous ethanolic extract of *Rubia cordifolia* (SERC) through HPLC analysis identified key phytochemicals, including p-coumaric acid, gallic acid, and kaempferol (we cite this research here because there is an overlap with the active constituents of spearmint). Thirty adult female rats were divided into two main groups: a normal control group (5 rats) and a disease-induced group (25 rats). Polycystic ovary syndrome (PCOS) was induced in the disease group by administering letrozole (1 mg/kg orally) for six weeks. Following induction, the disease-induced group was further subdivided into five groups: a PCOS control group, a metformin-treated group (20 mg/kg), and three SERC-treated groups receiving doses of 200, 400, and 600 mg/kg, respectively. Histopathological analysis demonstrated that PCOS induction led to a decline in the corpus luteum and developing follicles, along with an increase in cystic follicles. In contrast, treatment with SERC significantly improved ovulation by increasing the number of primary and developing follicles.

SERC administration also reduced serum insulin, luteinizing hormone (LH), and testosterone levels while elevating follicle-stimulating hormone (FSH), oestrogen, and progesterone levels. Moreover, SERC enhanced oxidative stress markers in the liver, improved the lipid profile, and normalized liver function parameters. These results suggest that SERC is effective in mitigating PCOS, likely through restoring aromatase activity and reducing ovarian inflammation (J. Zhang et al., 2024).

In summary, our goal in presenting these findings is to contribute to understanding the PCOS-improving and hormone-regulating effects of spearmint. These effects may be related to the experimental findings on individual compounds, as detailed above. Alternatively, they might result from the synergistic interaction of these compounds. To confirm these hypotheses, future studies should include more detailed mechanistic and animal experiments as well as clinical studies.

6. Traditional and folk medicinal uses

Spearmint has been traditionally used in folk medicine for treating gastrointestinal issues, respiratory problems, stomachaches, dandruff, bad breath, chronic bronchitis, and as a sedative, abortifacient, and emmenagogue (Conway & Slocumb, 1979).

More specifically, spearmint has been used in various cultures and regions for different medicinal purposes. For instance, in Pakistan, its decoction has been commonly used for its carminative, antispasmodic, and sedative effects. In Turkey and South Africa, both the infusion and decoction forms of spearmint have been considered treatment options for various ailments, especially respiratory diseases like colds and flu (Asowata-Ayodele et al., 2016; Cakilcioglu & Turkoglu, 2010). In Iran, spearmint, known by various names, has been widely used for numerous purposes, such as a flavouring agent, appetite stimulant, antacid, and for treating nausea, diarrhoea, and as an antihelmintic (Mosaddegh et al., n.d.). In Mexico, it has been employed to relieve colic pain, while in Nepal, its infusion has been used for treating diarrhoea, dysentery, and urinary retention. Additionally, in Nepal, the plant has been chewed in raw form to address diarrhoea and stomach aches. Besides internal applications, spearmint has also been used externally, with its use as a hair tonic noted in Iraq (Ahmad et al., 2016; Mahendran et al., 2021).

7. Preclinical studies

7.1. Antioxidant effects

Spearmint demonstrates notable antioxidant properties, mainly due to its phenolic compounds and key constituents such as eugenol, gamma-tocopherol, caffeic acid, rosmarinic acid, and alpha-tocopherol (Adam et al., 2009; Mkaddem et al., 2009). Air-dried spearmint extracts show peak efficacy during the flowering stage, attributed to higher flavonoid levels (Papageorgiou et al., 2008).

These air-dried spearmint extracts suppress lipid peroxidation, modulate antioxidant enzymes like glutathione-s-transferase and catalase, and outperform mate tea in antioxidant protection (Arumugam & Ramesh, 2009). However, their efficacy decreases under high heat in hydrogenated vegetable oil (Zandi & Ahmadi, 2000). While spearmint generally offers protective effects, it can induce oxidative stress in specific contexts, such as the hypothalamus of rats .

7.2. Antibacterial effects

Despite significant advancements in modern medicine, microbial contamination remains a serious threat to public health. There is a growing trend among consumers to move away from synthetic compounds traditionally used for microbial control in favour of substances with antimicrobial properties. In recent years, natural products have attracted considerable interest as valuable sources of innovative antimicrobials for the treatment of microbial infections and diseases (L.-L. Zhang et al., 2022).

Spearmint essential oil showed potent antibacterial activity, effectively killing bacteria in phosphate-buffered saline and inhibiting the growth of *Helicobacter pylori*, *Salmonella enteritidis*, *Escherichia coli* O157:H7, as well as MRSA and MSSA (Rasooli et al., 2009; Ulbricht et al., 2010) (**Table 1**).

Table 1. Antibacterial effect of spearmint oil and essential oil components

Strains	Component	Inhibitory effects
<i>Escherichia coli</i> <i>Staphylococcus aureus</i>	Carvone	Carvone showed low activity against <i>E. Coli</i> and <i>S. Aureus</i> (Moro et al., 2018).
<i>Escherichia coli</i> <i>Staphylococcus aureus</i>	Carvone	<i>E. coli</i> was strongly inhibited by carvone. Carvone showed no bactericidal activity against <i>S. aureus</i> (Lopez-Romero et al., 2015)
<i>Escherichia coli</i> <i>Staphylococcus aureus</i>	Carveol	<i>E. coli</i> and <i>S. aureus</i> were strongly inhibited by carveol (Lopez-Romero et al., 2015).
<i>Salmonella enterica</i> <i>Listeria monocytogenes</i> <i>Agrobacterium tumefaciens</i>	Carveol	Carveol was the effective compound against the three pathogens (Yang et al., 2020).
<i>Staphylococcus aureus</i> <i>Bacillus subtilis</i> <i>Bacillus cereus</i> <i>Listeria monocytogenes</i> <i>Salmonella typhimurium</i> <i>Escherichia coli</i> O157:H7	<i>Mentha spicata</i> essential oil (the major components being 78.76% carvone, 11.50% limonene and 11.23% β -bourbonene)	The essential oil moderately inhibited the growth of tested strains (Shahbazi & Shavisi, 2016).
<i>Xanthomonas sp</i>	<i>Mentha spicata</i> essential oil (the major components being 56.94% carvone and 11.63% limonene)	The oil exhibited remarkable activity against <i>Xanthomonas</i> sp (Bayar & Küsek, 2018).

7.3. Antifungal effects

Monoterpenes, a class of natural compounds, exhibit antifungal activity through diverse mechanisms. These include disrupting fungal cell membranes, inhibiting cell wall formation, impairing mitochondrial function, and blocking RNA/DNA synthesis or efflux pumps. Such actions make monoterpenes effective antifungal agents (Jager, 2014; L.-L. Zhang et al., 2022).

Carvone, a major component of spearmint essential oil disrupts fungal cell membranes and mitochondria. It inhibits *Aspergillus flavus* growth, reduces biomass and ergosterol levels, and halts aflatoxin production. It also affects *Candida* species by impairing membrane ATPase activity. In agriculture, carvone-rich essential oils from *Mentha spicata* control pathogens in strawberries and citrus fruits. Additionally, it combats dermatophytes like *Trichophyton* and *Microsporum* species (L.-L. Zhang et al., 2022).

Carveol also disrupts fungal membranes, showing activity against *Candida* strains and dermatophytic fungi. Oils like *Cymbopogon martinii* highlight its dermatophytic potential. Dihydrocarvone inhibits pathogens like *Fusarium* and *Candida albicans*, while dihydrocarveol and dihydrocarvyl acetate exhibit limited but notable antifungal effects (Ulbricht et al., 2010; L.-L. Zhang et al., 2022) (Table 2).

Table 2. Antifungal effect of spearmint oil and essential oil components

Strains	Component	Inhibitory effects
<i>Candida parapsilosis</i> <i>Candida tropicalis</i> <i>Candida albicans</i>	(4S)-Carvone	Carvone presented antifungal activity against <i>Candida</i> yeast (Moro et al., 2018).
<i>Candida albicans</i> ATCC 10261 <i>Candida albicans</i> ATCC 44829 <i>Candida albicans</i> ATCC 90028 <i>Candida tropicalis</i> ATCC750	Carvone	Carvone was found to be active against all <i>Candida</i> strains (Samber et al., 2015).

<i>Rhizoctonia solani</i> <i>Helminthosporium solani</i> <i>Phytophthora erythroseptica</i> <i>Fusarium coeruleum</i> <i>Pythium ultimum</i> <i>Phoma exigua</i> <i>Aspergillus flavus</i>	Carvone	Growth of strains were completely (100%) inhibited by carvone (Al-Mughrabi et al., 2013). With carvone, the growth of <i>A. flavus</i> was completely inhibited at a concentration of 1500 $\mu\text{g mL}^{-1}$ (Lasram et al., 2019).
<i>Sclerotinia sclerotiorum</i> <i>Alternaria alternata</i> <i>Fusarium oxysporum</i> <i>Penicillium sp.</i>	Carvone	Carvone inhibited the growth of <i>S. sclerotiorum</i>. (B. Ma et al., 2015). Carvone showed strong fungicidal activity on mycotoxigenic fungi (Morcia et al., 2011).
<i>Candida strains</i>	Carveol	Carveol exerted great antifungal activity against various <i>Candida</i> strains (Montenegro et al., 2019)
<i>Trichophyton sp.</i>	<i>Mentha spicata</i> L. essential oil (the major components being 62.9% carvone and 8.5% limonene)	The essential oil showed antidermatophytic activity, including <i>T. rubrum</i> and <i>T. verrucosum</i> (Piras et al., 2021).
<i>Botrytis cinerea</i>	<i>Mentha spicata</i> essential oil (the major components being 61.71% carvone and 20.22% limonene)	The essential oil showed a reduction of 100% in the disease incidence at a 10% concentration (Oliveira Filho et al., 2021).

7.4. Antiparasitic effect

Spearmint has been shown to possess potent antiparasitic properties. It effectively eliminated over 97% of *Varroa destructor* mites in honeybee colonies without evident toxicity (Ariana et al., 2002). Its essential oil proved lethal to red mites (*Dermanyssus gallinae*) in laboratory tests and served as a repellent in poultry environments (George et al., 2009; Kim et al., 2004). Spearmint has also been used to manage *Meloidogyne* (a type of roundworm) infestations, exhibited insecticidal activity against *Lycoriella ingenua* larvae, demonstrated nematicidal effects on root-knot nematodes, and reduced root galling in cucumber seedlings (Oka et al., 2000; Park et al., 2008; Walker & Melin, n.d.). Additionally, its volatile oils have protected against pests such as the cowpea weevil (*Callosobruchus maculatus*) and the greenhouse whitefly (*Trialeurodes vaporariorum*). Spearmint has also been toxic to mites like *Tetranychus urticae* and *Phytoseiulus persimilis*, as well as the grain weevil (*Sitophilus granarius*) (Choi et al., 2004; Raja et al., 2001). Furthermore, piperitenone oxide, a compound in spearmint, has shown toxic, repellent, and reproduction-inhibiting effects on the malaria vector mosquito *Anopheles stephensi* (Tripathi et al., 2004). However, its effectiveness is not universal; for example, crushed spearmint failed to protect roses from Japanese beetles (Held et al., 2003), and in Brazil, the exotic land snail *Achatina fulica* was observed feeding on spearmint plants .

7.5. Anti-inflammatory effect

Spearmint exhibits notable anti-inflammatory properties, demonstrated through various studies in animal models and *in vitro* experiments. Extracts of spearmint have been shown to alleviate both chronic and acute inflammation in rats by modulating *in vivo* antioxidant activity (Arumugam & Ramesh, 2009). Similarly, spearmint essential oil has been found to inhibit leukocyte migration into the peritoneal cavity of mice, primarily by reducing neutrophil accumulation (Abe et al., 2004). *In vitro* studies reveal that low concentrations of spearmint essential oil (0.0125%) suppress TNF-alpha-induced neutrophil adhesion, an effect also linked to the compound carvone (Abe et al., 2003). Moreover, monoterpenoid glycosides, specifically spicatoside A and spicatoside B, contribute to the anti-inflammatory activity of spearmint (J. Zheng et al., 2003). Collectively, these findings highlight spearmint as a potential natural agent for managing inflammation through diverse mechanisms (Ulbricht et al., 2010).

7.6. Effect on hormone levels

Firstly, when discussing preclinical studies, it is necessary to begin with the research conducted on the effects of peppermint tea on plasma testosterone, FSH hormone, and LH hormone in Wistar albino rats through *in vivo* studies. Because this chapters are the most interesting parts of our idea, which require focus, which served as the foundation for initiating this thesis. Subsequently, we will discuss on the other effects of spearmint and review the related research in the literature.

Forty-eight male Wistar albino rats were acquired (body weight 200 to 250 g) for a study and housed in a temperature-controlled, air-conditioned room set to an average of 24°C. The animals were divided into four groups, each consisting of 12 rats. These groups were further categorized based on the control group and the dosage and type of tea administered: 20 g/L of *Mentha piperita* (peppermint), 20 g/L of *Mentha spicata* (spearmint), and 40 g/L of *Mentha spicata*. The experimental groups showed a significant reduction in plasma total testosterone levels compared to the control group. In contrast, plasma LH levels were significantly elevated in the experimental groups relative to the control. Additionally, the 20 g/L *Mentha piperita* group had significantly higher plasma FSH levels than the control group. Similarly, the 20 g/L and 40 g/L *Mentha spicata* groups exhibited statistically significant increases in plasma FSH levels compared to the control group (Akdogan et al., 2004).

Following up on previous research, another study looked into the effects of spearmint tea on male hormone levels, this time using male albino rats. The doses of spearmint tea were chosen based on a past study (Akdoğan et al., 2004), with three different concentrations: 0 g/L (control), 20 g/L, and 40 g/L.

The rats were divided into these three groups and given the tea for different durations: 15, 25, and 35 days. After each period, the rats were anesthetized and sacrificed, and their androgen-dependent sexual tissues (testes, epididymis, seminal vesicles, and ventral prostate) were weighed. Blood samples were collected to measure serum testosterone, FSH, and LH levels using an immunoassay kit.

The findings were quite notable:

- 15-day group: There were no noticeable changes in the weights of sexual tissues or hormone levels.
- 25-day and 35-day groups: Significant reductions in tissue weights were observed:

- At 20 g/L dose: Testes, epididymis, seminal vesicle, and ventral prostate weights dropped by about 24%, 23%, 25%, and 41%, respectively.
- At 40 g/L dose: The reductions were even more pronounced, with weights decreasing by roughly 42%, 47%, 42%, and 52%, respectively.

One key difference from earlier studies was the effect on hormone levels. While the previous experiments primarily showed a decrease in testosterone with an increase in FSH and LH levels, this study found that FSH and LH also decreased significantly, especially at higher doses and longer treatment times. Specifically, serum LH, FSH, and testosterone levels decreased by 40%, 42%, and 41%, respectively, with 40 g/L spearmint tea compared to the control when treated for 25 days (Kumar et al., 2008).

In summary, there is a contradiction compared to the first study. Both studies agree that spearmint lowers testosterone levels, but this one also suggests that with higher doses or prolonged use, spearmint might reduce FSH and LH levels as well, showing a broader impact on male hormone regulation.

In another study, female Wistar albino rats were used. The rats were kept in rooms with a controlled temperature and humidity, following a 12-hour light/12-hour dark cycle and were provided with a standard diet. However, this study featured a different grouping compared to previous experiments. The groups were divided as follows: Control, PCOS, PCOS + Spearmint (150 mg/kg), and PCOS + Spearmint (300 mg/kg).

The hormone levels in each group were recorded as follows:

- Control Group: LH: 22.26 ± 1.76 ng/dl, FSH: 16.96 ± 3.76 ng/dl, Testosterone: 0.14 ± 0.02 mIU/ml
- PCOS Group: LH: 24.56 ± 1.98 ng/dl, FSH: 13.62 ± 0.65 ng/dl, Testosterone: 3.04 ± 0.69 mIU/ml
- PCOS + Spearmint (150 mg/kg) Group: LH: 21.88 ± 4.13 ng/dl, FSH: 13.61 ± 1.64 ng/dl, Testosterone: 0.20 ± 0.11 mIU/ml
- PCOS + Spearmint (300 mg/kg) Group: LH: 21.45 ± 2.63 ng/dl, FSH: 15.40 ± 3.86 ng/dl, Testosterone: 0.12 ± 0.01 mIU/ml

This experiment stands out due to its direct focus on the effects of spearmint on PCOS in female Wistar rats, differing from other similar studies. The most remarkable finding was the

significant reduction in testosterone levels in the PCOS and PCOS + treatment groups. However, there were no substantial changes observed in the LH and FSH levels across the groups (Sadeghi Ataabadi et al., 2017).

8. Clinical data

Some clinical studies suggest that drinking spearmint tea can reduce hirsutism in women with polycystic ovarian syndrome (PCOS) by lowering androgen production and testosterone levels (Akdoğan et al., 2007). Preliminary evidence indicates that an herbal combination containing spearmint may help in managing irritable bowel syndrome (IBS). The impact of spearmint on memory is still debated, with inconclusive results on whether spearmint itself or simply chewing gum improves memory (Baker et al., 2004). While patients with gastroesophageal reflux disease (GERD) are often advised to avoid spearmint and peppermint, clinical studies have not found evidence that spearmint reduces lower oesophageal sphincter (LES) function or worsens acid reflux in healthy individuals (Bulat et al., 1999; Ulbricht et al., 2010).

In a clinical study aimed at understanding and proving spearmint's antiandrogenic effects, its impact on humans was confirmed. The trial involved 21 women with hirsutism (12 due to PCOS and 9 with idiopathic causes). The Ferriman-Gallwey modified score was measured by the same physician. Participants consumed a cup (250 mL) of herbal tea brewed with *Mentha spicata* (20 g/L) twice daily for 5 days during the follicular phase of their menstrual cycle. After this 5-day spearmint tea treatment, there was a significant reduction in free testosterone (FT) (from 5.49 ± 2.94 to 3.92 ± 2.80 pg/mL $p < 0.05$), levels, along with a notable increase in LH (from 6.34 ± 4.53 to 8.04 ± 5.14 mIU/mL, $p < 0.05$), FSH (from 4.56 ± 1.49 to 5.36 ± 1.84 mIU/mL $p < 0.05$), and oestradiol (E2) (from 46.50 ± 29.01 to 63.43 ± 47.57 pg/mL $p < 0.05$) levels. However, no significant changes were observed in total testosterone (TT) or DHEA-S levels (Akdoğan et al., 2007). In another study, involving 42 women who were randomly divided into two groups. One group was given spearmint tea, while the other group received chamomile tea, which is known to have no endocrine effects. By the 30th day, the results were surprisingly striking. The group that drank spearmint tea showed a noticeable decrease in both free and total testosterone levels in their blood. Additionally, LH and FSH levels increased. Patients' self-ratings of their degree of hirsutism, as scored by the modified DQLI, were significantly reduced in the spearmint tea group (Grant, 2010).

9. Conclusion

This thesis was developed following clinical observations from the Yenişarbademli district of Isparta, where spearmint consumption appeared to be linked with noticeable anti-androgenic effects. Based on these local reports, the study aimed to collect and examine existing research that supports or explains these findings within a broader scientific context. The thesis provides an overall view of the phytochemical structure and pharmacological effects of spearmint, focusing especially on its influence on hormonal balance.

The main goal of this study was to explore the anti-androgenic effects of spearmint and look into the possible biological mechanisms behind these effects. A key part of the research is presented in Chapter 5.4, which focuses on individual compounds found in spearmint and how they may be related to hormonal and reproductive changes. This section brings together findings from various studies and discusses possible ways in which these compounds may work, offering a foundation for future research.

Although the amount of published research on this topic is still limited, this thesis tries to fill some of the gaps by offering evidence-based insights and pointing out trends that could be useful for future investigations. Besides its hormonal relevance, the thesis also looks at other properties of spearmint, such as its antioxidant, antimicrobial, and anti-inflammatory effects, along with its traditional medicinal uses. With this wide-ranging approach, the study hopes to serve as both a useful reference and a starting point for further scientific exploration.

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