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Critical Review

Sage Plant as a Natural Treatment for Polycystic Ovary Syndrome

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ABSTRACT:

The study sought to explore the potential therapeutic benefits of sage (*Salvia officinalis*) in managing polycystic ovarian syndrome (PCOS) through an extensive review of existing literature. The research focused on studies related to the bioactive compounds of sage and their proven effects on hormones, insulin resistance, antioxidant, and anti-inflammatory properties. Results indicated that sage might help regulate androgen and insulin levels, improving tissue sensitivity to these hormones, which may contribute to enhancing follicle development and ovulation in women with PCOS. The findings also suggest that sage could play a significant role in improving metabolic and reproductive health by reducing insulin resistance and promoting the secretion of female hormones, thus supporting overall ovarian function. However, further clinical research is needed to confirm these results and determine the optimal therapeutic doses.

KEYWORDS: Sage, Polycystic Ovary Syndrome, Insulin Resistance, Hormones, Ovulation, Herbal Treatment.

INTRODUCTION

Polycystic ovary syndrome (PCOS) is a common heterogeneous endocrine disorder and may be associated with metabolic disturbances such as hyperglycemia, insulin resistance, obesity, and an increased risk of cardiometabolic disorders, including type 2 diabetes (Rojas et al., 2014). PCOS affects approximately 8 to 13% of women of reproductive age; however, about 70% of cases remain undiagnosed worldwide. This syndrome is the most common cause of anovulation and the leading cause of infertility. It is also associated with a variety of long-term health issues that affect the physical and emotional aspects of well-being. Although PCOS is considered a genetic disorder, it manifests differently depending on ethnic variations, leading to diverse effects on individuals (WHO, 2023). Oxidative stress also seems to play a significant role in triggering hyperandrogenism in PCOS (Duleba et al., 2012).

PCOS has no definitive cure, but its symptoms can be effectively managed with appropriate treatments. Women experiencing menstrual disturbances, difficulty conceiving, or increased acne and hair growth are advised to consult healthcare professionals. Some PCOS symptoms can be mitigated by lifestyle changes, such as maintaining a healthy diet and engaging in regular physical activity, which contribute to weight reduction and a decreased risk of type 2 diabetes (WHO, 2023).

There is growing interest in using herbs to treat metabolic disorders commonly associated with PCOS. Among these herbs, *Salvia officinalis* L. (sage) is one of approximately 1,000 widely distributed species (Walker & Sytsma, 2007). According to Jafri and El-Gadi (1985), Libyan flora consists of 10 species of *Salvia* L., three of which are cultivated (Mahmoud, 2023). *Salvia* is a medicinal plant native to North Africa, Central and Southern Europe (ACSAD, 2024), and is extensively cultivated in various countries, including Canada, the United States, Turkey, India, Japan, Indonesia, Tanzania, South Africa, the Antilles, Brazil, Australia, New Zealand, Iran, and the Mediterranean basin (Grdiša et al., 2015).

Several studies have reported that *S. officinalis* L. possesses antioxidant, antidiabetic, and antimicrobial properties, and may offer protective effects against cardiovascular diseases and cancer (Grdiša et al., 2015). Sage extract is widely used in the pharmaceutical and cosmetic industries due to its antitumor (Murata et al., 2013), hepatoprotective (Santos et al., 2001), and anti-inflammatory properties (Bastos et al., 2011).

Some studies have also highlighted that parts of the plant, particularly its leaves and stems of sage are abundant in phenolic compounds known for their antioxidant properties (Jakovljević et al., 2019; Shan et al., 2005). Consuming sage tea has demonstrated potential benefits in enhancing the oxidative balance within the hepatic tissues of rats and mice, as reported by Lima et al. (2005). Sage has been consumed traditionally as a herb to treat diabetes, and it has been reported to possess glucose-lowering effects. Additionally, the aqueous extract of sage exhibits insulin-like activities (Christensen et al., 2010). Given the importance of sage, this study aims to explore its use as a natural remedy for PCOS.

Description of Sage (*Salvia officinalis* L.)

Salvia officinalis L. is part of the *Salvia* genus in the *Labiatae* family, which includes over 700 species of plants.

It has been used for thousands of years in various cultures, including Ayurvedic medicine and ancient Greek and Chinese civilizations, as a remedy for improving health (Scholey et al., 2011).

Salvia officinalis is a perennial evergreen shrub classified within the mint family (*Lamiaceae*), characterized by lance-shaped, opposite leaves covered with soft hair and purple, two-lipped flowers that bloom in clusters.

It is cultivated in well-drained soil under full sunlight and is drought-tolerant and adaptable to poor soil conditions. The dried leaves are commonly used as a culinary herb to enhance the flavor of foods, while its antibacterial essential oils are utilized for medicinal purposes (NParks | *Salvia Officinalis*, n.d.).

North Carolina Extension Gardener Plant Toolbox (n.d.) explains that the Latin name Salvia is derived from "salvare," meaning "to heal," reflecting its medicinal uses. Sage prefers full sun and can tolerate poor, dry soils, although it does not thrive in wet conditions.

Pruning is recommended to maintain its shape and prevent overgrowth. Its aromatic leaves are used fresh or dried in cooking, and light harvesting is advised in the first year.

Sage is ideal for herb or rock gardens and is available in various cultivars that add visual diversity to landscapes.

Figure:(1). Sage plant

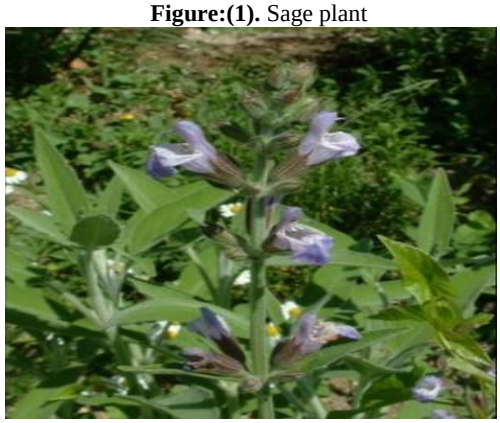

Figure2. Sage flower

Figure3. Sage leaves

Figure4. Sage fruits

Salvia officinalis L. is a robust, perennial shrub with herbaceous stems that become woody at the base. The plant is upright, highly branched, and covered with velvety hair, with square stems that can reach a height of approximately one meter.

These branches dry out each year. The plant has thick, aromatic, distinctive leaves arranged in opposite pairs, with petiolate leaves at the lower part of the stem and sessile ones at the upper part. The leaves are elliptical, oval, or oblong, with a grayish-green color due to the dense cottony hairs on their lower surface. The leaf blade measures between 1-8 cm in length and 35-8 mm in width, with a rounded or nearly truncated base and a crenate margin.

The flowers, about 2 cm long, are purple or blue, clustered in whorls containing 1-18 flowers, forming semi-spiky inflorescences that can be 4-18 cm long. The upper bracts of the flower are ovate with pointed tips, and the peduncle is about 3 mm long.

The calyx is around 1 cm but grows to 1.5 cm in the fruiting stage. The calyx is bilabiate (two-lipped) and hairy.

The corolla is also bilabiate, and the stamens are two in number with a connective about 3 mm long between the anther sacs. The fruit consists of four brown, nearly spherical nutlets, each with a diameter of about 2.5 mm (ACSAD, 2024).

Chemical Composition of Salvia officinalis (Sage)

Sage (Salvia officinalis) contains a diverse range of bioactive compounds, including alkaloids, carbohydrates, fatty acids, and glycosides, such as cardiac glycosides and flavonoid glycosides.

It also contains phenolic compounds, including coumarins, flavonoids, and tannins, as well as polyacetylenes, steroids, and various terpenes/terpenoids, such as monoterpenoids, diterpenoids, and triterpenoids. Additionally, sage contains waxes. The essential oil extracted from the plant contains over 120 compounds, Sage is rich in compounds such as borneol, camphor, caryophyllene, cineole, elemene, humulene, ledol, pinene, and thujone. Additionally, both alcoholic and aqueous extracts of sage contain flavonoids, including rosmarinic acid and luteolin-7-glucoside. (Ghorbani & Esmaeilizadeh, 2017).

The leaves contain volatile oil, with concentrations ranging from 0.08% to as high as 3.3%, and a significant amount of thujone. Additionally, the oil includes cineole, camphor, and borneol.

Sage also contains hydroxycinnamic acid derivatives, such as rosmarinic acid and chlorogenic acid, as well as diterpenes, including carnosolic acid and rosmanol.

Flavonoids present include apigenin and luteolin glycosides, while diterpenoids of the abietane type, such as salvianol and bitter lactone carnosol, are present, especially in dried or preserved plants.

Compounds like ursolic acid and oleanolic acid, which belong to the triterpene class, are also present, along with trace amounts of minerals like iron, magnesium, and zinc (ACSAD, 2024).

Classification of Sage

Sage (*Salvia officinalis*) belongs to the kingdom *Plantae* and is classified as a vascular plant (*Tracheobionta*) within the group of seed plants (*Spermatophyta*).

It is part of the division of flowering plants (*Magnoliophyta*) and the class of dicotyledons (*Magnoliopsida*), under the subclass *Asteridae*. Sage falls within the order *Lamiales*, the mint family (*Lamiaceae*), and the genus *Salvia*, known as common sage or kitchen sage (USDA Plants Database, n.d.).

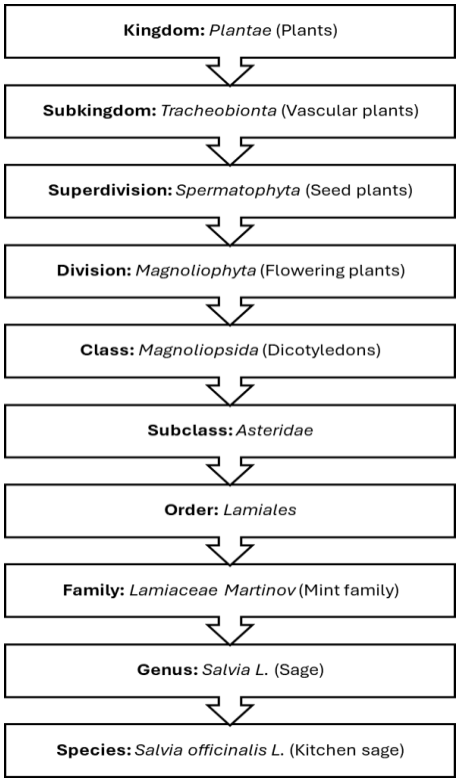

Figure:(5). Classification of the Plant Salvia officinalis L.

Understanding Polycystic Ovary Syndrome (PCOS)

Polycystic Ovary Syndrome (PCOS) is a hormonal disorder in women that primarily impacts ovarian function. The ovaries, responsible for producing the female hormones estrogen and progesterone that regulate the menstrual cycle, also generate small quantities of male hormones called androgens. In PCOS, this hormonal balance is disrupted, leading to various symptoms and complications. PCOS is commonly characterized by the absence of ovulation. Studies utilizing ultrasound and hormonal analyses have shown that PCOS causes approximately one-third of cases of amenorrhea (absence of menstruation) and 90% of cases of oligomenorrhea (infrequent menstruation) (Hull, 1989).

According to Haqq et al. (2014), women with Polycystic Ovary Syndrome (PCOS) often exhibit hormonal imbalances, including elevated luteinizing hormone (LH), decreased follicle-stimulating hormone (FSH), and increased levels of androgens and insulin. These changes contribute to irregular or absent menstrual cycles, a hallmark of the condition. Additionally, the reduced production of estrogen and the increased production of androgens like testosterone can result in additional symptoms, including the formation of small cysts on the ovaries, as well as hair and skin-related issues (Meena et al., 2019; Salley et al., 2007).

RESULTS AND DISCUSSION

This review study, based on peer-reviewed research, offers a comprehensive evaluation of sage's effectiveness in managing Polycystic Ovary Syndrome (PCOS). The analysis encompasses studies examining the impact of Salvia officinalis on PCOS, highlighting the following findings:

Sage (*Salvia officinalis*) is used as a beneficial dietary supplement in managing Polycystic Ovary Syndrome (PCOS). There is increasing interest in using herbal remedies to treat metabolic disorders globally. Due to its rich content of biologically active compounds, sage is a source of phenolic acids, including rosmarinic acid, caffeic acid, ferulic acid, and vanillic acid, as well as flavonoids such as luteolin, apigenin, and quercetin, sage has been utilized to treat various health conditions (Ghowsi et al., 2020).

Ghowsi et al. (2020) investigated the antioxidant, anti-diabetic, and lipid-lowering effects of sage tea in a testosterone-induced PCOS mouse model. Mice were treated with sage tea for two weeks, and the results revealed polycystic ovarian features, including the absence of a corpus luteum in the ovarian sections and significantly elevated testosterone levels compared to the control group. These findings confirmed that the testosterone injections induced PCOS

characteristics.

Notably, a significant reduction in fasting blood glucose levels was observed, aligning with the findings of Khedher et al., who reported that administering a low dose of sage methanolic extract to high-fat diet-fed mice for two weeks improved tissue insulin sensitivity and reduced plasma insulin concentrations in response to glucose (Khattab et al., 2012). Similarly, Lima et al. demonstrated that replacing water with sage tea for 14 days lowered plasma glucose levels in normal mice (Lima et al., 2006).

The anti-diabetic properties of sage are attributed to the inhibition of intestinal maltase and sucrase enzymes (Ga et al., 2016). Additionally, studies have shown that the aerial parts of sage contain flavonoids, such as kaempferol glycoside, which exhibit hypoglycemic effects and enhance glucose utilization in muscle tissues (Asadi et al., 2010). Furthermore, Eidi et al. found that consuming sage tea inhibited hepatic gluconeogenesis in streptozotocin-induced diabetic rats (Eidi et al., 2005).

Weight loss and preventing metabolic disorders associated with PCOS (such as insulin resistance) are key therapeutic strategies for women with PCOS (Pasquali et al., 2011). Amini et al. (2020) conducted a study that revealed the beneficial effects of a daily dose of 330 mg of sage extract over eight weeks on body composition and insulin resistance markers in women with polycystic ovary syndrome (PCOS). The findings showed a significant reduction in body weight, body mass index (BMI), waist circumference (WC), and diastolic blood pressure.

Several studies have suggested that sage consumption in traditional medicine is free of side effects (Ghorbani et al., 2017). Alrezaki et al. (2021) investigated the effects of different concentrations of sage extract on reproduction in female rats. The study found that low doses of sage extract (3.5 and 15 mg/kg) did not alter the secretion of steroid hormones, as levels of progesterone, estradiol, and testosterone remained stable. However, at the highest dose (60 mg/kg), a significant increase in estradiol levels was observed. Additionally, the expression of mRNA for genes associated with folliculogenesis and steroidogenesis showed a marked increase at the higher dose. This was accompanied by an increase in the number of growing follicles and a decrease in the number of abnormal follicles.

Research has shown that sage promotes growth, a property attributed to its rich content of bioactive compounds (Dadras et al., 2019). Gas Chromatography-Mass Spectrometry (GC-MS) analysis identified the primary components (each >1%) of sage as 1,8-cineole (47.40%), 13-epimanool (6.45%), 4,4-dimethyl-androst-5-en (5.90%), caryophyllene (5.11%), camphene (4.88%), alpha-pinene (4.40%), camphor (4.32%), beta-pinene (2.94%), and ledol (2.32%).

While the effects of these molecules on ovarian function remain unexplored, previous studies indicated that 1,8-cineole, the predominant component, caused no toxicity or fatalities in rats administered repeated injections at doses up to 1000 mg/kg for 50 days (Alrezaki et al., 2021; Caldas et al., 2016). Moreover, diterpenoid compounds like 13-epimanool and carnosol, which are significant constituents of sage, have demonstrated various pharmacological properties, including anti-proliferative effects due to their cytotoxic activity (Ruan et al., 2017).

Lienou et al. (2020) proposed that specific plant molecules, such as those in Senecio biverae (Asteraceae), can regulate female reproduction via the nervous system and are commonly used in traditional medicine to address female infertility. Based on this premise, it was hypothesized that high doses of sage extract, due to its abundance of

bioactive compounds, might enhance ovarian function by modulating estrogen signaling pathways, activating estrogen receptors, and influencing steroidogenesis within the ovary.

Alrezaki et al. (2021) found that sage extract may enhance the secretion of gonadotropin-releasing hormone (GnRH) and follicle-stimulating hormone (FSH), thereby stimulating the proliferation and differentiation of granulosa cells. This process contributes to the improvement of follicle growth and development. High doses of sage extract were found to increase the transcription of reproductive-related genes, such as INSL3, CCND2, IGF-I, and GDF, while also elevating estradiol levels. The increase in estradiol levels enhances follicle growth and differentiation, leading to a higher number of growing follicles. Additionally, the results showed an increase in the expression of genes associated with autophagy, such as ATG5, LC3, and ATG12, which help regulate cell survival and apoptosis. The evidence suggests that high sage doses may play a role in reducing ovarian disorders by stimulating apoptotic signaling pathways.

Shen et al. (2021) reported that sage extract enhances fertility in PCOS patients by improving uterine lining blood flow and increasing its receptivity to embryos. The extract also modulates fertility-related proteins like integrin and VEGF. Additionally, it helps reduce hyperandrogenism by altering androgen receptor expression and steroidogenic enzymes, improving reproductive hormone levels such as testosterone, LH, and FSH. The extract also positively affects insulin resistance and lipid levels by reducing triglycerides, total cholesterol, and LDL cholesterol and enhancing insulin sensitivity through adiponectin stimulation and reducing inflammation associated with insulin resistance. It also lowers fasting blood glucose and insulin levels.

CONCLUSION

Current research highlights that sage (Salvia officinalis) contains bioactive compounds that can mitigate several conditions associated with PCOS, including insulin resistance, hyperandrogenism, and weight gain. Key compounds in sage, such as phenolic acids and flavonoids, enhance insulin sensitivity, stabilize blood sugar levels, and reduce harmful lipids. Additionally, sage extract has demonstrated benefits for fertility by improving uterine blood flow and regulating reproductive hormones like testosterone, LH, and FSH.

Given the available evidence, sage can be considered a natural therapeutic option for PCOS patients looking to enhance fertility or manage hyperandrogenism and metabolic issues. It serves as an effective supplement for addressing PCOS symptoms, either by improving insulin sensitivity or supporting ovarian and reproductive health. Although additional clinical studies are necessary to confirm the safety and efficacy of higher doses of sage, existing research indicates that it could be a promising complement to treatment plans for PCOS.

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ETHICS

This study is a literature review and did not involve any direct human or animal experimentation, thus ethical approval was not required. However, the research adhered to all ethical standards regarding using previously published data, ensuring proper citation and acknowledgement of all sources.

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الملخص

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هدفت الدراسة إلى التعرف على نبات المريمية واستخداماته كعلاج محتمل لمتلازمة تكيس المبايض، باستخدام منهجية الدراسة المرجعية. تم الاعتماد على الأبحاث المتعلقة بالمكونات النشطة في نبات المريمية وتأثيراتها المثبتة على الهرمونات، مقاومة الأنسولين، والخصائص المضادة للأكسدة والالتهابات. أظهرت النتائج أن المريمية قد تساعد في تنظيم مستويات الأندروجينات والإنسولين، وتحسين حساسية الأنسجة لهذه الهرمونات، مما قد يسهم في تعزيز نمو الجريبات وتحسين عملية التبويض لدى النساء المصابات بمتلازمة تكيس المبايض. كما تشير النتائج إلى أن المريمية قد تلعب دورًا مهمًا في تحسين الصحة الأيضية والجنسية من خلال تقليل مقاومة الأنسولين وتعزيز إفراز الهرمونات الأنثوية، ما يؤدي إلى تحسين وظيفة المبيض بشكل عام. ومع ذلك، فإن هناك حاجة لإجراء المزيد من الدراسات السريرية لتأكيد هذه النتائج وتحديد الجرعات المناسبة للعلاج.

الكلمات المفتاحية: المريمية، متلازمة تكيس المبايض، مقاومة الأنسولين، الهرمونات، التبويض، العلاج النباتي.

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