

REVIEW ARTICLE

A Review of Therapeutic Properties and Uses of *Salvia officinalis*



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Abstract: Sage (*Salvia officinalis*) is an aromatic perennial herb belonging to the Lamiaceae family, renowned for its culinary and medicinal applications. Its essential oil and various phytochemical constituents, such as α -thujone, β -thujone, camphor, 1,8-cineole, and phenolic compounds like rosmarinic acid, carnosic acid, and carnosol, contribute to its diverse biological activities. The plant exhibits potent antioxidant, antimicrobial, anti-inflammatory, neuroprotective, and anti-diabetic properties. Numerous studies have explored its potential in combating various diseases, including cancer, Alzheimer's, cardiovascular disorders, and diabetes. The essential oil and extracts have demonstrated cytotoxic effects against various cancer cell lines, suggesting their potential as anticancer agents. Additionally, sage has shown promising results in improving cognitive function and memory, potentially benefiting individuals with neurodegenerative diseases like Alzheimer's. Its anti-diabetic effects, mediated through the inhibition of α -glucosidase and enhancement of insulin secretion, make it a valuable candidate for diabetes management. However, it is crucial to consider the potential toxicity associated with the thujone content in sage, as excessive intake may lead to adverse effects. Regulatory bodies have established safe limits for thujone consumption, ensuring responsible use of sage-based products. In conclusion, *Salvia officinalis* presents a promising avenue for further research and potential therapeutic applications, warranting rigorous scientific investigation to harness its full potential while ensuring safety.

Keywords: *Salvia officinalis*; Ethnomedicine; Anticancer; Alzheimer's disease; Diabetes; Cardiovascular disorders

1. Introduction

Salvia officinalis L., an aromatic and medicinal plant, is widely recognized for its pharmacological properties [1]. *S. officinalis* is a woody-stemmed, evergreen subshrub [2] with blue to purplish flowers and whitish leaves (Figure 1). Other common names for this plant include common sage, garden sage, and garden sage [3]. A member of the Lamiaceae family, *S. officinalis* is native to the Mediterranean region but has naturalized in various parts of the world [4]. It has a long history of being used as an ornamental garden plant, in culinary applications, and in traditional medicine. Numerous unrelated species are also known by the common name "sage." The use of *S. officinalis* has been associated with improved fertility [5, 6]. Historically, *S. officinalis* has been utilized as a stypic, a local anesthetic for the skin, and a diuretic [7]. Today, it has become naturalized in many regions, particularly in North America and Europe [8, 9]. The aerial parts of the *S. officinalis* shrub have a long history of use in traditional medicine and cooking [10]. Due to its ability to impart flavor and spice, this plant is frequently used in the preparation of various dishes.



Figure 1. Whole plant of *Salvia officinalis*

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In Asian and Latin American folk medicine, it has been employed to treat a variety of conditions, including seizures, ulcers, gout, rheumatism, inflammation, dizziness, tremors, paralysis, diarrhea, and hyperglycemia [11, 12]. In European traditional medicine, *S. officinalis* has been used to treat skin and throat inflammations, excessive perspiration, age-related cognitive problems, and mild dyspepsia (such as heartburn and bloating) [13, 14]. The German Commission E has approved the use of *S. officinalis* for the treatment of inflammation and dyspepsia [13, 14]. Numerous investigations have been conducted recently to document the traditional uses of *S. officinalis* and identify its novel biological properties [15]. These studies have revealed various pharmacological activities, such as anticancer, anti-inflammatory, antinociceptive, antioxidant, antimicrobial, antimutagenic, antidementia, hypoglycemic, and hypolipidemic effects [16, 17].

2. Pharmacognosy of *Salvia officinalis*

2.1. Plant profile

Sage (*Salvia officinalis*) is a fragrant herb belonging to the mint family (Lamiaceae), cultivated for its strong, edible leaves. Native to the Mediterranean region, sage is used as a flavoring in various dishes, especially in sausages and stuffings for pork and poultry. It can be used either fresh or dried [18, 19]

2.1.1. Classification

Kingdom: Plantae
Order: Lamiales
Family: Lamiaceae
Genus: *Salvia*
Species: *S. officinalis*.

2.1.2. Vernacular names

Hindi: Safakus
Sanskrit: Samudraphala, Shati, Vrddhadaru
Urdu: Sefakus (sepakass), sathi
Chinese: sage, Dan shen
English: Sage, lady salvia, magic mint, purple sticky, sally D, sage of the seers, and most widely salvia

2.1.3. Geographical distribution

Salvia officinalis is a perennial species native and endemic to the western Balkans and the Apennine Peninsula [20]

2.1.4. Morphology

In the Mediterranean region, *Salvia officinalis* L. is a member of the Labiatae/Lamiaceae family. It can be an annual or perennial bushy shrub. Aromatic and fragrant, sage varies in length from 40 to 100 cm [21]. Sage leaves are oval, 1-4 cm in diameter, and upright on the edges. They are also 4–10 cm long. The leaf margins are pilose, bitter, sharp, and green-grey in color. Excretions with aromatic odors are located on the lower surface of the leaf [22]. It has clusters of violet-like flowers. Each floral cluster contains 2–10, occasionally up to 40, flowers [23]. The plant organs can be exclusively female or both male and female. Two male organs are present [24]

2.1.5. Ethnomedical uses

Sage tea or infusion is a useful remedy for fever delirium and the anxious excitation that sometimes accompanies neurological and brain disorders. It has a good reputation as a remedy when taken in modest, frequent doses [25]. The active ingredients are well known for their antibacterial, antiallergic, antifungal, anti-inflammatory, and rubefacient properties [26]

3. Phytochemical constituents

The chemical composition of *S. officinalis* essential oil sold in the market is governed by the ISO 9909 standard. It specifies the following eleven compounds in recommended amounts: α -pinene (1.0–6.5%), camphene (1.5–7%), limonene (0.5–3%), 1,8-cineole (5.5–13%), total linalool and linalyl-acetate ($\leq 1\%$), α -thujone (18–43%), β -thujone (3.0–8.5%), camphor (4.5–24.5%), bornyl acetate ($\leq 2.50\%$), and α -humulene ($\leq 12\%$). An appropriate concentration of each individual molecule is necessary for physiological and pharmacological objectives, as an imbalance in the composition could result in a loss of therapeutic benefits or harmful effects [27, 28].

The essential oil of common sage appears to be the primary physiologically active ingredient. It contains compounds such as β -thujone, nicotinamide, fumaric acid, chlorogenic acid, caffeic acid, nicotinic acid, flavones, flavone glycosides, and estrogenic substances. Other compounds found in sage leaf include cineol, borneol, and tannic acid [29-32]

Table 1. Major Phytochemical Constituents of *Salvia officinalis*

Compound Class	Compounds
Monoterpenes	α -Thujone, β -Thujone, Camphor, 1,8-Cineole
Diterpenes	Carnosic Acid, Carnosol
Phenolic Acids	Rosmarinic Acid, Caffeic Acid
Flavonoids	Luteolin, Apigenin, Hispidulin
Other Compounds	α -Humulene, Viridiflorol, Manool

4. Pharmacological activities



Figure 2. Pharmacological activities of *S. officinalis*

4.1.1. Anti-inflammatory Activity

The topical anti-inflammatory activities of leaves from four distinct plant populations of *Salvia officinalis* L. were examined. An analysis of sage's chemistry and pharmacology indicated that ursolic acid is the primary ingredient responsible for its anti-inflammatory properties [32]. For quality control purposes, the determination of ursolic acid content in sage and sage-based therapies for the topical treatment of inflammatory diseases is recommended [33].

4.1.2. Antimicrobial Activity

The potential antibacterial and radical scavenging properties of *Salvia cryptantha* and *Salvia multicaulis* essential oils and methanolic extracts were investigated [34]. While little or no activity was observed for the polar and non-polar subfractions of the extracts, the essential oils exhibited antibacterial activity. The findings suggest that the essential oils of *S. cryptantha* and *S. multicaulis* possess free radical scavenging and antibacterial properties against pathogenic bacteria, making them potentially useful as antibacterial and antioxidant agents in the food industry [35, 36, 37]. Essential oils from *Salvia triloba* and *Salvia officinalis* were also examined and found to exhibit exceptional bacteriostatic and bactericidal activities against various bacteria, including *Aeromonas hydrophila*, *Aeromonas sobria*, *Bacillus cereus*, *Bacillus megatherium*, and *Klebsiella oxytoca* [38].

4.1.3. Anticancer and Antimutagenic Effects

The potential anticancer effect of *S. officinalis* has been investigated using animal cancer models and various malignant cell lines. Studies have shown that drinking sage tea can prevent the early stages of colon carcinogenesis [39]. Extracts from this plant have demonstrated pro-apoptotic and growth-inhibitory effects on cell lines of breast cancer (MCF-7), cervical adenocarcinoma (HeLa), colorectal cancer (HCT-116, HCT15, CO115, HT29), insulinoma (RINm5F), laryngeal carcinoma (Hep-2), lung carcinoma (A549), melanoma (A375, M14, A2058, B16), and oral cavity squamous cell carcinoma [40-43]. In addition to its antiproliferative activity, *S. officinalis* exhibits antimigratory and antiangiogenic properties [44-46].

4.1.4. Anticandidal Activity

Boonyanit Thaweboon demonstrated the anticandidal properties of *Salvia officinalis* L. (*S. officinalis*) essential oil against *Candida albicans* and its inhibitory effects on the adherence of *Candida albicans* to a polymethylmethacrylate (PMMA) resin surface [47]. The anticandidal properties of *S. officinalis* were initially investigated using the disc diffusion method, followed by the determination of the minimal lethal concentration (MLC) and minimal inhibitory concentration (MIC) using the modified membrane approach [48, 49]. The results showed that the essential oil of *S. officinalis* L. exhibited anticandidal activity against all strains of *C. albicans*, with an inhibition zone ranging from 40.5 to 19.5 mm. Therefore, it can be concluded that *S. officinalis* L. essential oil possesses anticandidal properties against *C. albicans*, and it can be utilized as an antifungal agent [50-52].

4.1.5. Antioxidant Activities

Oxidative stress plays a significant role in the onset and progression of various diseases, including cancer, cardiovascular disorders, diabetes, and neurological diseases [53-55]. Increased oxidative stress occurs when the production of reactive oxygen species (ROS) by the mitochondrial electron-transport chain, NADPH oxidase, uncoupled nitric oxide synthases, and xanthine oxidase exceeds the capacity of antioxidant defenses such as glutathione peroxidase, superoxide dismutase, and catalase [56]. Natural antioxidants can protect cells from the overproduction of reactive oxygen species and prevent tissue damage caused by oxidative stress [57-59]. Numerous studies have reported strong antioxidant properties of *S. officinalis* [60].

4.1.6. Anti-nociceptive Properties

Inflammation and pain are two major symptoms that arise from tissue injury. Non-steroidal anti-inflammatory drugs (NSAIDs) continue to play an essential role in the pharmacological management of these symptoms [61]. However, the clinical usefulness of NSAIDs is accompanied by undesirable side effects, such as digestive and cardiovascular issues [62]. Therefore, there is ongoing interest in exploring novel anti-inflammatory and antinociceptive drugs with fewer side effects. Pharmacological studies have demonstrated the anti-inflammatory and antinociceptive properties of *S. officinalis* [63-65].

4.1.7. Antiseptic Effects

Multiple lines of evidence support the antibacterial properties of *S. officinalis* [66]. The essential oil and ethanolic extract of *S. officinalis* exhibit strong bactericidal and bacteriostatic activities against both Gram-positive and Gram-negative bacteria [67]. Gram-positive pathogens such as *Bacillus cereus*, *Bacillus megatherium*, *Bacillus subtilis*, *Enterococcus faecalis*, *Listeria monocytogenes*, and *Staphylococcus epidermidis* have shown high susceptibility to *S. officinalis* [68-70].

4.1.8. Neuroprotective Effects

Several studies have investigated the neuroprotective potential of *S. officinalis*. One study demonstrated that the ethanolic extract of *S. officinalis* could protect neuronal cells from oxidative stress-induced cytotoxicity in vitro [71]. Another study reported that sage extract exhibited an inhibitory effect on acetylcholinesterase activity, suggesting its potential use in the treatment of Alzheimer's disease [72]. Additionally, *S. officinalis* has shown promising results in animal models of cognitive impairment and neurodegeneration [73, 74].

4.1.9. Hypoglycemic and Hypolipidemic Effects

S. officinalis has been traditionally used for the management of diabetes mellitus in various folk medicine systems [75]. Numerous preclinical studies have validated the hypoglycemic and hypolipidemic effects of *S. officinalis* extracts [76-78]. The proposed mechanisms of action include inhibition of enzymes involved in carbohydrate metabolism, stimulation of insulin secretion, and modulation of glucose transporters [79, 80]. Additionally, *S. officinalis* has been shown to improve lipid profiles and reduce the risk of associated complications, such as cardiovascular diseases [81, 82].

4.1.10. Hepatoprotective Effects

The hepatoprotective potential of *S. officinalis* has been explored in several studies. Extracts of *S. officinalis* have demonstrated protective effects against various hepatotoxic agents, including carbon tetrachloride, acetaminophen, and ethanol [83-85]. The proposed mechanisms involve the antioxidant and anti-inflammatory properties of *S. officinalis*, as well as its ability to modulate enzymatic activities involved in detoxification processes [86, 87].

4.2. Clinical Studies

While numerous preclinical studies have explored the therapeutic potential of *S. officinalis*, clinical studies in humans are relatively limited. However, some clinical trials have been conducted, yielding promising results.

Table 2. Details of clinical studies conducted on *S.officinalis*

Study	Participants	Intervention	Key Findings
Perry et al., 2003	11 patients with mild to moderate Alzheimer's disease	Salvia officinalis extract (60 drops/day) for 4 months	Improved cognitive performance and reduced agitation
Tildesley et al., 2003	20 healthy young volunteers	Single dose of Salvia lavandulaefolia extract	Enhanced memory performance, particularly long-term memory
Kianbakht et al., 2013	80 patients with hyperlipidemic type 2 diabetes	Salvia officinalis leaf extract (500 mg/day) or placebo for 3 months	Improved glycemic control, reduced triglycerides, and total cholesterol levels in the intervention group
Boutheina et al., 2019	In vitro study	Essential oils from Salvia officinalis and Salvia triloba	Demonstrated antibacterial activity against food-borne pathogens
Maistro et al., 2016	Ovalbumin-induced allergic mice	Salvia officinalis essential oil (100 mg/kg)	Reduced inflammatory cell infiltration and mucus production in the lungs
Farshchi et al., 2016	Male Wistar rats	Salvia officinalis leaf extract (200 and 400 mg/kg)	Improved memory retention, possibly through cholinergic system modulation

4.3. Toxicological Considerations

Despite the widespread use of *S. officinalis* in traditional medicine and culinary applications, there are concerns regarding the potential toxicity of its constituents, particularly thujone [88]. Thujone, a monoterpene ketone, has been associated with neurotoxicity and convulsions at high doses [89]. However, the levels of thujone present in culinary and medicinal preparations of *S. officinalis* are generally considered safe for consumption [90, 91]. Nonetheless, caution should be exercised, and further research is warranted to establish safe dosage ranges and potential interactions with other medications.

5. Conclusion

S. officinalis has a rich history of traditional use and continues to garner significant scientific interest due to its diverse pharmacological properties. The plant's extracts and essential oils have demonstrated promising therapeutic potential in various preclinical studies, particularly in the areas of cancer, inflammation, microbial infections, neurological disorders, metabolic disorders, and liver diseases. However, further research is needed to fully elucidate the mechanisms of action, identify the bioactive constituents responsible for specific pharmacological effects, and establish standardized extraction and formulation methods. Additionally, more clinical studies are necessary to evaluate the safety and efficacy of *S. officinalis* preparations in human populations. The integration of traditional knowledge with modern scientific techniques holds promise for the development of novel therapeutic agents derived from *S. officinalis*. Potential areas of focus include the development of standardized herbal formulations, isolation and characterization of bioactive compounds, and the exploration of synergistic effects with existing medications.

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