

Salvia Officinalis L.: A Review of its Bioactive Compounds, Pharmacological Activities, and Potential Health Benefits.

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Abstract

The plant *Salvia officinalis*, also known as Sage, belongs to the Labiatae/Lamiaceae family. Although it originated in the Middle East and the Mediterranean, it has now spread around the world. *S. officinalis* has been used in traditional medicine to treat a variety of conditions, such as rheumatism, ulcers, gout, seizures, inflammation, tremor, dizziness, paralysis, diarrhoea, and hyperglycaemia. This plant has been the focus of extensive research in recent years in an effort to chronicle its traditional use and uncover novel biological effects. Numerous pharmacological actions for *S. officinalis* have been identified by these investigations. The current study focusses on the most recent data about the pharmacological results that have been regularly reported for *S. officinalis*. These results include hypoglycemic, hypolipidemic, antioxidant, anticancer, anti-inflammatory, antinociceptive, antimicrobial, antimutagenic, and antidementia properties. Additionally, the chemical components that provide *S. officinalis* its pharmacological effects as well as the clinical research on this plant are discussed and given.

Keywords: Anticancer, Antimutagenic, Flavonoids Sage and *Salvia officinalis*.

1. Introduction

The Labiatae/Lamiaceae family includes the perennial round shrub known as "sage" (Fig. 1). With about 900 species, *Salvia* is the biggest genus in this family. The species of *S. officinalis* is indigenous to the Middle East and Mediterranean regions, however plants of this genus are found all over the world. It is now naturalised all over the world, but especially in North America and Europe. Traditional medicine and cooking have traditionally used the aerial parts of the *S. officinalis* plant.^{1,2} This plant has been utilised extensively in the making of numerous meals due to its flavouring and seasoning qualities. It has been used to treat a variety of conditions in Asian and Latin American traditional medicine, such as seizures, ulcers, gout, rheumatism, inflammation, dizziness, tremor, paralysis, diarrhoea, and hyperglycemia. *S. officinalis* has been used in European traditional medicine to treat age-related cognitive problems, excessive perspiration, skin and throat inflammations, and mild dyspepsia (heartburn and bloating). The German Commission E has approved the use of *S. officinalis* for a variety of medical conditions, such as dyspepsia and inflammation.³

Numerous investigations have been carried out recently to record the traditional use of *S. officinalis* and to identify novel biological properties of this plant. Numerous pharmacological actions, such as anticancer, anti-inflammatory, anti-nociceptive, antioxidant, antimicrobial, antimutagenic, antidementia,

hypoglycemic, and hypolipidemic effects, have been identified by these investigations.⁴ Every pharmacological discovery that has been regularly reported for *S. officinalis* has been attempted to be covered in this review. Additionally, the chemical components that give this plant its biological effects are described and examined. A brief summary of *S. officinalis*'s toxicity and undesirable consequences is provided.⁵

2. Bioactive compounds of *S. Officinalis*

The main phytochemicals found in *S. officinalis*'s stem, leaves, and flowers are clearly defined. Alkaloids, carbohydrates, fatty acids, glycosidic derivatives (such as cardiac glycosides, flavonoid glycosides, and saponins), phenolic compounds (such as coumarins, flavonoids, and tannins), polyacetylenes, steroids, terpenes/terpenoids (such as monoterpenoids, diterpenoids, triterpenoids, and sesquiterpenoids), and waxes are among the many different constituents that are present in *S. officinalis*. The structure of the primary terpenes and flavonoids that were separated from *S. officinalis*. The majority of the phytochemicals identified in *S. officinalis* came from its essential oil, butanol fraction, alcoholic extract, aqueous extract, and infusion preparation. The essential oil extracted from the aerial portions of *S. officinalis* has more than 120 components that have been identified.⁶ Borneol, camphor, caryophyllene, cineole, elemene, humulene, ledene, pinene, and thujone are the oil's primary constituents. *S. officinalis* extracts, both alcoholic and aqueous, are abundant in flavonoids, especially luteolin-7-glucoside and rosmarinic acid. The methanolic extract of *S. officinalis* has also been discovered to contain phenolic acids, including caffeic acid and 3-Caffeoylquinic acid. Several volatile components, including borneol, cineole, camphor, and thujone, as well as flavonoids, including chlorogenic acid, ellagic acid, epicatechin, epigallocatechin gallate, quercetin, rosmarinic acid, rutin, and luteolin-7-glucoside, have been identified in the infusion made from *S. officinalis*. The most prevalent flavonoids in the infusion extract of *S. officinalis* are ellagic acid and rosmarinic acid, which are followed by quercetin, rutin, and chlorogenic acid. The most abounding carbohydrates described in this plant are arabinose, galactose, glucose, mannose, xylose, uronic acids and rhamnose.⁷



Fig. 01. Aerial parts of *Salvia Officinalis* L.

When comparing the phytochemicals found in *S. officinalis*'s flowers, leaves, and stem, the most prevalent phytochemical in the stem is linalool; the highest concentrations of α -pinene and cineole are found in the flowers; and the most prevalent phytochemicals in the leaves are bornyl acetate, camphene, camphor, humulene, limonene, and thujone. It should be noted, nevertheless, that, similar to other plants, *S.*

officinalis's chemical makeup would vary based on environmental factors including height, climate, and water availability.⁸

3. Pharmacological activities

3.1 Anticancer and antimutagenic effects

Numerous malignant cell lines and animal models of cancer have been used to test *S. officinalis*' possible anticancer potential. Drinking sage tea has been shown to stop the early stages of colon carcinogenesis. On cell lines of breast cancer (MCF-7), cervix adeno carcinoma (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, extracts from this plant demonstrated pro-apoptotic and growth-inhibitory effects. *S. officinalis* exhibits antimigratory and antiangiogenic properties in addition to its antiproliferative impact. The extract from *S. officinalis* increases the cytotoxic effect by enhancing the release of TNF- α and nitric oxide from macrophages. *S. officinalis* contains a number of cytotoxic and anticancer chemicals that may be responsible for these effects.⁹ Among terpenes and terpenoids isolated from *S. officinalis*, the caryophyllene and α -humulene have been shown to inhibit growth of MCF-7 and HCT-116 tumor cells. Manool, a diterpene, induces selective cytotoxicity on human cervical adenocarcinoma and human glioblastoma. Also, ursolic acid, a pentacyclic triterpenoid, inhibits angiogenesis, neoplastic proteases, and invasion of melanoma cells. Caryophyllene and α -humulene are two terpenes and terpenoids that have been extracted from *S. officinalis* and have been demonstrated to suppress the growth of MCF-7 and HCT-116 tumour cells. A diterpene called manool selectively kills human glioblastoma and cervical cancer. Additionally, ursolic acid, a pentacyclic triterpenoid, prevents melanoma cell invasion, neoplastic proteases, and angiogenesis. Rosmarinic acid is one of the flavonoids of *S. officinalis* whose anticancer properties have been well investigated. Breast adenocarcinoma, colon carcinoma, prostate carcinoma, hepatocellular carcinoma, small cell lung carcinoma, and chronic myeloid leukaemia are among the human cancer cells that it prevents from growing. In animal experiments, rosmarinic acid prevented bone metastases from breast cancer and prevented skin tumours from forming in mice model of dimethylbenz(a) anthracene-induced skin carcinogenesis. This flavonoid's anticancer properties appear to be caused, at least in part, by the inhibition of the Mitogen-Activated Protein Kinase/Extracellular Signal-regulated Kinase pathway, the suppression of nuclear transcription factor-kappa B and reactive oxygen species (ROS), and the decrease in the expression of the proinflammatory gene cyclooxygenase-2. Additionally, it prevents endothelial cells from undergoing various stages of angiogenesis, including migration, adhesion, proliferation, and tube creation.^{10,11}

There is mounting evidence that *S. officinalis* has mutagenesis-inhibiting properties. Its essential oil has been demonstrated to lessen UV-induced mutations in *Saccharomyces cerevisiae* and *Escherichia coli*. In *Drosophila melanogaster*, its tea infusion lowers the frequency of mutations brought on by methyl methanesulphonate. Its methanolic extract protects rats from the genotoxicity caused by cyclophosphamide. In HepG2 cells, this plant also lessens oxidative DNA damage brought on by hydrogen peroxide and dimethoxy-1,4-naphthoquinone. The primary monoterpene chemicals found in *S. officinalis*, including limonene, camphor, thujone, and 1,8-cineole, are responsible for its antimutagenic properties. The antioxidant activity of *S. officinalis* may account for its protective impact on DNA.^{12,13,14}

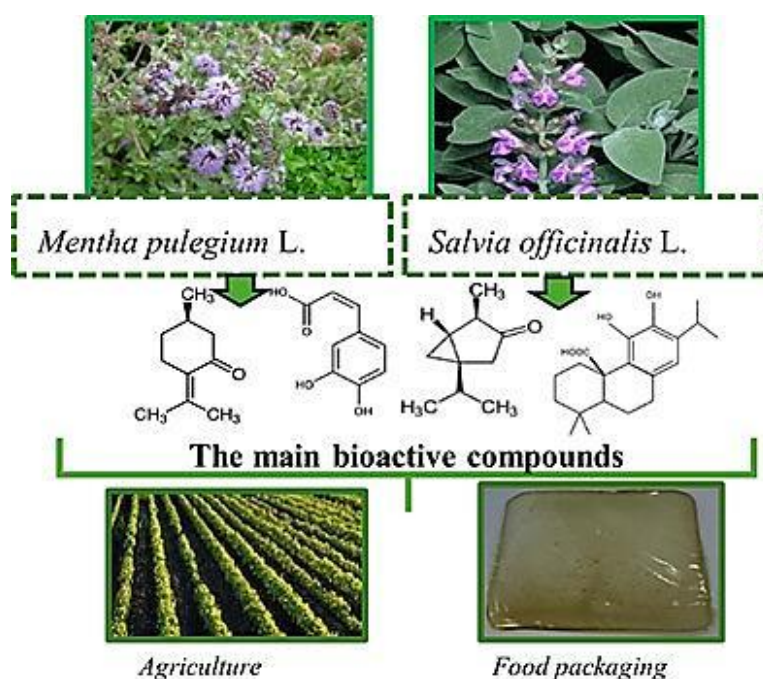


Fig. 02. Structure of *Salvia officinalis*.

3.2 Antioxidant activities

The development and course of a number of illnesses, including cancer, heart disease, diabetes, and neurological conditions, are significantly influenced by oxidative stress. When ROS production by the mitochondrial electron-transport chain, NADPH oxidase, uncoupled nitric oxide syntheses, and xanthine oxidase surpasses the capacity of antioxidant defences like catalase, glutathione peroxidase, and superoxide dismutase activities, enhanced oxidative stress results. Natural antioxidants can prevent tissue damage caused by oxidative stress because they shield cells from the overproduction of ROS. Numerous research have provided evidence of *S. officinalis*' strong antioxidant properties. Rat hepatocytes' tolerance to oxidative stress is increased when *S. officinalis* extract is added to their drinking water.¹⁵ By increasing glutathione peroxidase activity, it shields hepatocytes from DNA damage caused by dimethoxy naphthoquinone and hydrogen peroxide. Carnosol, rosmarinic acid, and carnosic acid are the most potent antioxidant components found in *S. officinalis*. These are followed by caffeic acid, rosmanol, rosmadial, genkwanin, and cirsimaritin. Carnosol has a similar effect to α -tocopherol in terms of scavenging radicals. Compared to trolox, a synthetic water-soluble vitamin E, the rosmarinic acid derivatives have 15–20 times the superoxide scavenging activity. Rosmarinic acid improves the activity of pancreatic catalase, glutathione peroxidase, glutathione-transferase, and superoxide dismutase in streptozotocin-induced diabetic rats. Other flavonoids of *S. officinalis*, including quercetin and rutin, exhibit potent antioxidant properties in addition to rosmarinic acid. For example, in our previous work we showed that rutin reversed hexachlorobutadiene-induced elevation of lipid peroxidation and depletion of thiol content in the kidney.¹⁶

3.3 Anti-inflammatory and antinociceptive properties

The two primary symptoms that arise from tissue injury are inflammation and discomfort. The pharmaceutical management of these symptoms still heavily relies on non-steroidal anti-inflammatory medications. However, these medications' clinical applications come with undesirable side effects include cardiovascular and gastrointestinal issues. As a result, the hunt for novel anti-inflammatory and antinociceptive drugs with fewer side effects is still an intriguing topic. According to pharmacological

research, *S. officinalis* has anti-inflammatory and antinociceptive properties..^{17,18} For instance, it has been demonstrated that this plant aids in the management of neuropathic pain in peripheral neuropathy brought on by chemotherapy. The chloroform extract of *S. officinalis* exhibits the strongest anti-inflammatory properties among the several extracts, whilst the methanolic extract and essential oil show the least amount of effect. The components that most likely contribute to the herb's anti-inflammatory and antinociceptive properties include flavonoids and terpenes. According to Mansourabadi et al., flavonoids derived from *S. officinalis* have a dose-dependent analgesic effect and decrease inflammation in the mouse carrageenan model. Osakabe et al. demonstrated that rosmarinic acid applied topically reduces inflammation of the epidermis. Among the terpenes/terpenoids with anti-inflammatory properties are manool, carnosol, and ursolic acid. Ursolic acid has a twofold stronger anti-inflammatory effect than indomethacin. The antinociceptive effect of *S. officinalis* in pharyngitis patients may be due to this activity of its components. *S. officinalis* does not, however, have a more potent impact than benzydamine hydrochloride in reducing postoperative pain following tonsillectomy or adenoidectomy..^{19,20}

3.4 Antiseptic effects

The antibacterial properties of *S. officinalis* are supported by multiple lines of data. Strong bactericidal and bacteriostatic properties against both Gram-positive and Gram-negative bacteria are demonstrated by *S. officinalis*' essential oil and ethanolic extract. High susceptibility to *S. officinalis* is demonstrated by the Gram-positive pathogens *Bacillus cereus*, *Bacillus megaterium*, *Bacillus subtilis*, *Enterococcus faecalis*, *Listeria monocytogenes*, and *Staphylococcus epidermidis*. The sort of extract that is utilised determines how *S. officinalis* affects Gram-negative bacteria. *Aeromonas hydrophila*, *Aeromonas sobria*, *E. coli*, *Klebsiella oxytoca*, *Klebsiella pneumoniae*, *Pseudomonas morgani*, *Salmonella anatum*, *Salmonella enteritidis*, *Salmonella typhi*, and *Shigella sonnei* are all significantly inhibited in their growth by the essential oil of *S. officinalis*, but *E. coli*, *Pseudomonas aeruginosa*, and *S. enteritidis* are only marginally affected..²²

3.5 Cognitive- and memory-enhancing effects

More and more data points to the potential benefits of *S. officinalis* for memory and cognition. Ethanolic extract of *S. officinalis* has been demonstrated in animal experiments to improve memory retention in rats that are learning passive avoidance. In healthy rats, the hydroalcoholic extract of *S. officinalis* and its primary flavonoid, rosmarinic acid, enhances cognition and prevents learning and memory impairments brought on by diabetes. Additionally, morphine-induced memory impairment is lessened by *S. officinalis* hydroalcoholic extract..²³

Clinical experiments have shown that *S. officinalis* improves cognitive function in both healthy individuals and patients with dementia or cognitive impairment, supporting the findings of animal studies. According to Moss et al., the scent of essential oil from *S. officinalis* may improve healthy people's prospective memory function. Additionally, Scholey et al. demonstrated that in healthy older participants, an ethanolic extract of this plant enhanced memory and attention. A randomized controlled trial by Akhondzadeh et al showed that a 4-month treatment with hydroalcoholic extract of *S. officinalis* improved cognitive functions in patients with mild to moderate Alzheimer's disease..²⁴

3.6 Metabolic effects

Clinical and Experimental studies have confirmed the beneficial effects of some medicinal plants on a body metabolism particularly glycemic status, serum lipids, lipolysis, and adipogenesis. Recent pharmacological investigations demonstrated that different extracts of aerial parts of *S. officinalis* are able to decrease blood glucose in a normal and diabetic conditions. The mechanisms suggested for

hypoglycemic effect of *S. officinalis* include an inhibition of hepatocyte gluconeogenesis and decrease of insulin resistance through stimulation of peroxisome proliferator-activated receptor γ (PPAR γ). Recently, one study group reported that *S. officinalis* extract increased plasma insulin in streptozotocin-induced diabetic rats. However, in their previous work they observed that the extract did not affect insulin releasing from the pancreas of normal or diabetic rats. Further studies required to elucidate whether stimulation of insulin release mediates hypoglycemic effect of *S. officinalis*.²⁵

Additionally, pharmacological research showed that various *S. officinalis* extracts lower serum lipid levels. Hernandez-Saavedra and associates reported that in rats given a diet that caused them to become obese, the infusion made from this plant decreased the levels of low density lipoproteins (LDL), total cholesterol, and serum triglycerides. Additionally, it reduced the animals' body weight and fat mass in the abdomen. In diabetic mice, *S. officinalis* has also been demonstrated to have positive effects on lipid profiles. In streptozotocin-induced diabetic rats, it may lower the levels of triglycerides, cholesterol, urea, uric acid, creatinine, aspartate amino transferase (AST), and alanine amino transferase (ALT). *S. officinalis* leaf extract has been shown in clinical trials to reduce blood levels of triglycerides, total cholesterol, LDL, VLDL, and 2 hours postprandial glucose in individuals with diabetes and hyperlipidaemia. Consuming tea from *S. officinalis* has also been shown to improve the blood lipid profile in healthy, non-diabetic participants. In high-risk patients, such as those with diabetes mellitus or hypercholesterolemia, *S. officinalis* may be useful for managing dyslipidaemia because it is a prevalent metabolic illness that contributes to mortality and morbidities from cerebrovascular and cardiovascular disorders. Flavonoids found in *S. officinalis* may be responsible for the plant's positive effects on dyslipidaemia. For instance, rosmarinic acid therapy lowers the blood triglyceride and cholesterol levels in rats with type 2 diabetes caused by streptozotocin and a high-fat diet. Additionally, rutin treatment lowers body weight and adipose tissue mass in rats who have been made obese by a high-fat diet. Furthermore, in skeletal muscle, this flavonoid increases the size, DNA content, and gene expression of mitochondrial biogenesis-related genes (e.g., nicotinamide adenine dinucleotide-dependent deacetylase, nuclear respiratory factor-1, transcription factor A, and PPAR γ coactivator1 α).²⁶

4. Toxicological studies

According to several clinical studies, ingesting *S. officinalis* does not cause serious adverse effects. However, some adverse effects, including vomiting, salivation, tachycardia, vertigo, hot flushes, allergic reactions, tongue swelling, cyanosis, and even convulsions, may arise after prolonged use or after an overdose of *S. officinalis*'s ethanolic extract and volatile oil (equivalent to more than 15 g of the leaves). Because *S. officinalis* oil directly affects the neurological system (at levels more than 0.5 g/kg), it has a proconvulsant effect. Terpene ketones, camphor, and thujone are thought to be the most harmful substances found in *S. officinalis*. These substances have the potential to harm both the foetus and the infant. Therefore, it is not advised to consume *S. officinalis* when pregnant or nursing. The LD₅₀ of *S. officinalis* oil (when taken orally) and the methanolic extract (when administered intraperitoneally) are 2.6 g/kg and 4 g/kg, respectively, according to findings from animal research. Tea from *S. officinalis* has been shown to increase the hepatotoxicity that CCl₄ causes in mice. Nevertheless, no hepatotoxic effects were identified in clinical trials.²⁷

5. Pharmaceutical use

Salvia is well known in traditional medicine as having antimicrobial properties, it being therefore used as

antiseptic, anti-scabies, anti-syphilis, and anti-inflammatory agent, and frequently used in skin and eye diseases. In some regions of the Middle East, *Salvia* was reported to be used in treating fever and some digestive diseases. The antibacterial properties of the *Salvia* oil have been attributed to the presence of cineole, thujone and camphor.

The antimicrobial properties of essential oil extracted from the *Salvia officinalis* have drawn the attention of researchers as they can be used in developing alternatives to traditional antibiotics which prove to be less and less efficient as bacterial resistance to them increases.²⁸

It is known that *Escherichia coli*, *Klebsiella pneumoniae* and *Klebsiella oxytoca* are pathogen agents responsible for diseases that can be more or less serious and are transmitted orally and have been detected in various foodstuff. Moreover, all these pathogen agents have become more and more resistant to synthetic antibiotics, which leads to inefficient treatments for some patients. For this reason, the interest in discovering natural antibacterial agents has increased, and these agents can be found in the essential oils of *Salvia officinalis*. The main advantage of using natural agents is that they do not induce antibiotic resistance, such as it happens with the long-term use of synthetic antibiotics.²⁹

Although, the anti-inflammatory effects of the ursolic acid contained by *Salvia officinalis* have been studied by Baricevic. *Salvia officinalis* tea has been traditionally used in treatment of the bronchitis, asthma, angina, mouth tissue inflammation, depressions or in various skin diseases. Carminative, antiseptic and antispasmodic properties of the *Salvia officinalis* essential oil have been reported. Their effects in the treatment of diseases of the nervous, circulatory and respiratory systems have been brought forth by Loizzo. Shaabani and Alizade explained the antimicrobial activity of the essential oil from *Salvia officinalis* against *Staphylococcus Aureus* and *Candida Albicans*.³⁰

Salvia essential oil is used in externally for inflammations and infections of the soft tissues (stomatitis, gingivitis and pharyngitis) and internally for excessive perspiration and dyspeptic symptoms. *Salvia* leaves and the essential oil possess carminative, antispasmodic, antiseptic and astringent properties.³¹

An infusion made of this plant is used for its hemostatic, estrogenic, antiperspirant, antineuralgic antiseptic, hypoglycemic effects, as well as other therapeutic effects, while the essential oil produced from this plant is used in large scale treatment of diseases of the nervous, circulatory, respiratory systems, as well as some digestive, metabolic/endocrine diseases. A recent study shows that hydroalcoholic extracts from *Salvia officinalis* are the active with the promastigote forms of *Leishmania major*.³²

Usually, cancer therapy involves surgery, irradiation and medicine in various combinations. An efficient medicine treatment should kill the cancerous cells without affecting the activity of the healthy ones. Therefore, the identification of new cytotoxic drugs with low effects upon the immune system has developed into a new field of immune-pharmacological studies. It is known that anti-cancer agents induce an apoptosis, so that the death of the apoptotic cell reduces the sensitivity to treatment. A wide range of natural components of the anti-cancer agents show significant cytotoxic activity that operates in apoptosis. For instance, in a recent study, Zhahneh and collaborators showed that the methanol extract from *Salvia officinalis* has significant benefic effects in the prophylaxis of leukemia.³³

The plant extracts used in the traditional medicine have similar properties. In facts, many diterpenes isolated from some species of a plants, belonging to the *Salvia* Gender have proved interesting pharmacological properties: antioxidant, antimicrobial, anti-inflammatory, analgesic, antipyretic, hemostatic, hypoglycemic and antitumor.³⁴

It is known that foodstuffs contain fatties and oils that are rich in polyunsaturated fatty acids, which suffer slight oxidation reactions that are not desired in the process of processing (heating up) and neither when

stored (addition of salt, freezing). In order to prevent the loss of quality or to delay the effects of oxidation, synthetic phenolic antioxidants are currently in use (butylhydroxytoluene, butylated hydroxyanisole, third-butyl hydroquinone). For this reason, recent studies have been carried out on the existence of some polyphenolic antioxidants in some plants such as *Salvia* or rosemary.³⁵

We used the method of oil stability in order to assess the antioxidant activities of some compounds such as: carnosol, rosmanol, epirosmanol, isorasmanol and the carnosic acid, which represented a remarkable activity comparable to that of the alpha-tocopherol. The rosmarinic acid and carnosol were the main components of all phenolic antioxidant extracts isolated from *Salvia officinalis*.³⁶

The increasing interest in the replacement of synthetic antioxidants with natural antioxidants showing the same efficiency could be beneficial both for the increase of foodstuff quality and for a positive influence upon the treatments of various human pathologies. For instance, it has been demonstrated that the raw ethanolic extract of *Salvia officinalis* has antioxidant properties comparable with butylhydroxytoluene.³⁷ *Salvia* is the rich source of phytochemicals, including flavonoids, sesquiterpenoids, diterpenoids, triterpenes and sesterpenes. Some are the active components such as the rosmarinic acid and acetyl homininon have been isolated from roots of *Salvia officinalis*. These compounds, extracts and essential oils reduce in vitro colon, breast and pulmonary cancer and leukemia and reduce the number of oncogenic cells.³⁸

6. Marketed Formulations

Salvia officinalis, commonly known as sage, is formulated into various products to harness its antioxidant, anti-inflammatory, and antimicrobial properties. Here are some marketed formulations:

- Topical Creams and Gels: Sage extract is incorporated into creams and gels for skin application, leveraging its therapeutic potential for wound healing, skin disorders, and anti-aging.
- Self-Emulsifying Systems: Researchers have developed self-nanoemulsifying drug delivery systems (SNEDDSs) to enhance the bioavailability and solubility of sage's active compounds, such as carnosol.
- Dermal Formulations: Sage-based formulations are designed for dermal application, utilizing surfactants and co-surfactants to improve skin penetration and efficacy.
- Cosmetic Products: Sage extract is used in various cosmetic products, including skincare creams, serums, and face masks, due to its antioxidant and anti-inflammatory properties.
- Pharmaceutical Preparations: Sage extract is being studied for its potential in managing inflammation, cancer, and other diseases, with researchers exploring its formulation into pharmaceutical products.

Some specific formulations include:

- SNEDDS-based Cream: A cream formulation containing *Salvia officinalis* extract, developed using Labrasol and Labrafil M as nonionic surfactants, Transcutol HP as the co-surfactant, and isopropyl myristate as the oily phase.
- SNEDDS-based Gel: A gel formulation containing *Salvia officinalis* extract, designed to improve skin penetration and efficacy.³⁹

These formulations aim to harness the therapeutic potential of *Salvia officinalis*, although more research is needed to confirm their long-term safety and efficacy.

Conclusion

Traditional remedies and herbal-based treatments are currently quite popular worldwide. As a result, a lot of clinical and experimental research on medicinal plants is being done, and the results need to be updated

and integrated. The available pharmacological findings that have been regularly reported for *S. officinalis* have been attempted to be discussed in this article. This plant exhibits anticancer, anti-inflammatory, antinociceptive, antioxidant, antibacterial, hypoglycemic, hypolipidemic, and memory-enhancing properties, according to the research currently in publication. Clinical research have verified *S. officinalis*'s efficacy as a medicinal plant that has antinociceptive, hypolipidemic, and memory-enhancing properties. In addition to the activities listed above, *S. officinalis* has been demonstrated in literature to have a variety of additional biological properties, including activating benzodiazepine receptors and preventing seizures brought on by pentylenetetrazole. Future research is required to clarify the potential therapeutic uses for these properties of *S. officinalis*. Future research is also required to pinpoint the precise molecular pathways underlying the toxicity, effects, and drug-drug interactions of *S. officinalis*.

References

1. Bisset NG, Wichtl M. Herbal Drugs and Phytopharmaceuticals: A Handbook for Practice on a Scientific Basis with Reference to German Commission E Monographs. 2nd ed. Boca Raton, FL: CRC Press; 2001:440-443.
2. Miura K, Kikuzaki H, Nakatani N. Apianane terpenoids from *Salvia officinalis*. Phytochemistry. 2001;58:1171-1175.
3. Physicians' Desk Reference (PDR) for Herbal Medicines. 3rd ed. Montvale, NJ: Thompson; 2004:698-701.
4. Zargari A. Medicinal Plants. 4th ed. Tehran: Tehran University Press; 1990: 59-64.
5. Garcia CSC, Menti C, Lambert APF, et al. Pharmacological perspectives from Brazilian *Salvia officinalis* (Lamiaceae): antioxidant, and antitumor in mammalian cells. An Acad Bras Ciênc. 2016;88:281-292.
6. Perry EK, Pickering AT, Wang WW, Houghton PJ, Perry NS. Medicinal plants and Alzheimer's disease: from ethnobotany to phytotherapy. J Pharm Pharmacol. 1999;51:527-534.
7. Adams M, Gmünder F, Hamburger M. Plants traditionally used in age related brain disorder: a survey of ethnobotanical literature. J Ethnopharmacol. 2007;113:363-381.
8. European Medicines Agency. Community Herbal Monograph on *Salvia officinalis* L., Folium. London: European Medicines Agency; 2009.
9. Badiie P, Nasirzadeh AR, Motaffaf M. Comparison of *Salvia officinalis* L. essential oil and antifungal agents against candida species. J Pharm Technol Drug Res. 2012;1:7.
10. Capek P, Hříbalová V. Water-soluble polysaccharides from *Salvia officinalis* L. possessing immunomodulatory activity. Phytochemistry. 2004;65:1983-1992.
11. El Hadri A, del Río MAG, Sanz J, et al. Cytotoxic activity of a-humulene and transcaryophyllene from *Salvia officinalis* in animal and human tumor cells. An R Acad Nac Farm. 2010;76:343-356.
12. Hayouni EA, Chraief I, Abedrabba M, et al. Tunisian *Salvia officinalis* L. and *Schinus molle* L. essential oils: their chemical compositions and their preservative effects against *Salmonella* inoculated in minced beef meat. Int J Food Microbiol. 2008;125:242-251.
13. Langer R, Mechtler C, Jurenitsch J. Composition of the essential oils of commercial samples of *Salvia officinalis* L. and *S. fruticosa* Miller: a comparison of oils obtained by extraction and steam distillation. Phytochem Anal. 1996;7: 289-293.
14. Lima CF, Carvalho F, Fernandes E, et al. Evaluation of toxic/protective effects of the essential oil of *Salvia officinalis* on freshly isolated rat hepatocytes. Toxicol In Vitro. 2004;18:457-465.

15. Lima CF, Andrade PB, Seabra RM, Fernandes-Ferreira M, Pereira-Wilson C. The drinking of a *Salvia officinalis* infusion improves liver antioxidant status in mice and rats. *J Ethnopharmacol*. 2005;97:383-389.
16. Lima CF, Fernandes-Ferreira M, Pereira-Wilson C. Drinking of *Salvia officinalis* tea increases CCl₄-induced hepatotoxicity in mice. *Food Chem Toxicol*. 2007;45:456-464.
17. Lima CF, Valentao PCR, Andrade PB, Seabra RM, Fernandes-Ferreira M, Pereira-Wilson C. Water and methanolic extracts of *Salvia officinalis* protect HepG2 cells from t-BHP induced oxidative damage. *Chem Biol Interact*. 2007;167:107-115.
18. Lu Y, Foo LY. Flavonoid and phenolic glycosides from *Salvia officinalis*. *Phytochemistry*. 2000;55:263-267.
19. Mitic-Culafic D, Vukovic-Gacic B, Knezevic-Vukcevic J, Stankovic S, Simic D. Comparative study on the antibacterial activity of volatiles from sage (*Salvia officinalis* L.). *Arch Biol Sci*. 2005;57:173-178.
20. Russo A, Formisano C, Rigano D, et al. Chemical composition and anticancer activity of essential oils of Mediterranean sage (*Salvia officinalis* L.) grown in different environmental conditions. *Food Chem Toxicol*. 2013;55:42-47.
21. Seidel V. Initial and bulk extraction. In: Sarker SD, Latif Z, Gray AI, eds. *Natural Product Isolation*. New Jersey, NY: Humana Press; 2006:27-46.
22. Velickovic DT, RanCelovic NV, Ristic MS, Velickovic AS, Smelcerovic AA. Chemical constituents and antimicrobial activity of the ethanol extracts obtained from the flower, leaf and stem of *Salvia officinalis* L. *J Serb Chem Soc*. 2003;68:17-24.
23. Venskutonis PR. Effect of drying on the volatile constituents of thyme (*Thymus vulgaris* L.) and sage (*Salvia officinalis* L.). *Food Chem*. 1997;59:219-227.
24. Wang M, Li J, Rangarajan M, et al. Antioxidative phenolic compounds from Sage (*Salvia officinalis*). *J Agric Food Chem*. 1998;46:4869-4873.
25. Wang M, Kikuzaki H, Zhu N, Sang S, Nakatani N, Ho CT. Isolation and structural elucidation of two new glycosides from sage (*Salvia officinalis* L.). *J Agric Food Chem*. 2000;48:235-238.
26. Hernandez-Saavedra D, Perez-Ramirez IF, Ramos-Gomez M, Mendoza-Diaz S, Loarca-Pina G, Reynoso-Camacho R. Phytochemical characterization and effect of *Calendula officinalis*, *Hypericum perforatum*, and *Salvia officinalis* infusions on obesity associated cardiovascular risk. *Med Chem Res*. 2016;25: 163-172.
27. Kianbakht S, Abasi B, Perham M, Hashem Dabaghian F. Antihyperlipidemic effects of *Salvia officinalis* L. leaf extract in patients with hyperlipidemia: a randomized double-blind placebo-controlled clinical trial. *Phytother Res*. 2011;25:1849-1853.
28. Fournomiti M, Kimbaris A, Mantzourani I et al. 2015 Antimicrobial activity of essential oils of cultivated oregano (*Origanum vulgare*), sage (*Salvia officinalis*), and thyme (*Thymus vulgaris*) against clinical isolates of *Escherichia coli*, *Klebsiella oxytoca*, and *Klebsiella pneumonia*, *Microbial Ecology in Health & Disease* 26 23289.
29. Baricevic D, Sosa S, Della Loggia R et al. 2001 Topical anti-inflammatory activity of *Salvia officinalis* L. leaves: the relevance of ursolic acid, *Ethnopharmacol* 75 125-132.
30. Walch S, Tinzoh L, Zimmerman B et al. 2011 Antioxidant capacity and polyphenolic composition as quality indicators for aqueous infusions of *Salvia officinalis* L, *Front Pharmacol* 2 29-44.

31. Khan A, Najeeb-ur-Rahman, Alkharfy K et al. 2011 Antidiarrheal and antispasmodic activities of *Salvia officinalis* are mediated through activation of K⁺ channels, J Bangladesh Pharmacol Soc 6 111–116.
32. Loizzo M R, Tundis R, Menichini F et al. 2007 Cytotoxic activity of essential oils from Labiatae and Lauraceae families against in vitro human tumor models, Anticancer Res 27 3293–3299.
33. Alizade A and Shaabani M 2012 Essential oil composition, phenolic content, antioxidant and antimicrobial activity in (*Salvia officinalis* L.) cultivated in Iran, Advances Environment Biol 6 221–226.
34. Istudor V 2001 Farmacognozie. Fitochimie. Fitoterapie, Editura Medicala, Bucuresti, Romania [25] Serakta M, Djerrou Z, Mansour-Djaalab H et al. Antileishmanial activity of some plants growing in Algeria: Juglans Regia, Lawsonia Inermis and *Salvia officinalis*, Afr J Tradit Complement Altern Med. 10 427–430.
35. Shahneh F Z, Valiyari S, Baradaran B et al. 2013 Inhibitory and Cytotoxic Activities of *Salvia officinalis* L. Extract on Human Lymphoma and Leukemia Cells by Induction of Apoptosis, Advanced Pharmaceutical Bulletin 3 51–55.
36. Cuvelier M E, Verset C and Richard H 1994 Antioxidant constituents in sage (*Salvia officinalis*), J Agr Food Chem 42 665–669.
37. Ben H A, Gajdoova D and Have J 2006 Analysis of *Salvia officinalis* plant extracts by capillary electrophoresis, J Sep Sci 29 1188–1192.
38. Angelo A J S, Vercellotti J, Jacks T et al. 1996 Lipid oxidation in foods, Crit Rev Food Sci Nutr 36 175–224.
39. Bodnár, Krisztina, et al. "Development of *Salvia officinalis*–Based Self-Emulsifying Systems for Dermal Application: Antioxidant, Anti-Inflammatory, and Skin Penetration Enhancement." *Pharmaceutics* 17.2 (2025): 140.