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Phytochemical and pharmacological aspects of *Salvia officinalis*

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Abstract

Worldwide interest in herbal remedies and traditional therapies is growing these days. As a result, a large number of clinical and experimental investigations on medicinal plants are being conducted, and the results need to be updated and integrated. This plant exhibits anticancer, anti-inflammatory, antinociceptive, antioxidant, antibacterial, hypoglycemic, hypolipidemic, and memory-enhancing properties, according to the literature that is currently available. Clinical experiments have established the efficacy of *S. officinalis* as an antinociceptive, hypolipidemic, and memory-enhancing medicinal herb. Apart from the aforementioned impacts, *S. officinalis* has also been linked to various other biological processes, including benzodiazepine receptor activation and inhibition of pentylenetetrazole-induced seizures, as shown in scientific literature. Future research must clarify the potential therapeutic uses for these actions of *S. officinalis*.

Key words: *S. officinalis,* herbal remedies, therapeutic uses

Introduction

At least 25% of medications in the current pharmacopeia are still sourced from plants, and many more are synthetic analogs based on plant-derived prototype chemicals. The growing expenses of prescribing medications for the preservation of one's health and well-being and the bioprospecting of novel plant-derived medications have stimulated interest in medicinal plants as a resurgent health assistance. expanding confidence in herbal therapy is one of the many factors contributing to the continued expanding acknowledgment of medicinal herbs. The World Health Organization states that the greatest place to find a wide range of medications is from medicinal plants. Consequently, research on these plants is necessary to comprehend their characteristics, safety, and effectiveness.

Numerous medications derived from plants or plant derivatives have been documented in India's Ayurvedic system; identifying these substances' morphological, pharmacological, and pharmacognostic properties can help clarify their active ingredients and mechanisms of action. Phytomedicines and plant-based pharmaceuticals with established medicinal benefits are typically prescribed drugs that have undergone

extensive toxicological and clinical testing before being authorized for sale. The survey found that 18% of the top 150 prescription medications in the world have plant-based ingredients. People have searched nature for medicines to treat their illnesses since ancient times. Like with animals, the medicinal plant was first employed based only on instinct. As medical studies progressed, it was determined that plants undergo processing in biosynthetic laboratories to extract chemical compounds that could cure illnesses. Many of the phytochemicals that scientists extract from medicinal plants are highly effective against a variety of illnesses. Phytochemicals such as morphine, nicotine, atropine, quinine, and aconitine are well-known examples. Research has recently shown an increasing tendency to support the biological actions of therapeutic herbs. Numerous scientific studies on the effectiveness and chemotherapeutic potential of medicinal plants in the management of various illnesses have been published. (1-5)

Plant profile

Classification

Kingdom: Plantae

Phylum: Streptophyta

Class: Equisetopsida

Subclass: Magnoliidae

Order: Lamiales

Family: Lamiaceae

Genus: *Salvia*

Species: *officinalis* (6-9)

Common Names: Sage, Common Sage, Garden Sage, Golden Sage, Kitchen Sage, True Sage, Culinary Sage, Dalmatian Sage, Broadleaf Sage. (6-9)

Synonym: *Salvia officinalis gallica, Salvia officinalis lavandulifolia, Salvia officinalis multiflora, Salvia officinalis officinalis, Salvia officinalis oxyodon.* (6-9)

Distribution

Although *Salvia officinalis* is native to the Mediterranean region, it has spread throughout the world. It has been utilized as an ornamental garden plant in recent times, and it has a long history of use in medicine and cuisine. (6-9)

Description

The tiny hairs on sage leaves are known as trichomes. Size, leaf and blossom color, foliage pattern, and variegated leaf kinds vary greatly amongst cultivars. The Old-World variety has flowers that might be white, pink, or purple, although lavender is the most common color. It reaches a height and width of around 60 cm. The plant blooms in the summer or late spring. The oblong leaves can measure up to 65 mm in length and 25 mm in width. The very small, silky hairs on the underside of the leaves give them a virtually white appearance. The leaves are grey-green. (6-9)

Traditional uses

Traditional medicine and cooking have long employed the aerial parts of the *S. officinalis* shrub. This plant's taste and seasoning qualities have led to its widespread usage in the cooking of numerous dishes. It has been

used to cure a variety of conditions in Asian and Latin American folk medicine, such as seizures, ulcers, gout, rheumatism, inflammation, dizziness, tremors, paralysis, diarrhea, and hyperglycemia. *S. officinalis* has been used in European traditional medicine to treat inflammations of the skin and throat, age-related cognitive problems, excessive perspiration, and moderate dyspepsia (such as heartburn and bloating). (6-9)

Bioactive compounds

S. officinalis contains a wide range of constituents, including alkaloids, carbohydrates, fatty acids, glycosidic derivatives (e.g., cardiac glycosides, flavonoid glycosides, saponins), phenolic compounds (e.g., coumarins, flavonoids, tannins), poly acetylenes, steroids, terpenes/terpenoids (e.g., monoterpenoids, diterpenoids, triterpenoids, sesquiterpenoids), and waxes. Since S. officinalis has essential oil, alcoholic extract, aqueous extract, butanol fraction, and infusion preparation, the majority of its phytochemicals have been identified from these sources. S. officinalis aerial parts were used to make an essential oil, of which more than 120 components have been identified. Borneol, camphor, caryophyllene, cineole, elemene, humulene, ledene, pinene, and thujone are among the principal ingredients of the oil. *S. officinalis* has a high content of flavonoids in both alcoholic and aqueous extracts, including luteolin-7-glucoside and rosmarinic acid.

Moreover, the methanolic extract of *S. officinalis* contains phenolic acids including caffeic acid and 3-Caffeoylquinic acid. The infusion made from *S. officinalis* contains a number of flavonoids, including borneol, cineole, camphor, and thujone, as well as a number of volatile ingredients, including quercetin, rosmarinic acid, epicatechin, epigallocatechin gallate, and luteolin-7-glucoside. In the S. officinalis infusion extract, rosmarinic acid and ellagic acid are the most prevalent flavonoids, followed by rutin, quercetin, and chlorogenic acid. The carbohydrates arabinose, galactose, glucose, mannose, xylose, uronic acids, and rhamnose are the most abundantly reported in this plant.

When examining the phytochemical content of *S. officinalis*, it can be observed that linalool is the most abundant in the stem, α-pinene and cineole are highest in the flowers, and bornyl acetate, camphene, camphor, humulene, limonene, and thujone are the most abundant in the leaves. It should be remembered, though, that *S. officinalis* chemical makeup would differ according to environmental factors like altitude, water availability, and climate, just like it would with other herbs. (6-9)

Reported Pharmacological Activities

G. Privitera et al. (2019) investigated the in vitro antiproliferative action of essential oil from *Salvia officinalis* and its main components on hormone-dependent cancer cell lines. At different dosages and time points, the effects of the essential oil and its three main constituents—thujone, 1,8-cineole, and camphor—were assessed in LNCaP cells (which represent prostate carcinoma), MCF-7 cells (which represent breast carcinoma), and HeLa cells (which represent cervical carcinoma). Utilizing the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide test, cell viability and proliferation were assessed. After 48 hours of incubation, the essential oil at concentrations of 100 µg/mL and 200 µg/mL significantly reduced the viability of the MCF7, LNCaP, and HeLa cell lines. Following a 48-hour incubation period, the cell lines exhibited reduced viability upon treatment with a blend of the essential oil's three primary components at concentrations of 100 µg/mL and 200 µg/mL. These primary findings may help in the development of novel antiproliferative treatment drugs. (10)

Stan et al. (2019) reported the *in vivo* antitumor effect of hydroalcoholic extract of *Salvia officinalis* leaves and the association between the extract and Doxorubicin increase the antitumor effect of Doxorubicin. The antiproliferative effects against experimentally implanted cancer cells (EAC) were found to be enhanced by combined therapy, with modest hematological parameter protection and no extra cytotoxicity. Doxorubicin and *Salvia officinalis* may interact to suppress the immune system; however, tumor growth inhibition may also play a role in preventing leukocytosis. (11)

Yinrong Lu et al (2001) reported the antioxidant activities of polyphenols from *Salvia officinalis*. The ability of the sage polyphenols, which include flavone glycosides and many rosmarinic acid derivatives, to scavenge superoxide anion radicals and DPPH as well as to convert Mo (VI) to Mo (V) was assessed as an indicator of their antioxidant activity. In three different test systems, the rosmarinic acid derivatives all demonstrated strong antioxidant activity. In particular, their ability to convert Mo (VI) to Mo(V) and their superoxide radical scavenging activity, with values ranging from 220 to 300 SOD units/mg, were 4-6 and 15-20 times greater than trolox, respectively. The catechols that scavenge free radicals and the caffeic acid moieties that inhibit xanthine oxidase may be responsible for the high SOD activity of rosmarinic acids. The flavonoids' antioxidant activity varied, with luteolin glycosides—which have a catechol B-ring—having a higher level of activity than those that don't (apigenin glycosides). (12)

Dana Maria Copolovici et al (2022) evaluated the chemical and biochemical characteristics and the potential aromatherapy applications of the essential oil (EO) of aerial parts of *Salvia officinal*is within a hospital environment. ATR-FTIR spectroscopy and gas chromatography with mass spectrometry were used to determine the chemical makeup. In this study, three different types of sage essential oils were examined: one produced through in-house hydrodistillation and two commercial oils. These EOs were assigned to various chemotypes following the results. The in-house sage EO exhibited a high amount of 1,8-cineole, borneol, and α-thujone, similar to the Dalmatian type, whereas the first two samples were similar to the most prevalent chemotype (α-thujone > camphor > 1,8-cineole > β-thujone). The latter sample was chosen for examination of its antioxidant and medicinal properties since borneol, a bicyclic monoterpene, is recognized in traditional Asian medicine as having anesthetic and analgesic properties. According to the study, sage EO has a minor antioxidant ability (33.61% and 84.50% inhibition, respectively, as assessed by DPPH and ABTS assays). However, hospitalized patients may find greater enjoyment if they inhale sage EO with a high borneol concentration. (13)

Zakaria Khiya et al (2019) investigated the Valorization of the *Salvia officinalis* Leaves of the Morocco bioactive extracts to explore its antioxidant activity and corrosion inhibition using two methods: potentiodynamic polarization and impedance spectroscopy (EIS) measurements. The presence of flavonoids, saponins, terpenoids, polyphenols, catechics, and gallic tannins was highlighted by the phytochemical screening. The results indicated that the methanolic extract had high levels of flavonoids (0.037 ± 0.003 mg EQ/g of extract) and total phenols (1.044 ± 0.004 mg GAE/g of extract). The essential oil production was $4.13 \pm 0.01\%$, and its GC–MS analysis revealed that Trans-Thujone, 1,8-cineol, Camphor, Caryophyllene, α-pinene, Dehydra-Aromadendrane, and Guaiol were the predominant compounds. The DPPH method's results of the antioxidant activity measurement made it possible to calculate the oil's IC50, which came out to be

309.42 mg/ml. At a concentration of 4 g/l, the latter has demonstrated an inhibition effectiveness of 83.06% and 70.58% for both techniques, respectively, while the methanolic extract has demonstrated an inhibition efficiency of 91.62% and 49.70%, respectively, at the same concentration. (14)

Müberra Koşar et al. (2010) reported the composition and antioxidant-related activities of methanol: acetic acid (99:1, v/v) soluble crude extract isolated from *S. officinalis* leaves. Gallic acid equivalents were used to estimate the total phenol content, and high-performance liquid chromatography with photodiode array detection was used to quantify the qualitative-quantitative phenolic content. Ferric reductive capacity, 1,1-diphenyl-2-picrylhydrazyl, and hydroxyl free radical scavenging measurements were used to assess the antioxidant potential. The chromatographic and spectral characteristics of caffeic acid, carnosic acid, luteolin, luteolin-7-O-glucoside, and rosmarinic acid were used to identify and quantify the constituents of the crude extract, which also contained hydroxybenzoic acids, hydroxycinnamic acids, flavonoids, and diterpenoids. All of the fractions except the n-hexane fraction showed variable levels of efficiency in the antioxidant-related assays less effective at reducing iron (III) than the positive controls, ascorbic acid, BHA, and BHT and significantly more effective than pycnogenol, a commercial preparation high in proanthocyanidins. (15)

Yinrong Lu et al (2001) reported the isolation of Salvianolic acid, a potent phenolic antioxidant from *Salvia officinalis.* 7,8-dihydroxy-2-(3,4-dihydroxyphenyl)-1,2-dihydronaphthalene-1,3-dicarboxylic acid di(1-carboxy-2-(3,4-dihydroxyphenyl)) ethyl ester was found to be salvianolic acid. Additionally, two new hydrolytic products were identified and characterized: 7,8-dihydroxy-2-(3,4-dihydroxyphenyl)-1,2-dihydronaphthalene-1,3-dicarboxylic acid, as well as the corresponding 3-monoester. For superoxide anion and DPPH radicals, it demonstrated potent free radical scavenging properties. (16)

Mohadese Azarsina et al. (2015) evaluated the clinical effects of a mouthwash containing *Salvia officinalis* leaves extracts on *Streptococcus mutans* (SM) causing dental plaque in school-aged children. 70 girls, ages 11 to fourteen, who shared the same socioeconomic circumstances and dental hygiene standards participated in a double-blind clinical trial study at a dormitory. The colony count was considerably lowered by the mouthwash. In the test group, the average number of colonies per plaque sample was 3900 at baseline and 300 following the use of mouthwash. The pre-test colony count in the control group was 4400; this was subsequently reduced to 4000, albeit the difference was not statistically significant. (17)

Lato Pezo et al (2022) investigated the chemical composition of steam distillate essential oil and corresponding hydrolate obtained from *S. officinalis* as well as the influence of weather conditions on their chemical profiles. By figuring out the minimal inhibitory and biocidal concentrations, their antibacterial efficacy was examined in vitro. The primary constituents of the essential oil were cis-thujone, which was followed in order by camphor, trans-thujone, and 1,8-cineole. In contrast, the hydrolate's primary constituents were camphor, cis-thujone, and 1,8-cineole. *Klebsiella oxytoca* showed the highest sensitivity to the evaluated endotoxins (EOs), with minimum inhibitory concentration (MIC) and minimum bactericidal/fungicidal concentration (MBC/MFC) values of 14.20 and 28.4 μL mL^{-1}, respectively, among the microorganisms examined. Other studied bacteria had MIC and MBC values ranging from 28.40 to 227.25 μL mL^{-1}, whereas *Candida albicans* had MIC/MFC values between 28.40/56.81 and 56.81–113.63 μL mL^{-1}. (18)

Juman D. Alkhayoun et al (2020) evaluated in vitro antimicrobial effect of *Salvia officinalis* leaf extracts on the salivary *Lactobacilli* in comparison to chlorhexidine. By using the agar diffusion technique, it was demonstrated that both alcoholic and aqueous sage extracts inhibited the growth of *Lactobacilli*. The diameter of the inhibition zone grew as the sage extract concentration increased, but the aqueous extract's effect was less pronounced than the alcoholic extract's. Aqueous and alcoholic sage extracts had minimum bactericidal concentrations of 50% and 20%, respectively. Salivary *Lactobacilli* are more inhibited by alcoholic sage extract than by aqueous extract. (19)

Mohammad Akram Randhawa et al (2018) investigated the activity of methanolic extract of aerial parts of S. officinalis against ATCC strains of some bacteria (*Staphylococcus aureus, Enterococcus faecalis, Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa*), Methicillin Resistant *Staphylococcus aureus* (MRSA), Multi-drug resistant *Acinetobacter baumannii* and some fungi (*Candida albicans* and *Aspergillus flavus*). To find the minimal inhibitory doses of S. officinalis methanolic extract against test organisms, the Agar dilution method was employed. The extract exhibited strong action (MICs 5–10 mg/ml) against *Staphylococcus aureus*, MRSA, and the multidrug-resistant *Acinetobacter baumanni*; moderate activity (MICs 10–20 mg/ml) against *Candida albicans*; and mild activity (MICs 20–40 mg/ml) against *Aspergillus flavus* and Gram-negative bacilli. The multidrug-resistant *Acinetobacter baumannii*, MRSA, *Staphylococcus aureus*, and *Candida albicans* are among the resistant and opportunistic infections that the methanolic extract of S. officinalis exhibits good effectiveness against. (20)

Miroslava Císarová et al (2018) reported the antimicrobial activity of sage oil, some of its pure components (1,8-cineole, borneol, and α-ß thujone) and sage extract were studied against selected strains of Gram-positive bacteria (*Enterococcus faecalis, Staphylococcus aureus*) and Gram-negative bacteria (*Klebsiella pneumoniae, Escherichia coli*). The antimicrobial activities were determined by using the micro broth dilution method. The absorbance on a microplate was measured to calculate the percentage of bacterial growth. Sage essential oil was shown to have the best minimum inhibitory concentration (MIC) of 96.05 µg/mL against the Gram-positive bacteria S. aureus. Antimicrobial drugs block more Gram-positive bacterial strains than Gram-negative bacterial strains, according to the results of the percentage growth of the tested bacteria. The gas chromatography-mass spectrometry (GC-MS) technique was used to examine the chemical makeup of sage essential oil (EO). Primarily, ƶ-thujone, borneol, camphor, (−)-Isopulegol, ß-thujone, and 1,8-cineole (8.00%) are present in sage essential oil. The scavenging impact of sage oil and sage propylene glycol extract on DPPH radical activity was used to determine their antioxidant capabilities. Sage EO had a higher level of antioxidant activity (71.55%), whereas sage propylene glycol extract had the lowest level (60.93%). The pharmaceutical industry may be able to address the issue of microbe resistance to traditional antibiotics by producing antibacterial medications as a result of the studied antimicrobials from sage having antibacterial action. (21)

Samy Selim et al (2022) investigated the antimicrobial and antibiofilm effects of essential oil (EO) obtained from *Salvia officinalis* against *S. enterica*. It had been found that the inhibitory zones for EO from S. officinalis leaves had a diameter of 21 mm. A notable in vitro inhibitory action was demonstrated by *S. officinalis* EO at a concentration of 5% towards the biofilm formation of various S. enterica isolates. GC-MS analysis of the EO revealed discrete components that made up 89.94% of the entire oil component. The three most noticeable

substances were β-caryophyllene, α-terpineol, and 1,8-cineole. Therefore, it is appropriate to pay attention to the use of *S. officinalis* EO as a food preservative and supplementary treatment for bacterial food-borne illnesses. (22)

Abdelsamed I. Elshamy et al. (2022) reported *in-vivo* anticonvulsant and Analgesic Activities of Sclareol Isolated from *Salvia officinalis*. Using the MES protocol, sclareol (50 mg/kg) reduced tonic convulsions from 100% (positive control) to 33.33% with 16.66% mortality. Moreover, convulsions were reduced to 16.66% with no fatalities at 100 mg/kg. It provided dose-dependent protection against progressively increasing electric shock in the MEST test, similar to that of phenytoin. A 100% fatal dose of pentylenetetrazole caused global clonic convulsions. A considerable incidence reduction in fatality was observed with a prolonged latency to 1-3 phases of clonic convulsions following scraleol administration. was not neurotoxic in the rotarod test at any dose. Scalaneol demonstrated an analgesic effect in the hot-plate test 60 and 90 minutes after the drug was administered. Finally, sclareol has no adverse effects on the central nervous system and, in addition to its central anti-nociceptive activity, protects against seizures generated by chemicals and/or electrical stimulation. This implies that sclareol might be a key ingredient in a novel antiepileptic and analgesic medication. (23)

Dadfar Fereshteh et al (2019) evaluated the effect of *Saliva officinalis* on the decreasing of the severity of the menopausal symptoms in postmenopausal women. Thirty postmenopausal women, ages 46 to 58, with varying degrees of postmenopausal symptoms participated in the study. A Menopause Rating Scale is used to record the degree of menopausal symptoms. For four weeks, each participant received a 100 mg pill of sage extract. Four weeks of sage extract ingestion was followed by a comparison of the severity of postmenopausal symptoms. The severity of hot flashes, nocturnal sweats, anxiety, exhaustion, and focus were found to alter significantly before and after sage extract use, according to the results. (24)

Carsten Tober et al (2019) reported the Modulation of neurological pathways by *Salvia officinalis* and its dependence on the manufacturing process and plant parts used. An acetylcholinesterase enzyme assay and multiple receptor binding assays (adrenergic alpha 2A, GABA (benzodiazepine site), GABAB; muscarinic M3, μ-opioid, serotonin 5-HT1A, serotonin 5-HT2B, serotonin 5-HT2C, and serotonin transporter) were performed on a hydroalcoholic, thujone-free extract obtained from recently harvested Salvia officinalis leaves. It was also investigated how the manufacturing method affected other extracts from various fresh or dry plant components. 50% of specific ligand binding to GABAA and GABAB receptors was substituted by the Salvia officinalis extract, with an inhibitory concentration (IC50) of 89 and 229 μg/ml, respectively. The muscarinic M3 receptors, μ-opioid receptors, adrenergic α2A receptors, and serotonin 5-HT1A receptors all showed strong binding affinity, with IC50 values of 15 μg/ml, 20 μg/ml, 25 μg/ml, and 19 μg/ml, respectively. The human serotonin transporter, 5-HT2B, and 5-HT2C receptors were all shown to be moderately interfered with; their IC50 values were all greater than 32 μg/ml. Two women, ages 51 and 37, provided native female hypothalamus tissue from which Salvia extract receptor binding data were verified. When fresh Salvia leaves were used instead of extracts from dried plants or stipes, the activity was 2- to 4-fold higher and the IC50 values were lower. These findings imply that the alcoholic extract's mechanism of action is the strong modulation of neuro-receptors and serotonin transporters, which may restore normal thermoregulation and menopausal mental impairment. (25)

Roaa A. Alkhairat et al. (2018) reported the effects of *Salvia officinalis* on cognitive impairment in Saudi Aging People. The purpose of this study was to determine whether giving older persons an oral sage tea extract for four weeks would improve their cognitive function. An MMSE score was used to assess cognitive function both before and after sage tea. All question scores showed a significant difference between the pre-and post-month periods, except the registration score, where the average score was higher the month following. This shows that giving sage herbs to older persons can enhance their cognitive function; this effect may be attributed to the herb's active ingredients. (26)

Hassan Barakat et al (2022) investigated the Antioxidative, Antidiabetic, and Hypolipidemic Properties of fermented camel milk (FCM)Combined with S. *officinalis* hydroalcoholic extract (SOHE) of Leaves in Streptozotocin-Induced Diabetes in Rats. High levels of phenolics with exceptional antioxidant activity were found in *S. officinalis,* according to phytochemical analysis and antioxidant capacity. Following this, HPLC examination revealed the presence of flavonoids and phenolic acids in significant proportions, with resveratrol and ferulic acid being the most prevalent, respectively. When FCM and SOHE were combined at 25 or 50 mg kg−1, they showed a synergistic effect that reduced random blood glucose (RBG) and fasting blood glucose (FBG) considerably and increased the percentage of weight gain recovery. FCM plus 50 mg of gallic acid equivalents (GAE) SOHE kg−1 had a significantly greater hypolipidemic effect than using FCM or SOHE alone. Triglycerides (TG), total cholesterol (CHO), high- and low-density lipoproteins (HDL and LDL), and very-low-density lipoproteins (VLDL) were noted to be attenuated. Moreover, metformin, FCM, or SOHE alone did not improve liver and kidney functions as much as a dose of 25 or 50 mg kg^{-1}. Furthermore, when compared to the STZ group (G2), FCM with 50 mg SOHE kg^{-1} demonstrated a notable improvement in the activity of antioxidant enzymes, reduced glutathione, catalase, superoxide dismutase, and a considerable reduction in malonaldehyde levels with 53.75%, 89.93%, 63.06%, and 58.69%, respectively. Histopathological analysis revealed that both the islets of Langerhans cells and the acini had normal histological structures when FCM + 25, 50 mg SOHE kg^{-1}, or 50 mg kg^{-1} metformin was administered. To sum up, the combination of FCM and SOHE demonstrated both therapeutical and synergistic effects. It might be advantageous and profitable for preventing oxidative stress and managing problems from diabetes mellitus. (27)

Saeed Kianbakht et al (2016) reported a Randomized Clinical Trial of *Salvia officinalis* Leaf Extract as Add-on to Statin Therapy in Hypercholesterolemic Type 2 Diabetic Patients. The DPPH radical scavenging assay was used to measure the antioxidant activity of the plant extract. Measurements were also taken of the capsules containing the plant extract's total flavonoid, total phenolic, and quercetin concentrations. Additionally, the effects of a two-month extract intake (500 mg capsule three times a day) on blood levels of fasting glucose (FG), two hours postprandial glucose (2hPPG), glycosylated hemoglobin (HbA1c), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), triglyceride, high-density lipoprotein cholesterol (HDL-C), serum aspartate aminotransferase (AST), serum alanine aminotransferase (ALT), creatinine, and body mass index were investigated in fifty patients and compared with the placebo group. In the DPPH experiment, the ascorbic acid IC_{50} was 5.626±0.001 µg/mL, whereas the extract IC_{50} was 87.26±0.003 µg/mL. The plant extract capsule's total flavonoid, total phenolic, and quercetin contents were 39.76±3.58 mg of rutin equivalents, 30.33±1.23 mg of gallic acid, and 0.13 mg, respectively. At the endpoint, the extract was superior to the placebo

in terms of HDL-C level but decreased FG, 2hPPG, HbA1c, TC, LDL-C, and triglyceride levels. Due to its strong antioxidant activity, the extract may help avoid the cardiovascular problems associated with DDMT2. (28)

S Akhondzadeh et al (2003) evaluated a double-blind, randomized, and placebo-controlled trial of *Salvia officinalis* extract (60 drops/day) in the treatment of patients with mild to moderate Alzheimer's disease. The primary efficacy metrics during the 16 weeks were the differences between the baseline and ADAS-cog and CDR-Sum of Boxes scores. Furthermore, a checklist was used to thoroughly record side effects throughout the investigation. At four months, the *S. officinalis* extract significantly outperformed the placebo in terms of cognitive functions. Regarding reported side effects, there were no appreciable variations between the two groups; nevertheless, agitation seemed to be more common in the placebo group. The study's findings show that *S. officinalis* extract is effective in treating mild to moderate Alzheimer's disease. (29)

Conclusion

Plants in the Labiatae/Lamiaceae family include *Salvia officinalis,* or sage. Originating in the Middle East and Mediterranean regions, it has now spread throughout the globe through naturalization. Several conditions, including seizures, ulcers, gout, rheumatism, inflammation, disorientation, tremors, paralysis, diarrhea, and hyperglycemia, have all been treated with S. officinalis in traditional medicine. To chronicle its traditional use and discover novel biological effects, this plant has been the focus of several studies in recent years. The pharmacological actions of S. officinalis are diverse in this research. The pharmacological results for S. officinalis that have been regularly reported are highlighted in this review with the most recent data. Hypoglycemic, hypolipidemic, anticancer, anti-inflammatory, antinociceptive, antioxidant, antibacterial, and antimutagenic properties are among the findings.

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