

Species (Family)

Salvia officinalis L. (Labiatae)

Synonym(s)

Dalmatian Sage, Garden Sage, True Sage
Red Sage refers to *Salvia haematodes* Wall.
Greek Sage refers to *Salvia triloba*⁽¹⁾
Spanish Sage refers to *Salvia lavundaefolia*

Part(s) Used

Leaf

Pharmacopoeial and Other Monographs

BHP 1996^(G9)
BP 2001^(G15)
Complete German Commission E^(G3)
ESCOP 1996^(G52)
Martindale 32nd edition^(G43)
PDR for Herbal Medicines 2nd edition^(G36)
Ph Eur 2002^(G28)

Legal Category (Licensed Products)

GSL^(G37)

Constituents^(G2,G22,G41,G52,G58,G62,G64)

Acids Phenolic—caffeic, chlorogenic, ellagic, ferulic, gallic and rosmarinic.⁽²⁾

Flavonoids 5-Methoxysalvigenin.

Terpenes Monoterpene glycosides. Diterpenes, abietanes including carnosic acid and derivatives, e.g. carnosol. Triterpenes, oleanolic acid and derivatives.

Tannins 3–8%. Hydrolysable and condensed.^(2,3)

Volatile oil 1–2.8%. Pharmacopoeial standard not less than 1.0% cut herb.^(G15,G28) Major components are α - and β -thujones (35–50%, mainly α). Others include 1,8-cineole, borneol, camphor, caryophyllene, linalyl acetate and various terpenes.^(4,5)

It has been noted that commercial sage may be substituted with *Salvia triloba*.⁽¹⁾ In contrast to *S. officinalis*, the principal volatile oil component of *S.*

triloba is 1,8-cineole, with α -thujone only accounting for 1–5%.⁽¹⁾ Compared to *S. officinalis*, volatile oil yield of various *Salvia* species is lower, with lower total ketone content and higher total alcohol content.⁽⁶⁾

Food Use

Sage is commonly used as a culinary herb. It is listed by the Council of Europe as a natural source of food flavouring (category N2).^(G16) This category indicates that sage can be added to foodstuffs providing the concentration of thujones (α and β) present in the final product does not exceed 0.5 mg/kg, with the exceptions of alcoholic beverages (10 mg/kg), bitters (35 mg/kg), food containing sage (25 mg/kg) and sage stuffing (250 mg/kg).^(G16) In the USA, sage is listed as GRAS (Generally Recognised As Safe).^(G65)

Herbal Use^(G2,G4,G7,G32,G43,G52,G54,G64)

Sage is stated to possess carminative, antispasmodic, antiseptic, astringent and antihidrotic properties. Traditionally, it has been used to treat flatulent dyspepsia, pharyngitis, uvulitis, stomatitis, gingivitis, glossitis (internally or as a gargle/mouthwash), hyperhidrosis, and galactorrhoea. The herbals of Gerard, Culpeper and Hill credit sage with the ability to enhance memory.⁽⁷⁾ The German Commission E approved internal use for dyspeptic symptoms and excessive perspiration, and external use for inflammation of mucous membranes of mouth and throat.^(G3)

Dosage

Leaf 1–4 g or by infusion three times daily;^(G7) 4–6 g daily.^(G3)

Liquid extract 1–4 mL (1:1 in 45% alcohol) three times daily.^(G7)

Gargles, rinses 2.5 g/100 mL water.^(G3)

Pharmacological Actions

In vitro and animal studies

Hypotensive activity in anaesthetised cats, CNS-depressant action (prolonged barbiturate sleep) in anaesthetised mice, and an antispasmodic action *in*

vitro (guinea-pig ileum) have been reported for a sage extract⁽⁸⁾ and for the essential oil.⁽⁹⁾

Antispasmodic activity Inhibition of contractions induced by acetylcholine, histamine, serotonin and barium chloride by 60–80% has been noted for a total sage extract, with lesser activity exhibited by a total flavonoid extract.⁽⁸⁾ An initial spasmogenic action exhibited by low doses of sage oil has been attributed to the pinene content.⁽⁹⁾ Antispasmodic activity *in vivo* (guinea-pigs) has been reported for sage oil administered intravenously, which released contraction of Oddi's sphincter induced by intravenous morphine.⁽⁵⁾

Anticholinesterase activity Early herbals claim that sage enhances the memory.⁽⁷⁾ The anticholinesterase activity of several *Salvia* species and their constituents have been investigated in the search for new drugs for the treatment of Alzheimer's disease. The inhibition of anticholinesterase *in vitro* by an ethanolic extract of *S. officinalis* (2.5 mg/mL) was 68%, and by oils of *S. officinalis* and *S. lavandulaefolia* (0.1 µg/mL) was 52% and 63%, respectively.⁽¹⁰⁾ The IC₅₀ value of *S. lavandulaefolia* oil is reportedly 0.03 µg/mL.⁽¹¹⁾ The monoterpenes 1,8-cineole and α-pinene from the oil have been identified as the inhibitors of acetylcholinesterase with IC₅₀ values of 0.67 and 0.63 mmol/L, respectively.⁽¹¹⁾ Rats given *S. lavanadulaefolia* oil (20 µL or 50 µL for five days) were sacrificed, and acetylcholinesterase activity assessed for striatum, cortex and hippocampus of brain left hemisphere.⁽¹²⁾ At the lower dose, there was a decrease in acetylcholinesterase activity in the striatum, but not in the hippocampus or cortex of treated rats. At the higher dose, there was a decrease in striatal acetylcholinesterase activity. It was concluded that the oil inhibited acetylcholinesterase in selective areas of the brain.

Hypoglycaemic activity Hypoglycaemic activity *in vivo* (rabbits) has been reported for *S. lavandulaefolia*.⁽¹³⁾ and for mixed phytotherapy preparations containing various *Salvia* species, including *S. officinalis*.⁽¹⁴⁾ Activity in normoglycaemic, hypoglycaemic and in alloxan-diabetic rabbits was observed, although no change in insulin concentrations was noted.⁽¹³⁾

Antimicrobial and antiviral activity Antimicrobial activity of the volatile oil has been attributed to the thujone content.⁽⁴⁾ Antimicrobial activity *in vitro* was noted against *Escherichia coli*, *Shigella sonnei*, *Salmonella* species, *Klebsiella ozanae* (Gram-negative), *Bacillus subtilis* (Gram-positive), and against various fungi (*Candida albicans*, *C. krusei*, *C. pseudotropicalis*,

Torulopsis glabrata, *Cryptococcus neoformans*).⁽¹⁵⁾ No activity was observed versus *Pseudomonas aeruginosa*.⁽⁴⁾ Microencapsulation of sage oil into gelatin-acacia capsules introduced a lagtime with respect to antibacterial activity and inhibited antifungal activity.⁽⁴⁾ Diterpene constituents of *S. officinalis* are reported to be active against vesicular stomatitis virus.^(G52)

Other activities An aqueous ethanolic extract of sage (50%) strongly inhibited collagenolytic activity of *Porphyromonas gingivitis*.^(G52) In addition to anticholinesterase activity, other biological activities have relevance in the treatment of Alzheimer's disease. In this context, *S. lavanadulaefolia* and its individual constituents have been assessed for antioxidant, anti-inflammatory and oestrogenic activities.⁽¹¹⁾ An ethanolic extract of dried herb (5 mg/mL) and the monoterpenes α- and β-pinene and 1,8-cineole (0.1 mol/L) inhibited bovine brain liposome peroxidase activity. Anti-inflammatory activity was demonstrated by weak inhibition of thromboxane B₂ and leukotriene B₄ synthesis, and possible oestrogenic activity of sage oil (0.01 mg/mL) and geraniol (0.1–2 mmol/L), demonstrated by induction of β-galactosidase in yeast cells.

Other species Various activities in rats, mice and rabbits have been reported for a related species, *S. haematodes* Wall. (commonly known as red sage), including wound-healing, anti-inflammatory, analgesic, anticonvulsant and hypotensive, and positive inotropic and chronotropic actions (*in vitro*).^(16,17) *In vivo* studies have indicated different activities for *S. triloba* and *S. verbenaca*, compared with *S. officinalis*.⁽⁸⁾

Clinical studies

Excessive sweat induced by pilocarpine was inhibited by a dialysate of an aqueous extract of fresh sage.^(G52) In an open study, 40 patients were given dried aqueous extract of sage (440 mg, equivalent to 2.6 g herbs) and 40 were given infusion of sage (4.5 g herb daily). Reduction of sweat (less than 50%) was achieved in both groups of patients with idiopathic hyperhidrosis.^(G52) It should be noted, however, that this study did not include a control group.

A double-blind, placebo-controlled, crossover study involving 20 healthy volunteers compared the effects of 50 µL, 100 µL and 150 µL of *S. lavandulaefolia* oil and sunflower oil.⁽¹²⁾ Cognitive assessment indicated improvements in both immediate and delayed word recall scores, coupled with decrements in accuracy and speed of attention, with sage oil 50 µL. At this dose, self-related alertness at 2.5 hours and

calmness at 4 hours and 6 hours were reported to be reduced. The results suggest that the effects of sage oil in modulating mood and cognition are worth further investigation.

Side-effects, Toxicity

A case of human poisoning has been documented following ingestion of sage oil for acne.⁽¹⁸⁾ Convulsant activity in both humans and animals has been documented for sage oil.^(19,20) In rats, the subclinical, clinical and lethal doses for convulsant action of sage oil are estimated as 0.3, 0.5, and 3.2 g/kg.⁽¹⁹⁾ This toxicity has been attributed to the ketone terpenoids in the volatile oil, namely camphor and thujone. Acute LD₅₀ values for sage oil are documented as 2.6 g/kg in rats for oral administration and 5 g/kg in rabbits for intradermal administration.⁽²¹⁾ *S. officianalis* has no mutagenic or DNA-damaging activity in either the Ames test or *Bacillus rec*-assay.^(G52)

Sage oil is reported to be a moderate skin irritant⁽²¹⁾ and is not recommended for aromatherapy.^(G58)

Contra-indications, Warnings

Sage oil is toxic (due to the thujone content) and should not be ingested. *S. lavandulaefolia* oil has a much lower content of thujone than *S. officianalis* oil.⁽¹²⁾ In view of the toxicity of the essential oil, sage extracts should be used with caution and not ingested in large amounts. Sage may interfere with existing hypoglycaemic and anticonvulsant therapies, and may potentiate sedative effects of other drugs.

Pregnancy and lactation Sage is contra-indicated during pregnancy. Traditionally, it is reputed to be an abortifacient and to affect the menstrual cycle.^(G30) The volatile oil contains a high proportion of α - and β -thujones, which are known to be abortifacient and emmenagogic.

Pharmaceutical Comment

The characteristic components of sage to which its traditional uses can be attributed are the volatile oil and tannins. However, the oil contains high concentrations of thujone, a toxic ketone and should not be ingested. Sage is commonly used as a culinary herb and presents no hazard when ingested in amounts normally encountered in foods. However, extracts of the herb should be used with caution and should not be ingested in large amounts or over prolonged periods. *S. lavandulaefolia* oil is being investigated for symptomatic treatment of Alzheimer's disease.⁽¹¹⁾ However, at present, there is a lack of well-designed

clinical studies investigating the reputed effects of sage.

References

See also General References G2, G3, G9, G10, G15, G16, G22, G28, G30, G31, G32, G36, G37, G41, G43, G52, G54, G58, G62 and G64.

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