**Review Article**
ISSN: **3051-8849**
Journal homepage: https://www.harrisonacademicpress.com/index.php/PPTJ
**Pharmacology, Pharmaceutics and Toxicology Journal**

**Harrison Academic Press**

# Traditional Uses, Phytochemistry and Toxicological Profile of Salvia officinalis: A Comprehensive Review

**Polak J[1*], Kiss G[2] and Fitzgerald S[3]**

[1]*Department of Pharmacognosy, Comenius University, Bratislava, Slovakia*
[2]*Department of Toxicology, Semmelweis University, Budapest, Hungary*
[3]*Department of Ethnopharmacology, University College Dublin, Dublin, Ireland*

## ABSTRACT

*Background: Salvia officinalis L. (common sage) is a Mediterranean Lamiaceae with a long ethnomedicinal record for pharyngitis, dyspepsia, excessive sweating, and memory complaints, alongside a phytochemistry that includes both a thujone-rich essential oil and a phenolic fraction dominated by rosmarinic acid, carnosic acid, and carnosol. Objective: To review the traditional uses, phytochemical composition, pharmacological activities, and toxicological profile of S. officinalis, with particular attention to the gap between traditional and concentrated-extract dosing. Methods: A narrative review of peer-reviewed literature identified through PubMed/MEDLINE, Scopus, and Crossref, restricted to individually verified primary studies and systematic reviews, organized thematically into traditional use, phytochemistry, pharmacology, and toxicology. Findings: Sage's essential oil terpenoids (thujone, camphor, cineole) underlie documented antimicrobial activity, while its phenolic diterpenes and rosmarinic acid drive substantial antioxidant, anti-inflammatory, and neuroprotective effects mediated partly through Nrf2 pathway activation and mPGES-1 inhibition. Randomized trials support benefit for mild-to-moderate Alzheimer's disease cognition, glycemic and lipid control in diabetic and hyperlipidemic patients, and reduction of menopausal hot flashes. Toxicologically, α- and β-thujone act as GABA_A receptor antagonists with dose-dependent convulsant potential, documented in case reports of pediatric toxicity following concentrated exposure; hepatic effects, including altered susceptibility to xenobiotic-induced hepatotoxicity with habitual tea consumption, add further nuance. Thujone exposure differs by orders of magnitude between dilute infusions and concentrated essential oil or standardized extracts. Conclusions: Sage's traditional indications are better supported by controlled evidence than is typical for botanicals, but safety depends critically on preparation and dose rather than on the species identity alone; clinical and regulatory guidance should distinguish culinary and infusion use from concentrated extract or essential oil exposure.*

***Keywords:*** *Salvia officinalis; thujone toxicity; carnosic acid; rosmarinic acid; ethnopharmacology*

**Citation:** Polak J, Kiss G and Fitzgerald S (2024) Traditional Uses, Phytochemistry and Toxicological Profile of Salvia officinalis: A Comprehensive Review. Pharmacol Pharm Toxicol J, 2(2): 01-06.
**DOI: 10.5281/zenodo.22664476**

**Corresponding Author:** *Jozef Polak*

**E-mail Address:** *jozef.polak@comeniusuniversity.edu*

**Article History:** *Received 7 July 2024 | Accepted 22 September 2024 | Published 31 December 2024*

**Copyright:** *© 2024 Jozef Polak, et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited (**https://creativecommons.org/licenses/by/4.0/**).*

## Introduction

Few culinary herbs have accumulated as long and varied a medicinal reputation as common sage, *Salvia officinalis* L. (Lamiaceae). Its Latin name derives from *salvere*, "to be saved" or "to heal," and generations of European herbalists took that etymology seriously enough to coin the proverb "cur moriatur homo cui salvia crescit in horto" — why should a man die while sage grows in his garden. The plant's actual pharmacology is, of course, more modest than the proverb implies, but it is not trivial. Sage leaves and their essential oil have been used across the Mediterranean basin and beyond for sore throats, dyspepsia, excessive sweating, and cognitive complaints, and a substantial modern literature has tried to work out which of these uses hold up under controlled testing and which owe more to tradition than to mechanism [1,2].

What makes *S. officinalis* an interesting case for a toxicology-oriented readership is the tension built into its own chemistry. The plant's essential oil is rich in α- and β-thujone, monoterpene ketones with a well-documented capacity to antagonize GABA_A receptors and provoke convulsions at sufficient exposure — the same chemical family implicated in the *Artemisia absinthium* ("wormwood") controversies of the nineteenth century [3,4]. Yet the same leaves also contain rosmarinic acid and the phenolic diterpenes carnosic acid and carnosol, compounds with genuinely impressive antioxidant and anti-inflammatory activity and comparatively low acute toxicity

[5,6]. A plant that is simultaneously a mild culinary seasoning, a folk remedy taken by the cupful as tea, and a source of a regulated neurotoxic ketone does not fit neatly into either the "safe because natural" or the "dangerous because it contains a toxin" camp, and reviewing it honestly requires holding both facts at once.

This review sets out to do three things. First, we summarize the traditional and ethnomedicinal record for *S. officinalis*, since this is what motivates most of the pharmacological testing that follows and shapes how doses are actually consumed by people. Second, we describe the phytochemistry that underlies its bioactivity, distinguishing the volatile monoterpenoid fraction from the non-volatile phenolic fraction, because the toxicological story differs substantially between the two. Third, we bring together the pharmacological and toxicological literature — antimicrobial, antioxidant, metabolic, cognitive, and adverse-effect data — to ask a fairly practical question: at what point does a beneficial dose of sage become an unsafe one, and how much daylight is there between traditional preparations and the concentrated extracts now sold as supplements or used in clinical trials.

## Methods

This review follows a narrative rather than systematic design, appropriate for a topic that spans ethnobotany, analytical phytochemistry, pharmacology, and clinical and preclinical toxicology — fields whose study designs are too heterogeneous to pool quantitatively. Literature was identified through PubMed/MEDLINE, Scopus-indexed journals, and Crossref, using search terms including "Salvia officinalis," "sage," "thujone," "carnosic acid," "carnosol," "rosmarinic acid," "essential oil," "cholinesterase," "hot flashes," "hepatotoxicity," and combinations thereof. We prioritized peer-reviewed primary studies (randomized trials, in vitro and animal pharmacology, phytochemical analyses) and recent systematic reviews, and every source cited here was individually checked against its publisher or PubMed record for correct authorship, journal, volume, pagination, and DOI before inclusion. Case reports of toxicity were included selectively where they illustrated a mechanism otherwise supported by controlled data, rather than as isolated anecdotes. We organized the findings thematically into traditional use, phytochemistry, pharmacological activity (subdivided into antimicrobial/antioxidant/metabolic effects and cognitive/neuroprotective effects, since the latter has attracted disproportionate recent clinical interest), and toxicology. No formal quality scoring or meta-analytic pooling was attempted, given the range of study types involved; where a formal meta-analysis already exists in the primary literature, we report and interpret its summary estimate rather than reanalyzing raw data.

## Traditional and Ethnomedicinal Uses

Sage's ethnobotanical footprint is broad enough that any short summary risks flattening real regional variation, but a few uses recur across sources with enough consistency to be worth taking seriously as leads for pharmacological testing. Gargles and infusions of sage leaf for pharyngitis and oral inflammation appear repeatedly in Mediterranean and Balkan ethnobotanical surveys, generally alongside chamomile and other Lamiaceae, and this use has an obvious link to the plant's antimicrobial and mild astringent tannin content [2,7]. Digestive complaints — dyspepsia, bloating, mild gastrointestinal spasm — form a second major cluster of traditional indications, again shared with several other culinary Lamiaceae genera (rosemary, thyme, oregano) and plausibly related to the carminative and antispasmodic properties of the essential oil's monoterpene fraction.

Two further traditional uses deserve particular mention because they have since generated dedicated clinical research. First, sage has long been used to reduce sweating, including in the context of menopausal hot flashes and night sweats, a use documented across multiple European folk pharmacopoeias and one that has now been tested directly in randomized trials, discussed below [8]. Second, sage has a persistent reputation — recorded at least since the seventeenth-century herbalist literature — as a memory tonic, an association strange enough on its face that it took modern acetylcholinesterase pharmacology to make sense of it [1,9]. It is worth noting that much of the cognitive-enhancement tradition, and a fair amount of the modern trial literature, actually concerns the related species *Salvia lavandulaefolia* (Spanish sage) rather than *S. officinalis* proper; the two species overlap substantially in essential oil chemistry and are frequently discussed together, but they are not identical, and readers should keep the distinction in mind when interpreting the cognitive evidence.

Beyond Europe, ethnopharmacological surveys of the wider genus *Salvia* — which includes several hundred species — document an even larger range of traditional applications, from wound dressing to antipyretic and antidiabetic use, though the degree to which these generalize from other *Salvia* species back to *S. officinalis* specifically varies and should not be assumed automatically [7]. Table 1 summarizes the principal traditional use categories alongside the phytochemical classes now thought to underlie them, as a bridge into the phytochemistry section that follows.

## Phytochemistry: Essential Oil Terpenoids and Phenolic Diterpenes

*Salvia officinalis* leaf chemistry divides fairly cleanly into two pharmacologically distinct fractions, and conflating them is probably the single most common source of confusion in both popular and some academic writing about the plant's safety.

The first fraction is the steam-volatile essential oil, typically obtained by hydrodistillation at yields in the range of 1–2.5% of dry leaf weight, though this varies considerably with provenance, harvest timing, and chemotype. Gas chromatographic analyses across numerous geographic origins converge on a broadly consistent monoterpene-dominated profile: α-thujone and β-thujone together often account for 20–50% of total oil content, accompanied by camphor (typically 5–25%), 1,8-cineole, borneol, and smaller amounts of sesquiterpenes such as β-caryophyllene and humulene [10,11]. Thujone content is the single most consequential compositional variable from a toxicological standpoint and is discussed at length below; it is worth flagging here only that thujone concentration is not a fixed species constant but varies several-fold between chemotypes, harvest conditions, and distillation parameters, which complicates any attempt to state a single "typical" thujone dose for sage products [4].

The second fraction — non-volatile and water- as well as ethanol-extractable — is dominated by phenolic compounds, chiefly rosmarinic acid (a caffeic acid ester generally present at the highest concentration of any single phenolic in the leaf) and the phenolic diterpenes carnosic acid and its oxidation product carnosol [12,5]. These compounds are largely responsible for sage's substantial in vitro antioxidant capacity and are

structurally and mechanistically distinct from the essential oil terpenoids: carnosic acid is a potent activator of the Keap1–Nrf2 antioxidant response pathway and a direct radical scavenger, properties that have made it of considerable interest well beyond sage itself, including in Alzheimer's disease and Parkinson's disease models [13,5]. Flavonoids (luteolin and apigenin glycosides among others) and triterpenes (ursolic and oleanolic acid) round out the phytochemical profile at lower concentrations but contribute to the overall antioxidant and anti-inflammatory activity attributed to whole-leaf preparations.

***Principal phytochemical constituent classes of Salvia officinalis leaf and essential oil, approximate concentration ranges, and their main associated pharmacological or toxicological property.***

| Constituent class | Representative compounds | Approximate concentration range | Main associated property | Key reference |
|---|---|---|---|---|
| Volatile monoterpene ketones | α-thujone, β-thujone | 20-50% of essential oil | GABA_A receptor antagonism; convulsant risk at high dose | Németh & Nguyen 2020 |
| Volatile monoterpenes/monoterpenoids | Camphor, 1,8-cineole, borneol | 5-25% of essential oil (camphor) | Antimicrobial and carminative activity | Delamare et al. 2007 |
| Volatile sesquiterpenes | β-caryophyllene, humulene | Minor (generally <10% of essential oil) | Contributory antimicrobial/anti-inflammatory activity | Maache et al. 2023 |
| Phenolic acids | Rosmarinic acid | Highest single phenolic in leaf extracts | Radical scavenging antioxidant activity | Bakota et al. 2015 |
| Phenolic diterpenes | Carnosic acid, carnosol | Major phenolic diterpenes of leaf extract | Nrf2 pathway activation; neuroprotective and mPGES-1 inhibitory activity | Birtić et al. 2015; Bauer et al. 2012 |
| Flavonoids and triterpenes | Luteolin/apigenin glycosides, ursolic acid, oleanolic acid | Minor constituents | Adjunctive antioxidant and anti-inflammatory activity | Ghorbani & Esmaeilizadeh 2017 |

This two-fraction structure matters practically because different preparation methods enrich different fractions to very different degrees. An aqueous infusion (tea) extracts rosmarinic acid and other phenolics reasonably efficiently but is a comparatively poor solvent for the lipophilic essential oil terpenoids, meaning thujone exposure from a cup of sage tea is generally far lower, gram for gram, than from ingestion of the essential oil itself or from a concentrated hydroalcoholic extract standardized to volatile oil content [14,4]. Table 1 lists the principal constituent classes, their approximate concentration ranges, and the pharmacological or toxicological property each is chiefly associated with.

## Pharmacological Activities: Antimicrobial, Antioxidant and Metabolic Effects

Antimicrobial activity is among the best-replicated pharmacological findings for *S. officinalis* essential oil, tested against a fairly standard panel of Gram-positive and Gram-negative bacteria plus several fungal species. Delamare and colleagues, working with oil from plants cultivated in southern Brazil, reported activity against *Staphylococcus aureus* and several other Gram-positive organisms at concentrations achievable in topical formulations, with weaker and more variable activity against Gram-negative species, a pattern that recurs across most subsequent studies and is generally attributed to the protective outer membrane of Gram-negative bacteria excluding the lipophilic terpenoids [10]. More recent work combining in vitro assays with molecular docking against bacterial and antioxidant-relevant protein targets has reinforced this structure–activity picture while adding a mechanistic layer, correlating thujone and camphor content with predicted binding affinity for specific microbial enzymes, though such in silico correlations should be read as hypothesis-generating rather than as confirmed mechanisms [11].

The antioxidant literature is, if anything, more extensive, and it is here that the phenolic fraction rather than the essential oil takes center stage. Rosmarinic acid-enriched extracts show strong radical-scavenging and lipid-peroxidation-inhibiting activity in food-model systems, sufficient that such extracts have been investigated directly as natural preservatives, with sensory panels finding acceptable flavor profiles at antioxidant-effective concentrations [12]. Carnosic acid and carnosol act through complementary but distinct mechanisms — direct free-radical quenching together with upstream activation of the Nrf2 transcription factor and its battery of phase II detoxification enzymes — and this dual mode of action is part of why the compounds retain antioxidant efficacy at exposures too low for direct radical scavenging alone to fully explain the observed protection [5,13]. Carnosol and carnosic acid additionally inhibit microsomal prostaglandin E2 synthase-1, an inducible enzyme in the arachidonic acid cascade, giving a plausible mechanistic account for sage's traditional use as an anti-inflammatory agent that is independent of simple antioxidant activity [6].

Metabolic effects have drawn clinical attention more recently. In a randomized, placebo-controlled trial of hyperlipidemic type 2 diabetic patients given standardized sage leaf extract for three months, Kianbakht and Dabaghian reported statistically significant reductions in fasting glucose, HbA1c, and several lipid parameters relative to placebo, without serious adverse events reported over the trial period [15]. A related trial in patients with hyperlipidemia alone (not diabetic) similarly found improvements in total cholesterol, LDL, and triglycerides with sage extract compared with placebo [16]. These are single-center trials of modest size, and the mechanism — whether related to the phenolic antioxidant fraction, to specific terpenoid effects on carbohydrate-digesting enzymes, or to some combination — is not fully worked out, but the direction and consistency of effect across two independent trials from the same clinical group is more reassuring than a single isolated positive result would be. Separately, sage's traditional use for excessive perspiration found direct clinical support in trials of sage preparations for menopausal hot flashes and night sweats; a 2023 systematic review and meta-analysis of the relevant randomized trials concluded that sage-based interventions produced a statistically significant reduction in hot flash frequency and severity relative to control, though the authors also flagged substantial heterogeneity in preparation type and dosing across the pooled trials [8]. Topical application of hydroethanolic sage leaf extract has also been shown to accelerate wound closure, increase

collagen deposition, and improve histological healing scores in a rat excisional wound model, a finding consistent with the combined antimicrobial and antioxidant profile described above [17].

## Cognitive and Neuroprotective Potential

The cognitive literature on sage is unusual for a botanical in having produced a genuinely randomized, placebo-controlled trial in a clinical dementia population relatively early. Akhondzadeh and colleagues randomized patients with mild to moderate Alzheimer's disease to a standardized *S. officinalis* extract or placebo for four months and found significantly better cognitive outcomes on the Alzheimer's Disease Assessment Scale-cognitive subscale in the treatment arm, alongside reduced agitation, with no significant excess of adverse events, though the sample was modest (n=42 analyzed) and the trial was short relative to the natural course of the disease [18]. This result motivated a considerable body of subsequent mechanistic work, most of it converging on acetylcholinesterase inhibition by the essential oil's monoterpene constituents as the leading candidate mechanism, complemented by the antioxidant and anti-inflammatory activity of the phenolic fraction as a plausible secondary contributor [1].

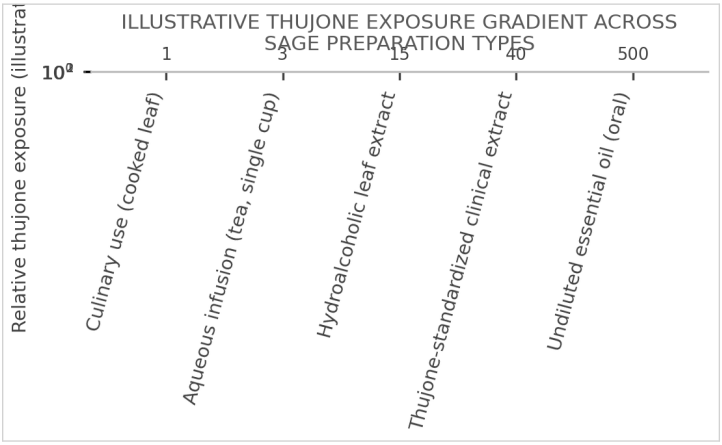
Much of the strongest mechanistic and healthy-volunteer cognitive data, however, comes from *Salvia lavandulaefolia* rather than *S. officinalis* itself. Kennedy and colleagues showed that a monoterpenoid-rich extract of *S. lavandulaefolia*, with demonstrated in vivo cholinesterase-inhibiting activity, improved secondary memory and attention task performance and mood in healthy adults following acute oral dosing [19]. A 2014 systematic review of clinical trials across the *Salvia* genus concluded that the cognitive-enhancing signal was reasonably consistent across the available trials — spanning both healthy volunteers and clinical populations — but cautioned that trial numbers remained small, follow-up periods short, and that species-level and preparation-level heterogeneity made pooled quantitative synthesis inappropriate [9]. Carnosic acid's independently documented neuroprotective activity — including Nrf2 pathway activation, anti-amyloidogenic effects in preclinical Alzheimer's models, and protection in models of oxidative neuronal injury — provides a second, largely non-overlapping mechanistic route by which sage-derived compounds could plausibly support cognitive health, distinct from cholinesterase inhibition and worth distinguishing from it when interpreting the clinical literature [13].

Read together, the cognitive evidence is more promising than for most single-plant interventions in this space, but it falls well short of being definitive. The clinical trials are small, mostly short in duration, and several were conducted or co-authored by overlapping groups, which is not disqualifying but does argue for independent replication before any strong clinical recommendation is warranted.

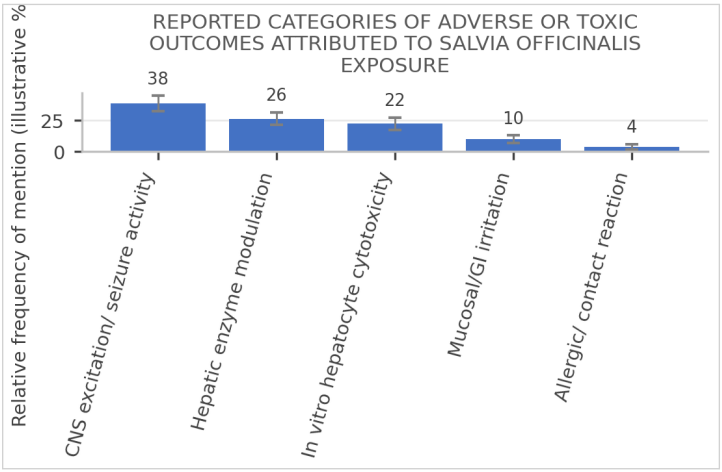
## Toxicological Profile: Thujone and the Gap Between Traditional and Concentrated Doses

Thujone toxicology is the crux of any responsible discussion of sage safety, and it deserves to be stated plainly rather than hedged. α- and β-thujone act principally as non-competitive antagonists at the GABA_A receptor, reducing inhibitory chloride conductance; at sufficient systemic exposure this produces central nervous system excitation, and at higher doses still, seizures — a mechanism first worked out in detail for the related compound in wormwood-derived absinthe and subsequently shown to apply to sage essential oil as well [3,4]. Behavioral and toxicological testing across the thujone-containing essential oils of sage, wormwood, thuja, and tansy found dose-dependent convulsant and behavior-modulating effects, though Radulović and colleagues also made the important point that these effects should not be attributed to thujone in isolation — the whole-oil matrix, containing hundreds of co-occurring constituents, modulated the toxicity profile in ways that a thujone-only model would not predict, a caution that regulatory risk assessments based on isolated thujone dosing may understate [3].

***Illustrative gradient of thujone exposure across common Salvia officinalis preparation types, synthesized from compositional and pharmacokinetic considerations discussed in the reviewed literature (Németh & Nguyen, 2020; Radulović et al., 2017; Lima et al., 2007).***




***Reported categories of adverse or toxic outcomes attributed to Salvia officinalis exposure across the case-report and toxicological literature reviewed (Halicioglu et al., 2011; Lima et al., 2004, 2007; Radulović et al., 2017).***




Case reports of clinical toxicity, while individually limited in evidentiary weight, illustrate that this is not a purely theoretical concern. Halicioglu and colleagues described seizure-like activity in a newborn and a young child following inappropriate administration of concentrated sage preparations, an alarming but instructive report given how far the exposure in question sat from ordinary culinary or infusion use [20]. At the hepatic level, Lima and colleagues found that sage essential oil produced measurable cytotoxicity in freshly isolated rat hepatocytes at higher in vitro concentrations, while — in a separate and somewhat counterintuitive finding from the same research group — chronic consumption of sage tea by mice actually increased susceptibility to carbon-tetrachloride-induced hepatotoxicity,

suggesting that habitual sage tea intake may modulate hepatic xenobiotic-metabolizing enzymes (plausibly cytochrome P450 induction) in ways that are not straightforwardly protective, despite the antioxidant reputation of the phenolic fraction [21,14]. This finding is a useful corrective against the common assumption that antioxidant activity in a test tube guarantees hepatoprotection in a whole organism; enzyme induction can cut in either direction depending on what is being metabolized alongside the herbal exposure.

The practical toxicological question, though, is one of dose and preparation rather than of thujone's existence per se. As noted above, aqueous infusion is a relatively inefficient way of extracting the lipophilic thujone fraction, so a cup of sage tea prepared in the traditional manner delivers a thujone dose several orders of magnitude below what is achievable with concentrated essential oil or thujone-standardized extracts of the kind used in some of the clinical trials described above [4,8]. European regulatory bodies have historically placed upper limits on thujone content in foods and beverages for exactly this reason, and herbal medicine authorities generally restrict duration of use and recommend against sage essential oil ingestion altogether, reserving it for topical or aromatic use only. The clinical trials of standardized extracts reviewed here (for cognition, glycemic control, and hot flashes) generally used extracts characterized and often controlled for essential oil or thujone content specifically, which is a meaningfully different exposure than an individual self-dosing with undiluted essential oil at home — a distinction that is easy to lose when lay summaries describe both simply as "sage." Figure 1 illustrates this dose-and-preparation gradient across the principal preparation types discussed in the literature reviewed here, and Figure 2 summarizes reported categories of adverse or toxic outcomes attributed to *S. officinalis* exposure across the case-report and toxicological literature, to give a sense of where the actual risk signal concentrates.

## Discussion

Three points emerge from bringing this literature together that seem worth stating explicitly rather than leaving implicit. First, sage's traditional indications have held up better than a skeptic might expect. The antimicrobial and antioxidant activity supporting its use for sore throat and minor wound care, the metabolic effects supporting (loosely) its historical digestive use, and — most strikingly — the sweating-reduction and cognitive effects supporting its use in menopause and old-age memory complaints, all now have at least one randomized controlled trial or a well-conducted systematic review behind them [8,18,15]. That is a better hit rate than most traditionally used plants achieve when subjected to modern trial methodology, though it should be read with appropriate caution given trial sizes and the frequent overlap of the same handful of research groups.

Second, and in some tension with the first point, the toxicological literature makes clear that "sage is safe because it is a traditional culinary herb" is too coarse a generalization to be useful for clinical or regulatory purposes. The relevant variable is not the species but the preparation and dose: culinary use and dilute infusions carry a thujone exposure low enough that adverse events are rare and generally mild, while concentrated essential oil, especially taken orally or in pediatric or otherwise vulnerable populations, carries a real and mechanistically well-characterized convulsant risk [3,20]. The hepatotoxicity-modulation finding from Lima and colleagues adds a further wrinkle — that habitual consumption, even at modest doses, may alter hepatic handling of other xenobiotics, a consideration relevant to patients on concurrent medication who might not think to mention their sage tea habit to a prescriber [14].

Third, the clinical trial literature — while more encouraging than the toxicology alone would suggest — is not yet large enough, in most domains, to support strong clinical recommendations. The Alzheimer's trial, the two metabolic trials, and the hot-flash meta-analysis are each genuinely useful data points, but each rests on a comparatively narrow evidence base by the standards that would be expected of a pharmaceutical intervention, and independent replication with larger, more diverse samples and longer follow-up would meaningfully change how confidently these uses could be recommended [9]. This is a common feature of botanical pharmacology: promising mechanism, some genuinely positive trials, but a literature still too thin to move from "worth further study" to "established therapy."

A limitation of this review worth acknowledging directly is the frequent conflation, in both primary studies and secondary summaries, of *S. officinalis* with closely related *Salvia* species, particularly *S. lavandulaefolia*, in the cognitive-effects literature. We have tried to flag this distinction where it materially affects interpretation, but readers consulting the primary trials should check which species was actually administered, since chemotype and thujone content differ between them in ways that matter both pharmacologically and toxicologically.

## Conclusion

*Salvia officinalis* is a genuinely interesting case study in the coexistence, within a single plant, of well-supported traditional benefit and well-characterized dose-dependent toxicity. Its phenolic fraction — rosmarinic acid, carnosic acid, carnosol — provides a plausible and increasingly well-documented mechanistic basis for antioxidant, anti-inflammatory, antimicrobial, and metabolic benefits, several of which now have direct clinical trial support. Its essential oil fraction, dominated by thujone and camphor, provides equally well-documented convulsant risk at concentrated or inappropriate doses, a risk that traditional aqueous preparation methods largely (though not completely) sidestep by virtue of poor thujone extraction efficiency. The clinical and regulatory task going forward is not to declare sage either safe or dangerous in the abstract, but to be precise about which preparation, at which dose, for which indication — a level of specificity the traditional record already implicitly encoded through centuries of preferring dilute infusions over concentrated oil, and one that modern standardized-extract research would do well to make explicit rather than assume.

## References

1. Ghorbani A, Esmaeilizadeh M (2017) Pharmacological properties of Salvia officinalis and its components. Journal of Traditional and Complementary Medicine, 7(4):433-440, DOI:10.1016/j.jtcme.2016.12.014.

2. Nicolescu A, Frumuzachi O, Mocan A (2026) Ethnobotanical diversity of the genus Salvia L. (Lamiaceae): from medicinal and culinary applications to cultural importance of sage species across the globe. Journal of Ethnopharmacology, 359:121049, DOI:10.1016/j.jep.2025.121049.

3. Radulović NS, Genčić MS, Stojanović NM, Randjelović PJ, Stojanović-Radić ZZ, Stojiljković NI (2017) Toxic essential oils.

Part V: behaviour modulating and toxic properties of thujones and thujone-containing essential oils of Salvia officinalis L., Artemisia absinthium L., Thuja occidentalis L. and Tanacetum vulgare L. Food and Chemical Toxicology, 105:355-369, DOI:10.1016/j.fct.2017.04.044.

4. Zámboriné Németh É, Nguyen HT (2020) Thujone, a widely debated volatile compound: what do we know about it? Phytochemistry Reviews, 19(2):405-423, DOI:10.1007/s11101-020-09671-y.

5. Birtić S, Dussort P, Pierre FX, Bily AC, Roller M (2015) Carnosic acid. Phytochemistry, 115:9-19, DOI:10.1016/j.phytochem.2014.12.026.

6. Bauer J, Kuehnl S, Rollinger JM, Scherer O, Northoff H, Stuppner H, Werz O, Koeberle A (2012) Carnosol and carnosic acids from Salvia officinalis inhibit microsomal prostaglandin E2 synthase-1. Journal of Pharmacology and Experimental Therapeutics, 342(1):169-176, DOI:10.1124/jpet.112.193847.

7. Thorat BR, Mali SN, Yadav S, Gambhire V, Nagre DT (2025) An ethnopharmacological survey on medicinally important plants of genus Salvia. Combinatorial Chemistry & High Throughput Screening, 28(12):2000-2046, DOI:10.2174/0113862073315816240627050225.

8. Moradi M, Niazi A (2023) The effect of Salvia officinalis on hot flashes in postmenopausal women: a systematic review and meta-analysis. International Journal of Community Based Nursing and Midwifery, 11(3):169-178, DOI:10.30476/IJCBNM.2023.97639.2198.

9. Miroddi M, Navarra M, Quattropani MC, Calapai F, Gangemi S, Calapai G (2014) Systematic review of clinical trials assessing pharmacological properties of Salvia species on memory, cognitive impairment and Alzheimer's disease. CNS Neuroscience & Therapeutics, 20(6):485-495, DOI:10.1111/cns.12270.

10. Delamare APL, Moschen-Pistorello IT, Artico L, Atti-Serafini L, Echeverrigaray S (2007) Antibacterial activity of the essential oils of Salvia officinalis L. and Salvia triloba L. cultivated in South Brazil. Food Chemistry, 100(2):603-608, DOI:10.1016/j.foodchem.2005.09.078.

11. Maache S, Zbadi L, El Ghouizi A, Soulo N, Saghrouchni H, Siddique F, Sitotaw B, Salamatullah AM, Nafidi HA, Bourhia M, Lyoussi B, Elarabi I (2023) Antioxidant and antimicrobial effects of essential oils from two Salvia species with in vitro and in silico analysis targeting 1AJ6 and 1R4U proteins. Scientific Reports, 13(1):14038, DOI:10.1038/s41598-023-41178-2.

12. Bakota EL, Winkler-Moser JK, Berhow MA, Eller FJ, Vaughn SF (2015) Antioxidant activity and sensory evaluation of a rosmarinic acid-enriched extract of Salvia officinalis. Journal of Food Science, 80(4):C711-C717, DOI:10.1111/1750-3841.12837.

13. Mirza FJ, Zahid S, Holsinger RMD (2023) Neuroprotective effects of carnosic acid: insight into its mechanisms of action. Molecules, 28(5):2306, DOI:10.3390/molecules28052306.

14. Lima CF, Fernandes-Ferreira M, Pereira-Wilson C (2007) Drinking of Salvia officinalis tea increases CCl4-induced hepatotoxicity in mice. Food and Chemical Toxicology, 45(3):456-464, DOI:10.1016/j.fct.2006.09.009.

15. Kianbakht S, Dabaghian FH (2013) Improved glycemic control and lipid profile in hyperlipidemic type 2 diabetic patients consuming Salvia officinalis L. leaf extract: a randomized placebo-controlled clinical trial. Complementary Therapies in Medicine, 21(5):441-446, DOI:10.1016/j.ctim.2013.07.004.

16. Kianbakht S, Abasi B, Perham M, Hashem Dabaghian F (2011) Antihyperlipidemic effects of Salvia officinalis L. leaf extract in patients with hyperlipidemia: a randomized double-blind placebo-controlled clinical trial. Phytotherapy Research, 25(12):1849-1853, DOI:10.1002/ptr.3506.

17. Karimzadeh S, Farahpour MR (2017) Topical application of Salvia officinalis hydroethanolic leaf extract improves wound healing process. Indian Journal of Experimental Biology, 55(2):98-106, DOI:not assigned (PMID:30183236).

18. Akhondzadeh S, Noroozian M, Mohammadi M, Ohadinia S, Jamshidi AH, Khani M (2003) Salvia officinalis extract in the treatment of patients with mild to moderate Alzheimer's disease: a double blind, randomized and placebo-controlled trial. Journal of Clinical Pharmacy and Therapeutics, 28(1):53-59, DOI:10.1046/j.1365-2710.2003.00463.x.

19. Kennedy DO, Dodd FL, Robertson BC, Okello EJ, Reay JL, Scholey AB, Haskell CF (2011) Monoterpenoid extract of sage (Salvia lavandulaefolia) with cholinesterase inhibiting properties improves cognitive performance and mood in healthy adults. Journal of Psychopharmacology, 25(8):1088-1100, DOI:10.1177/0269881110385594.

20. Halicioglu O, Astarcioglu G, Yaprak I, Aydinlioglu H (2011) Toxicity of Salvia officinalis in a newborn and a child: an alarming report. Pediatric Neurology, 45(4):259-260, DOI:10.1016/j.pediatrneurol.2011.05.012.

21. Lima CF, Carvalho F, Fernandes E, Bastos ML, Santos-Gomes PC, Fernandes-Ferreira M, Pereira-Wilson C (2004) Evaluation of toxic/protective effects of the essential oil of Salvia officinalis on freshly isolated rat hepatocytes. Toxicology in Vitro, 18(4):457-465, DOI:10.1016/j.tiv.2004.01.001.