

Pharmacological Activities and Therapeutic Potentials of *Salvia* sp. (Lamiaceae) Based on Practical and Clinical Evidence: A Literature Review

Seno Aulia Ardiansyah^{1*}, Fawza Isra Albadria¹, Miranda Wulandari¹, Qitsania Bilqis Syabani¹

¹ Indonesian School of Pharmacy, Jl Soekarno-Hatta No 354 Bandung, West Java, Indonesia

*Corresponding author: senoauliaardiansyah@stfi.ac.id

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ABSTRACT

The Lamiaceae family, particularly the genus *Salvia*, has long been valued in ethnopharmaceutical practices due to its rich secondary metabolites, including phenolics, flavonoids, and diterpenoids, which exhibit a wide spectrum of pharmacological activities. This review synthesizes findings from 22 scientific publications evaluating the pharmacological potential of *Salvia* species in managing degenerative, metabolic, inflammatory, and infectious diseases. Active compounds such as tanshinone IIA, rosmarinic acid, cryptotanshinone, and magnesium lithospermate B demonstrated significant cardioprotective, anticancer, antidiabetic, neuroprotective, and antioxidant effects. Key mechanisms include inhibition of MMP-9, upregulation of TIMP-1, α -glucosidase and acetylcholinesterase inhibition, as well as increased expression of GLUT4 and caspase-3/-9. Scientific evidence from *in vitro*, *in vivo*, and preliminary clinical studies highlights *Salvia* as a promising candidate for the development of standardized herbal therapies. However, further research is needed on its bioavailability, chronic toxicity, and drug interactions to ensure safe and effective clinical application.

Keywords: Bioactive Compounds; Degenerative Diseases; Ethnopharmacy; *Salvia* Sp., Lamiaceae; Pharmacological Activity.

INTRODUCTION

The *Lamiaceae* family, also known as the *mint* family, is one of the largest and most widespread groups of flowering plants, comprising more than 240 genera and about 7000 species that are mostly aromatic and have long been used in traditional medicine, culinary, and cosmetic products (1). Plants in this family are widely distributed throughout the world, especially in the Mediterranean region, Western Asia, and Eastern Europe, with very high ecological adaptation to both dry and humid environments (2).

The uniqueness of *Lamiaceae* lies in its richness of secondary metabolite compounds, such as flavonoids, phenolic acids, diterpenoids, sesquiterpenes, and complex essential oils. These compounds are known to have diverse biological activities such as antioxidant, antimicrobial, anti-inflammatory, anticancer, as well as effects on the central nervous system (3). Therefore, *Lamiaceae* has become an important subject in pharmaceutical bioprospection and plant-based phytopharmaceutical development (4).

One of the most prominent genera of this family is *Salvia*, which includes more than 900 species and is widely distributed in Eurasia, North America, and North Africa. In the context of ethnopharmacology, various *Salvia* species have been used to treat digestive disorders, inflammation, pain, and respiratory disorders (5). Modern studies have shown that *Salvia* not only has potential as a traditional therapeutic agent, but also as a strong candidate for the development of modern scientific evidence-based therapeutic agents.

Species such as *Salvia miltiorrhiza*, *Salvia officinalis*, *Salvia syriaca*, and *Salvia verticillata* have been intensively studied in various *in vitro*, *in vivo*, and clinical trials for their pharmacological activities against various diseases.

Research shows that these species have significant potential in the management of cardiovascular diseases such as *stable angina pectoris*, *myocardial ischemia-reperfusion injury*, and *acute ischemic stroke* (6); metabolic diseases such as diabetes mellitus and insulin resistance common in patients with polycystic ovary syndrome (8); and neurodegenerative diseases such as *Alzheimer's disease* (10). In addition, the anticancer potential of the active compounds in *Salvia* has also been observed, particularly against pancreatic, prostate, and breast cancer (11, 12).

Antimicrobial and antifungal capabilities against pathogens such as *Staphylococcus aureus*, *Candida albicans*, and *Escherichia coli* also reinforce *Salvia*'s role as a natural anti-infective agent (13), along with significant anti-inflammatory and antioxidant activities in addressing oxidative stress and systemic inflammation (1, 3). All these findings indicate that various *Salvia* species possess a broad spectrum of bioactivities against various degenerative, metabolic, infectious and inflammatory disorders, making them an important subject in plant-based pharmaceutical research.

In the pharmaceutical world, compounds such as *tanshinone IIA*, *cryptotanshinone*, *rosmarinic acid*, *carnosic acid*, *magnesium lithospermate B*, and *lithospermic acid A/B* have been shown to have specific pharmacological activities, such as lowering blood glucose levels, inhibiting platelet aggregation, modulating ROS, and suppressing the expression of genes involved in inflammation and cancer cell proliferation (11, 14).

In addition, the potential of *Salvia* in modulating target enzymes has also been studied, such as *acetylcholinesterase* (AChE) inhibition in *Alzheimer's*, α -glucosidase in diabetes, as well as MMP-9 inhibition and TIMP-1 enhancement in blood-brain barrier protection in *stroke* (10, 14). This suggests that the multi-target approach of *Salvia*'s active compounds provides adaptive and prospective therapeutic advantages for the therapy of complex and chronic diseases.

With the increasing prevalence of degenerative diseases and resistance to synthetic drugs, the exploration of medicinal plants such as *Salvia* from the *Lamiaceae* family becomes highly relevant in the context of new drug development, adjuvant therapy, and modern-traditional medicine system integration. Therefore, this review aims to summarize recent scientific evidence on the pharmacological activities, bioactive compounds, and potential mechanisms of action of *Salvia* species in pharmaceutical and ethnopharmaceutical settings, as a basis for the development of further research and evidence-based herbal-based formulations.

METHODS

This article is a literature review that synthesizes and evaluates findings from scientific publications regarding the pharmacological activity and therapeutic potential of various species in the genus *Salvia*. The review assessed evidence from 22 scientific publications focused on the management of degenerative, metabolic, inflammatory, and infectious diseases. The summarized data were derived from *in vitro*, *in vivo*, and preliminary clinical trial studies to provide a comprehensive overview of the ethnopharmaceutical and modern therapeutic applications of *Salvia sp.*

RESULT AND DISCUSSION

The pharmacological benefits of the *Salvia* genus are largely attributed to its diverse bioactive compounds, such as *tanshinone IIA*, *cryptotanshinone*, and *rosmarinic acid*, which exert effects on specific molecular pathways. In this section, the mechanisms of action are systematically presented according to major disease categories.

Cardiovascular Disease (CVD) and Myocardial Ischemia

Compounds derived from *Salvia miltiorrhiza*, particularly tanshinone IIA and its derivatives, demonstrate cardioprotective effects by inhibiting platelet aggregation, downregulating MMP-9, upregulating TIMP-1, and protecting the blood–brain barrier. These vasodilatory and antioxidant effects also contribute to improved endothelial function and stabilization of atherosclerotic plaques.

Diabetes Mellitus and Hypoglycemia

Extracts from *Salvia officinalis*, *S. nemorosa*, and *S. syriaca* exhibit inhibitory activity against α -glucosidase and α -amylase enzymes, thereby reducing fasting blood glucose and insulin levels. In addition, their phenolic compounds enhance GLUT4 expression and suppress gluconeogenesis, which is highly relevant for managing hyperglycemia and insulin resistance.

Polycystic Ovarian Syndrome (PCOS) and Insulin Resistance

Short-term administration of *S. officinalis* extract in clinical trials improved insulin sensitivity, as indicated by increased QUICKI and decreased HOMA-IR. These improvements were further supported by anti-inflammatory effects and the reduction of oxidative stress, both of which play key roles in the pathophysiology of insulin resistance.

Acute Ischemic Stroke

The application of sodium tanshinone IIA sulfonate (STS) as an adjuvant therapy following rtPA administration was shown to decrease blood–brain barrier leakage by downregulating claudin-5 and increasing TIMP-1 expression. This mechanism, mediated by reduced MMP-9 activity, contributes to improved neurological recovery and vascular protection in the brain.

Pancreatic, Prostate and Breast Cancer

Bioactive compounds such as tanshinone and cryptotanshinone derived from *S. miltiorrhiza* promote apoptosis via the ROS–FOXO3–AKT pathway, suppress anti-apoptotic proteins (e.g., Bcl-2), and inhibit cancer cell proliferation. Their cytotoxic effects are further supported by the downregulation of STAT3, VEGF, and NF- κ B signaling pathways, suggesting potential anticancer applications across multiple malignancies.

Neurodegenerative Disease (Alzheimer's Disease)

Rosmarinic acid and essential oils from *S. syriaca* and *S. verticillata* inhibit acetylcholinesterase (AChE) and butyrylcholinesterase (BChE), thereby increasing synaptic acetylcholine levels. This activity provides symptomatic benefits in Alzheimer's disease and is complemented by the modulation of neuroinflammation.

Inflammation and Oxidative Stress

Most *Salvia* species display potent anti-inflammatory and antioxidant properties by reducing pro-inflammatory mediators such as IL-1 β , TNF- α , and nitric oxide (NO). In parallel, they enhance endogenous antioxidant activity, further mitigating oxidative damage and systemic inflammation.

Bacterial and Fungal Infections

Essential oils extracted from *S. officinalis*, *S. lavandulifolia*, and *S. syriaca* demonstrate antimicrobial activity against pathogens such as *Staphylococcus aureus*, *Escherichia coli*, and *Candida albicans*. Compounds including camphor and α -pinene are believed to exert their effects by disrupting microbial cell membranes.

As shown in Table 1, many studies have documented the specific bioactive compounds and mechanisms of various *Salvia* species.

Table 1. Summary of Pharmacological Activities of Various *Salvia* Species

No.	Common Name	Species Name	Parts used	Active Substance	Pharmacological Activity/Potency	Mechanism	Author and Year
1	Red sage	<i>Salvia miltiorrhiza</i>	Root	Salvianolic acids, magnesium lithospermate B, rosmarinic acid, sodium tanshinone IIA sulfonate, tanshinones	cardioprotective, neuroprotective, anticancer	↓inflammation, antioxidant effects, vasodilation, BBB protection (↓MMP-9, ↑TIMP-1), apoptosis induction (↑ROS, ↑caspase-3/9)	(14);(15); (16)
2	Common sage	<i>Salvia officinalis</i> L.	Leaves	salvianolic acid, rosmarinic acid, caffeic acid, flavonoids	anti-inflammatory, antioxidant, antidiabetic	↓PGE ₂ , ↓TNF-α, ↑SOD, ↑CAT, ↑GLUT4 expression, ↓α-glucosidase activity	(18);(19)
3	Clary sage	<i>Salvia sclarea</i> L.	Essential oil	essential oil	anxiolytic	↓corticosterone, modulation of stress-related behaviour	(20)
4	Greek sage	<i>Salvia fruticosa</i> Mill.	Aerial parts	rutin, luteolin	anti-inflammatory, antioxidant	DPPH radical scavenging, ↓edema formation	(21)
5	Spanish sage	<i>Salvia officinalis</i> subsp. <i>lavandulifolia</i>	Leaves	rosmarinic acid, salvianolic acid, camphor, eucalyptol	antioxidant, antimicrobial, memory-protective	inhibition of lipid peroxidation, ↑SOD, ↑CAT, ↓MIC of microbes	(22); (23)
6	Chia / sweet sage	<i>Salvia hispanica</i> L	Seeds	polyphenols, flavonoids, omega-3 fatty acids	antidiabetic, antioxidant, hypolipidemic, hepatoprotective	improved glucose tolerance, free-radical scavenging, modulation of redox balance	(24); (25)

7	Diviner's sage	<i>Salvia divinorum</i>	Leaves	salvinorin A	psychoactive	selective κ -opioid receptor agonism	(26)
8	Scarlet sage	<i>Salvia splendens</i> Sellow	Aerial parts	rosmarinic acid, rutin, polyphenols	antioxidant, anti-inflammatory, antihyperglycemi	$\uparrow$ SOD, $\uparrow$ CAT, $\downarrow$ fasting glucose, $\downarrow$ carrageenan-induced edema	(27)
9	Jerusalem sage	<i>Salvia reuterana</i> Boiss.	Leaves	flavonoids, polyphenols	anxiolytic	$\uparrow$ time spent in open arms (EPM), modulation of anxiety pathways	(28)
10	not reported	<i>Salvia glutinosa</i> L	Aerial parts	phenolic acids, flavonoids	antioxidant, anti-inflammatory, antidiabetic, antiproliferativ	DPPH & ABTS scavenging, $\downarrow$ NO, $\downarrow$ α -glucosidase, $\downarrow$ viability of cancer cell lines	(29)
11	not reported	<i>Salvia atropatana</i> Bunge	Roots	-	anticancer	$\uparrow$ Bax/Bcl-2 ratio, activation of caspase-3, $\downarrow$ cell viability	(30)
12	not reported	<i>Salvia syriaca</i> L.	Aerial parts	spathulenol, rutin, rosmarinic acid, apigenin, quercetin	antidiabetic, anti-Alzheimer's, antioxidant	$\downarrow$ α -glucosidase, $\downarrow$ α -amylase, $\downarrow$ AChE, $\downarrow$ BChE	(9)
13	not reported	<i>Salvia nemorosa</i> L	Leaves and flowers	rosmarinic acid, caffeic acid, quercetin	antioxidant, antibacterial, antifungal, antidiabetic, anti-Alzheimer's	DPPH scavenging, $\downarrow$ α -glucosidase, $\downarrow$ AChE, antimicrobial effects	(9)

The Lamiaceae family occupies a strategic position in ethnopharmaceuticals due to its taxonomic diversity and similarity of secondary metabolite profiles such as phenolics and terpenoids. Research on the *Salvia* genus confirms that its extensive pharmacological benefits are due to the content of bioactive compounds such as rosmarinic acid, luteolin, and apigenin that exert antioxidant and anti-inflammatory effects, while *tanshinone* specifically shows cardioprotective and anticancer potential. Preclinical results in myocardial ischemia models have consistently shown that *Salvia miltiorrhiza* (*danshen*) extract is able to lower blood pressure and reduce oxidative damage to heart tissue. Specifically, *Tanshinone IIA Sulfonate Sodium* (STS) was shown to decrease MMP-9 levels and increase TIMP-1 expression, which provided significant protection to the blood brain barrier post-ischemia.

The anticancer activity of *Salvia*, particularly for pancreatic cancer, was demonstrated through *tanshinone-induced* apoptosis that triggers oxidative stress and modulates the ROS/AKT-FOXO3/SOD2 signaling pathway. Nutritionally, chia seeds (*Salvia hispanica*) are rich in alpha-linolenic acid (omega-3), fiber, and protein. This combination not only has a positive impact on the regulation of serum lipid profile, but also slows glucose absorption, making it a promising antidiabetic supplement. Various *Salvia* extracts have also shown antidiabetic activity through inhibition of α -glucosidase and α -amylase enzymes, as well as increased GLUT4 expression and improved insulin sensitivity in clinical trials.

Although preclinical evidence and some early-stage clinical trials are promising, there are still research gaps in many other *Salvia* species. Further studies on toxicity, pharmacokinetics, and drug interactions are needed to ensure their safe and effective use. Studies on molecular mechanisms related to modulation of cellular signaling pathways such as NF- κ B by phenolic compounds or epigenetic changes triggered by *tanshinone* are also still wide open for exploration. Optimizing the use of Lamiaceae for therapeutic applications requires multidisciplinary collaboration to develop safe, effective, and standardized formulations to improve the quality of public health globally.

CONCLUSION

Species of the *Salvia* genus, belonging to the Lamiaceae family, exhibit a broad spectrum of pharmacological activities supported by both preclinical and preliminary clinical evidence. These activities are primarily mediated by bioactive compounds such as phenolics, flavonoids, alkaloids, tanshinones, and omega-3 fatty acids, which contribute to antioxidant, anti-inflammatory, antiplatelet, antihypertensive, anticancer, and antidiabetic effects. Given the large number of *Salvia* species with unexplored potential, future research should prioritize refining extraction standards, optimizing dosage and formulation, and conducting large-scale clinical and molecular studies to ensure safety, efficacy, and to maximize the therapeutic and nutritional applications of this genus.

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