OPEN ACCESS

Global Journal of Research in Agriculture & Life Sciences
ISSN: 2583-4576 (Online)
Volume 04 | Issue 04 | July-Aug. | 2024
Journal homepage: https://gjrpublication.com/gjrals/

Review Article

Exploring Sage (*Salvia officinalis L.*) in Uzbekistan for Enhanced Medicinal Application Potential

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DOI: 10.5281/zenodo.13334158 **Submission Date:** 10 July 2024 | **Published Date:** 17 Aug. 2024

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Abstract
Sage (*Salvia officinalis L.* Lamiaceae), with commonplace occurrence and ample availability in Uzbekistan, also largely cultivated worldwide, is widely used in the food, pharmaceutical and cosmetic industries. As is evident from contemporary global research trends, *Salvia* is being aggressively investigated in many countries, on account of its precious bioactive constituent yielding potential. Extensive searches of databases such as PubMed, Scopus, Web of Science, and Google Scholar reveal Sage as a well-known aromatic and medicinal mediterranean plant with multiple industrial and pharmaceutical future applications, species of which are native in the coastal regions of the western Balkan and southern Apennine peninsulas and elsewhere in Central Asia. Recent trends in pharmaceutical research also clearly reiterate these and other novel benefits, describing newer extraction methods and solvents for more efficient extraction capable of qualitative and quantitative gains in the phytochemical ingredient recovery. Elaborating enhanced anti-inflammatory activities, current research also stresses the evaluation of Salvia's latent potential for combating oxidative stress and inflammatory diseases. With these objectives, following the recent research by Hakimova (2023), we highlight expanded regional application and export possibilities, also appraising novel ways of productive crop cultivation.

Keywords: *Salvia Officinalis*, geographic diversity, cultivation potential, Bioactive phytochemicals, anti-inflammatory properties.

Introduction
The botanical family *Lamiaceae*, which comprises around 230 genera and 7100 species worldwide, is of great importance in terms of medicine, cooking, cosmetics, and the cultivation of medicinal and aromatic plants. Notable members include Sage, Mint, and Sideritis. *Salvia officinalis*, commonly known as garden sage, Dalmatian sage, or common sage, is widely used in traditional medicine. An infusion of dried sage leaves with boiling water (sage tea) has been traditionally used to treat mouth, throat, and bronchial inflammations, as well as coughs and stomach pain (Vieira *et al*., 2020).

The use of complementary medicine such as herbal extracts in the treatment of dementia has also since long been documented among different cultural traditions. In orthodox Western medicine, however, pharmacological properties of traditional plants that improve cognition or memory have not been widely studied in the context of modern models of Alzheimer's and other diseases. Some old European reference books on medicinal herbs describe *Salvia officinalis* and *Melissa officinalis* (Lemon balm) as ones having memory-enhancing properties, and cholinergic activity has recently been detected in extracts of these plants (Perry *et al.*, 1999).

More recently, extracts prepared from the leaves and stems of the sage plant have been shown to have cytotoxic effect on the membranes of red blood cells, implying that the biologically active substances contained in the plant have a strong hemolytic effect, even in low concentrations. In another recent study by Viera *et al*. (2020), antioxidant properties of *Salvia officinalis* decoction extract and the mechanism of its protective effect on ethanol-induced liver and kidney damage were evaluated for the hepato- and nephroprotective effects of *Salvia officinalis* decoction extract (SODE) against ethanol (EtOH)-induced oxidative stress in rats, suggesting possible mechanisms behind the resultant protection. It has been thus concluded that SODE has a potential protective effect against EtOH-induced inflammation and oxidative stress in rat organs. The study also recommends that consumption of sage flowers is beneficial for patients suffering from hepatotoxicity and nephrotoxicity (Vieira *et al.,* 2020).

Cognitive health is of great public interest, as age-related risk factors for neuroinflammation and systemic inflammation are associated with cognitive decline. Several herbal ingredients have been suggested to have benefits in this area, including *Salvia officinalis* (sage), which has demonstrated anti-inflammatory effects and has caused promising cognitive improvements in numerous human studies. Another study by Margetts *et al*. (2022) has demonstrated anti- inflammatory effects of *S. officinalis* in a wide range of *in vitro* models in human cells, adding further evidence supporting modulation of acetylcholine and monoamine neurotransmitter levels as mechanisms that possibly contribute to the herb's beneficial effects on cognitive health. This study presents significant evidence to support modulation of acetylcholine and monoamine neurotransmitter levels as mechanisms that contribute in the benefits of the herb on cognitive health.

Elsewhere, *Salvia officinalis* has traditionally been used for excessive sweating and menopausal complaints, including hot flashes. Sabry *et al*. (2022) have inferred that the ethanolic extract of *S. officinalis* and the ferulic acid it contains may be useful as a safe natural source of estrogenic activity, substantiating its traditional use for improving postmenopausal symptoms. *Salvia* leaf extract also has been further shown to have antioxidant effects and stimulates increased new bone formation in the expanded midpalatal suture, after maxillary expansion in rats (Kelayar *et al.,* 2022).

Uniqueness for Medicinal Properties

Various studies on the chemical constituents of *Salvia* reveal the presence of several valuable active compounds, including terpenoids, flavonoids and phenolic compounds, unique pharmacological properties of sage having been attributable mainly to those (Akacha *et al.,* 2024). As for example, phenolic compounds of plants belonging to this genus have shown to exhibit the role of active-oxygen scavengers such as superoxide anion, hydroxyl radical and singlet oxygen, as also with the activity to inhibit lipid peroxidation, as Sage has been credited with a long list of medicinal uses. *Salvia officinalis, S. lavandulifolia, S. miltiorrhiza, and S. leriifolia*, among others, have demonstrated potential for antioxidant properties, an effect currently being thought as relevant to the prevention and treatment of Alzheimer's disease and other neurodegenerative diseases. In the recent years, furthermore, there has been increased evidence to suggest that many degenerative diseases, such as brain dysfunction, cancer, heart diseases, ageing processes and immune system decline could be the result of cellular damage caused by free radicals. Antioxidants have therefore been regarded as noteworthy in playing important role in preventing diseases caused by oxidative stress.

Sage leaf extract since long has been valued as an excellent source of bioactive compounds, mainly due to its high content of phenols, widely known as natural antioxidants. *Salvia officinalis* leaves are known to contain up to 2.5% essential oil, the components of which are cineole (up to 15%), linalool, α- and β-pinene, borneol and its acetate, thujone, linalyl acetate and other terpene compounds. The leaves also contain tannins, vitamins P and PP; flavonoids: hispidulin, genquanine, 6-methoxygenquinine, salvitin, luteolin, 6- hydroxyluteolin, cirziliol, cinaroside, nepetin; alkaloids, resinous substances; triterpenoids: ursolic and oleanolic acids; salvin diterpene; phenolcarboxylic acids: chlorogenic, noochlorogenic, cryptochlorogenic, caffeic, rosemary; bitterness, and phytoncides.

Studies on the chemical constituents of *Salvia* by Porres-Martinez *et al*. (2018) are focused on a host of therapeutically active compounds, including terpenoids, flavonoids and phenolic compounds, since pharmacological properties of sage have been attributed chiefly to them. As for instance, some of the key phenolic compounds of plants belonging to this genus have shown activity of active-oxygen scavengers such as superoxide anion, hydroxyl radical and singlet oxygen and activity to inhibit lipid peroxidation. *Salvia officinalis*, *Salvia lavandulifolia*, *Salvia miltiorrhiza* and *Salvia leriifolia*, among others, have since long been demonstrated potential antioxidant properties, an effect currently relevant to the prevention and treatment of Alzheimer's disease and other neurodegenerative diseases. In recent years, there has been further evidence to suggest that many degenerative diseases, such as brain dysfunction, cancer, heart diseases, ageing processes and immune system decline, could be the result of cellular damage caused by free radicals, as the role of antioxidants gets elaborated in preventing diseases caused by oxidative stress. Stress in the current research is being placed on precise analysis of antioxidant activity and pharmacological uses of species of *Salvia* to provide a better understanding of their therapeutic application.

Current research also emphasizes the antioxidant properties of *S. officinalis* due to its flavonoids and phenolic acids. Both in vitro and in vivo studies demonstrate its effectiveness against bacterial infections. Recent research also suggests that *S. officinalis* has the potential to extend the shelf life of various foods by reducing lipid oxidation, making it an important ingredient in the food industry as a natural food additive.

Global Distribution

Salvia spp. (sage) is the largest genus of the family *Lamiaceae* (formerly *Labiatae*). This important genus includes about 900 species widespread throughout the world. Their species have been cultivated worldwide due to their excellent medicinal values, pharmaceutical applications and for culinary purposes. The native range of this species is SW. Germany to S. Europe. It is a subshrub and grows primarily in the temperate biome. It is traditionally used as a poison and a medicine, has environmental uses and for food (Anon., 2024 a, b).

The genus *Salvia* L., one of the largest genera in the Lamiaceae family (Nepetoidae subfamily), includes hundreds of relatively lesser-known species widespread in the Old and New World's regions (Akacha *et al.*, 2024). The main centers of their speciation are the eastern Mediterranean, southwest Asia, South Africa, and the Americas. Sage is widespread and is mainly found in Croatia, Serbia, Montenegro, Bosnia and Herzegovina, Bulgaria, France, Italy, Spain, the United Kingdom, Turkey, Morocco, Greece, South Africa, the USA, Central and South America, India and Southeast Asia. In the European countries, the genus *Salvia* is represented by 36 species.

The principal diversity centers for *Salvia* genus are in Southwest Asia and South America. *Salvia* is widely cultivated in different parts of the world as well as in Iran (Porres-Martinez, *et al.*, 2016). Some species of this genus are used in folk medicine. Also, some *Salvia* species have medicinal attributes such as anti-inflammatory, anti-platelet, and anti-thrombotic effects. Essential oils and terpenoids are abundant chemical components in *Salvia* species.

Central Asian Diversity:

Analysis of regional genetic diversity levels among plant germplasm is essential for establishing, managing and ensuring the long-term success of plant-breeding programs (Perry *et al.*, 1999). Knowledge of such genetic diversity is also important for effective plant breeding programs and their long-term conservation. The diversity of *Salvia* in Central Asia has still not been fully explored. Some studies indicate up to 34 species, including 20 endemics, in this region (Anon, 2024b). Further research is needed to understand the mechanism of diversity of Central Asian Sage forms.

Marker-Based Diversity Studies

Following remarkable progress in the field of plant functional genomic research realizes in the recent years, novel gene-targeted molecular marker techniques are being progressively employed for deeper insight into genetic diversity, especially target region amplification polymorphism (TRAP), conserved region amplification polymorphism (CoRAP), and conserved DNA-derived polymorphism (CDDP). In one such recent analysis of genetic variability and relationships among *Salvia* ecotypes/species revealed by TRAP-CoRAP markers (Fabriki-Ourang, *S., et al.*, 2018; Restnik *et al.*, (2016), eight microsatellite markers were employed to investigate the evolutionary history of indigenous populations, as well as genetic diversity and structure within and among indigenous and cultivated/naturalized populations distributed across the Balkan Peninsula. The results have shown a remarkable pattern of clear separation between the indigenous and cultivated/naturalized groups, with the cultivated material shown as originating from one restricted geographical area. Most of the genetic diversity between the groups was attributable to differences among individuals within populations, although spatial genetic analysis of indigenous populations indicated the existence of isolation by distance. Geographical structuring of indigenous populations was found using clustering analysis, with three sub-clusters of indigenous populations. The highest level of gene diversity and the greatest number of private alleles were found in the Central part of the eastern Adriatic coast, while decreases in gene diversity and number of private alleles were evident towards the northwestern Adriatic coast and southern and eastern regions of the Balkan Peninsula. These results have revealed the versatility of both TRAP and CoRAP markers as useful for *Salvia* germplasm fingerprinting, virtually for improving germplasm management and promoting germ-plasm utilization.

Recent Initiatives in Uzbekistan

In Uzbekistan, significant measures were recently initiated to enhance import-substituting, effective medicines based on biologically active compounds that can be made readily available from native plants such as *Salvia* grown locally, to facilitate the ease of manufacture and uses of new and affordable effective medicines. An important part of the implementation task in this direction, as elaborated in the 4th Directive of the Action Strategy for the Development of the Republic of Uzbekistan, prioritizes development of the pharmaceutical industry, based on possible improvement in the provision of relatively inexpensive, high-quality medicines and medical supplies. Anticipating increase in the general population, several essential innovations are aptly listed for medical research institutions, while also provisioning more funds and qualified manpower towards exploration and exploitation of the locally available known resources of medicinal and aromatic plants of high value, thereby countering unjustified increases in prices for medicines, all of which are listed as important tasks for the implementation of prevention measures. To achieve the listed goals, as it is duly

stressed, estimating their range and investigating in depth the role of biologically active constitutive compounds extractible from regionally cultivated medicinal plants, determining their chemical composition and studying their effect on cellular processes, are also listed, emphasizing those currently as alternatively powerful and safer remedies against chronic diseases requiring highly expensive treatment. Thus, accelerated work in the fields of evaluation and creation of new effective drugs possible from local raw materials is being duly stressed as accentuated regional priority (Hakimova, 2023).

New Directives for Cultivation and Economic Importance in Uzbekistan

Sage, also known locally as Mavrak, is a heat-loving, drought-resistant crop that can be locally grown and used for 4-5 years to get high yields. As per new directives emerging from recent agronomic investigations, it is recommended that for greater benefits, it is also beneficial to grow Sage on irrigated lands, taking full advantage of the favorable factors of soil and its climate in the Republic of Uzbekistan (Anon., 2024b). Current research further reveals that akin to the medicinal plants growing in the wild, the content of biologically active substances in the current Mavrak cultivars interestingly remain well preserved to date despite the modernization of their cultivation. Proper and timely collection of plant raw materials is highly stressed in these studies for extraction and preservation of valuable components along with the richness of their composition, facilitating the optimized use of these substances in medicine.

Recent Studies by Hakimova:

From previous studies on subject, changes in the thymocytes cell volume have been known to be related to their development, affecting their development and function impacting the overall immune response.

A thymocyte is an immune cell present in the thymus, before it undergoes transformation into a T cell which plays a crucial role in the immune system. Thymocytes are precursor to T cells and their development occurs in the thymus. This process involves several stages, each characterized by distinct metabolic and cellular changes. Thymic stromal cells, including thymic epithelial cells, are known to play a crucial role in providing the necessary signals for thymocyte development and homeostasis (Anon, 2024 c). Thomas *et al.* (2020) elaborates how the immune system aging is characterized by the paradox of immunosenescence (insufficiency) and inflammaging (over-reaction), which incorporate two sides of the same coin, resulting in immune disorder. Immunosenescence is thus considered as highly important in reference to disruption in the structural architecture of immune organs and dysfunction in immune responses, resulting from both aged innate and adaptive immunity (Thomas *et al*., 2020).

A series of detailed experiments was recently carried out by Hakimova (2023), employing hemolysis method in both human and mice cells, in which extracts were prepared from the stems and leaves of sage plants were used as treatments. It has been inferred that the locally grown sage plant extract was capable of inhibiting thymocyte cell volume control system at low concentrations and completely block it at high concentrations. Thus, the results of these and the other studies provide concrete evidence to encourage cultivation and utilization of endemic sage plants shown to be vitally useful in the future control of several chronic diseases.

Conclusion: Emerging importance of Sage with Versatile Applications

Multiple findings cited in global databases have served to underscore potential medicinal applications of *S. officinalis*, appreciating its value for pharmacological, antioxidant and antibacterial properties, as well as its significant role in food preservation. According to some researchers, *S. officinalis* conclusively proves to be a natural and healthier alternative for various ingredients, favoring today's consumer preferences for natural and sustainable products. Chronic inflammation is characterized by an overproduction of several inflammatory mediators (e.g., reactive species and interleukins -IL) that play a central role in numerous diseases. Available therapies are often associated with serious side effects and, consequently, the need for safer drugs is of utmost importance.

Stressing the global spectrum of industrial and medicinal application benefits of considerable economic importance, decades of studies listed above provide robust basis favoring advanced research for exploiting the numerous precious biological and pharmacological properties of the sage plant. Furthermore, considering the advantages of soil and its climate prevalent in the Republic of Uzbekistan, it becomes imperative to grow sage as a preferential field crop on fertile irrigated lands, capable of assuredly yielding more and superior quality raw materials.

Dominating research on the group of plants traditionally regarded as versatile is uses, including in the treatment of inflammatory conditions (Vieira *et al.*, 2020), *Salvia officinalis* decisively retains its well-known status as a precious regional resource deserving greater attention.

References

1. Akacha, B. B., Kačániová, M., Mekinić, Wirginia Kukula-Koch, I. G., Koch, W., Orhan, I. E., Čmiková, N, Taglieri, I., Venturi, Samartin, F. C., Bouteraa, M. T., Ben Saad, R., Mnif, W., Garzoli, S. and Hsouna, A. B., 2024. Sage (Salvia officinalis L.): A botanical marvel with versatile pharmacological properties and sustainable applications in functional foods, South African Journal of Botany, 169, 361-382.
2. Anonymous, 2024a. Salvia officinalis L. | Plants of the World Online | Kew Science

3. Anonymous, 2024b. Institute of Botany, Academy of Sciences, Tashkent. https://uzbbg.uz/en/plants/kop-yillik/salvia-officinalis-l
4. Anonymous, 2024c. Thymocyte. https://en.wikipedia.org/wiki/Thymocyte
5. Fabriki-Ourang, S., & Yousefi-Azarkhanian, M., 2018. Genetic variability and relationships among *Salvia* ecotypes/species revealed by TRAP-CoRAP markers. *Biotechnology & Biotechnological Equipment*, *32*(6), 1486–1495. https://doi.org/10.1080/13102818.2018.1534555
6. Hakimova, Sevara H. 2023, d. Determining the influence of local plant extracts on the permeability of cell membranes. M.Ss. Thesis. Denov Institute of Entrepreneurship and Pedagogy, Denov, Uzbekistan, 2023. 69 p
7. Kayalar E., Goger F., Tas Deynek, G., Tok, O.E., and Kucuk, S. 2022. New bone-generative effect of Salvia officinalis L. in the expanded midpalatal suture: An in vivo and in vitro study. J Orofac Orthop. 2022 Oct;83(Suppl 1):85-95.
8. Margetts G, Kleidonas S, Zaibi, N. S, Zaibi, M. S, and Edwards, K. D. 2022. Evidence for anti-inflammatory effects and modulation of neurotransmitter metabolism by Salvia officinalis L. BMC Complement Med Ther. 2022 May 12;22(1):131. doi: 10.1186/s12906-022-03605-1. PMID: 35550086; PMCID: PMC9101933.
9. Perry, E. K., Pickering, A., Wang, A. T., Houghton, P. J. and Perry, N. S., 1999. Medicinal plants and Alzheimer's disease: from ethnobotany to phytotherapy. Pharm Pharmacol. 1999 May;51(5):527-34.
10. Porres-Martínez, M., González-Burgos, E., Emilia Carretero, M., Pilar Gómez-Serranillos, M., 2017. Salvia spp. An Update on Antioxidant Activity and Pharmacological Uses. In: Georgiev, V., Pavlov, A. (eds) Salvia Biotechnology. Springer, Cham. https://doi.org/10.1007/978-3-319-73900-7_4
11. Rešetnik, I., Baričevič, D., Batîr Rusu, D. and Carović-Stanko, K., 2016, Genetic Diversity and Demographic History of Wild and Cultivated/Naturalised Plant Populations: Dalmatian Sage (*Salvia officinalis* L.) https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0159545
12. Sabry M. M., Abdel-Rahman, R. F., El-Shenawy, S. M., Hassan, A. M., and El-Gayed. S. H., 2022. Estrogenic activity of Sage (Salvia officinalis L.) aerial parts and its isolated ferulic acid in immature ovariectomized female rats. J Ethnopharmacol. 2022 Jan 10;282:114579.
13. Thomas R., Wang W., and Su, D. M., 2020.Contributions of Age-Related Thymic Involution to Immunosenescence and Inflammaging. Immun Ageing. 2020 Jan 20;17:2. doi: 10.1186/s12979-020-0173-8. PMID: 31988649; PMCID: PMC6971920.
14. Vieira, S. F, Helena Ferreira, H., and Neves, N., 2020. Antioxidant and Anti-Inflammatory Activities of Cytocompatible Salvia officinalis Extracts: A Comparison between Traditional and Soxhlet Extraction.2020. https://pubmed.ncbi.nlm.nih.gov/33233648/
15. Vieira S.F., Ferreira H., and Neves, N. M., 2020. Antioxidant and Anti-Inflammatory Activities of Cytocompatible *Salvia officinalis* Extracts: A Comparison between Traditional and Soxhlet Extraction. Antioxidants (Basel). 2020 Nov 20;9(11):1157. doi: 10.3390/antiox9111157. PMID: 33233648; PMCID: PMC7699719.

Citation
Hakimova, S.H., Roziev, O.A., & Dani, R.G. (2024). Exploring Sage (Salvia officinalis L.) in Uzbekistan for Enhanced Medicinal Application Potential. In Global Journal of Research in Agriculture & Life Sciences (Vol. 4, Number 4, pp. 44–48). https://doi.org/10.5281/zenodo.13334158