Phytochemical and Biochemical Studies of Sage (*Salvia officinalis* L.)

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Abstract

Salvia is one of the major genuses belonging to Lamiaceae family. It is historically well known by its therapeutic applications. *Salvia officinalis* L. is a common herbal plant known as common sage. It is used in the food and beverage industries due to its powerful antimicrobial activity against several gram positive and negative bacteria. It contains high percentage of the essential oil due to the presence of external glandular structures that produce volatile oil. It is rich in the biologically active constituents which are represented mainly by polyphenolic compounds. These phenolic compounds are characterized by presence of one or more aromatic rings with one or more hydroxyl groups. The previous studies showed that water extract of this plant prevented growth of colorectal cancer and human prostate carcinoma cells. This might refer to its ability to decrease the tissue lesions occurred as a result of oxidative stress. It showed radioprotective effect against irradiation through lowering lipid peroxidation, protein carbonyl and NO in brain tissue and elevating activities of the antioxidant enzymes. It showed antiinflammatory effects by reducing marrow acute phase response and NO synthesis. Also, it showed antagonistic effect against Aluminum neurotoxicity due to reducing the oxidative stress and improving the antioxidant status and particularly by inhibiting the acetylcholinesterase activity.

1 Introduction

Lamiaceae (*Labiatae*) is one of the plant families which are the most diverse and widespread among the dicotyledons¹. This plant family includes approximately 230 genera and 7100 species all over the world. Abdelkader *et al.* (2014)² postulated that this family includes several species which have great value due to their effect in medicament, cooking, makeup, beauty products and production of essential oils (fig-1).

Salvia is one of the major genuses of Lamiaceae family². This genus includes about 900 species which cultivated in many countries due to its traditional usefulness in folk medicine and for domestic applications³. This plant is historically well known from the early 1960s till now by its therapeutic and domestic applications due to its high economic value⁴. The recent studies suggested that the plant extracts is naturally rich sources of antioxidants which used in the prevention of diseases occurred as a result of oxidative stress and free radical attack⁵.

Behradmanesh *et al.* (2013)⁶ showed that this plant is used in the food and beverage industries due to its tasty and spicy flavor. Also, it is added to several food products as preservative⁷. This is due to its powerful antimicrobial activity against several gram positive and negative bacteria such as *L. monocytogenes*, *B. cereus*, *B. subtilis*, *E. coli S. aureus* and all various food borne pathogens⁸.⁹

Miura *et al.* (2002)¹⁰ postulated that this plant species used widely for treatment of some diseases. The botanical name of sage is a clear reference to the curative properties of the plant. They added that the genus name *Salvia* comes from the Latin names *salvāre* meaning to heal and *officinalis* means medicinal.
The recent studies reported by Behradmanesh et al. (2013) emphasized that *Salvia officinalis* L. is a common herbal plant known as sage, common sage, garden sage, golden sage, true sage, culinary sage, kitchen sage and broadleaf sage. Antioxidant and antimicrobial activities of the extracts depend on the type of plant material and the extraction conditions.

2 Bioactive compounds

2.1 Essential oil

It is known that *S. officinalis* L. contains high percentage of the essential oil. This may refer to the presence of external glandular structures that produce volatile oil.

Aroma and fragrance of this plant species may refer to the presence of the essential oil which is consisting of mixture of volatile compounds of terpenes with low molecular weight (mainly monoterpenes and sesquiterpenes), triterpenoids, ursolic acid and oleanolic acid.

Recently, it was found that the oil was rich in oxygenated monoterpenes, with its range varying from 59.43 to 70.68%. This oil is complicated in its composition mainly α-thujone, α-humulene, 1,8-cineole, E-caryophyllene, camphor, borneol, bornyl acetate, α-pinene, β-pinene, α-thujene, β-thujone, eucalyptol and myrcene. The previous studies confirmed that the good quality of sage oil refer to presence of high amount of epimeric α- and β- thujones (50% or more) and a low quantity of camphor (less than 20%).

The essential oil differs in its composition. This may occur due to time of collection and the area of the planting.

2.2 Phenolic compounds

The plants produce different phenolic compounds through the shikimate, mevalonate and phenyl propanoid pathways. Role of these products are important pigmentation, pollination, protection against UV-B irradiation and pathogen. The studies which were compiled by Abdelkader et al. (2014) showed that *S. officinalis* L. is rich in the biologically active constituents which are represented mainly by polyphenolic compounds. They added that these polyphenolic compounds can be classified into phenolic acids and flavonoids. The phenolic compounds are characterized by presence of one or more aromatic rings with one or more hydroxy groups. For this reason, these compounds are classified as phenolic acids, flavonoids, stilbenes, coumarins, and tannins.

Sarhan et al. (2013) reported that the phenolic acids which include carnosic acid and carnosol, rosmarenic acid, methyl rosmarenamate, caffeic acid, cinnamic acid, chlorogenic acid, quinic acid and salvianolic acids. While the flavonoid include ferulic acid, apigenin, luteolin and quercetin. This was in addition to luteolin-7-glucoside and other phenolic glycosides.

All these compounds have effective therapeutic properties and useful in the human health.
S. officinalis L leaves are characterized by antioxidant properties and the antioxidants are effective against blood sugar\(^5\). It was reported that S. officinalis L has wide range of biological activities, such as antioxidant\(^{27,28}\), antibacterial\(^{29}\), fungistatic, virustatic, astringent, anti-hydrotic \(^{30,31}\), hypoglycemic\(^{32}\) and anti-inflammatory properties\(^{33}\). The literature data showed that carnosic acid, carnosol and methyl carnosate are responsible for the antioxidant properties of sage extracts\(^{34,35}\). Due to presence of the essential oil, this species showed hypotensive properties, central nervous system-depressant actions and anti-spasmodic activity\(^{36}\).

Abdelkader \textit{et al}. (2014)\(^2\) concluded their studies that the high polyphenol content in S. officinalis leaves’ extracts is responsible for the strong antioxidant activities compared to that of the standard compounds such as Ascorbic acid and Butylated hydroxy Toluene. The Fig. 2 showed the most common polyphenolic compounds present in S. officinalis L leaves.

The flavonoids and polyphenolic compounds in this species are responsible for antimicrobial and radical-scavenging properties\(^{37,38}\). As shown in the Fig. 3, the presence of carnosic acid, rosemarinic acid and caffeic acid are responsible for protection of the body against the oxidative stress and free radicals attack\(^{25}\). S. officinalis L is a plant which has been used in a variety of food preparations. This may refer to its ability to inhibit the bacterial growth. This occurs due to the presence of essential oils in addition to the other phenolic compounds\(^{39}\).

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{fig2.png}
\caption{S. officinalis extract is rich in the common polyphenolic compounds}
\end{figure}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{fig3.png}
\caption{Showing the scavenging mechanism of the phenolic compounds in S. officinalis against the oxidative stress and free radicals attack}
\end{figure}

This plant species is claimed to be beneficial to diabetic patients. It was suggested that its extracts have hypoglycaemic effects in normal and diabetic animals. This may refer to presence of the essential oil which increased hepatocyte sensitivity to insulin and inhibited gluconeogenesis\(^{40}\).
Eidi and Eidi, (2009)\textsuperscript{61} postulated that the doses 0.2 and 0.4 g/kg body weight of the \textit{S. officinalis} L. leaves extract for 14 days exhibited a significant reduction in serum glucose, triglycerides, total cholesterol, urea, uric acid, creatinine, AST, ALT and increased plasma insulin in streptozotocin-induced diabetic rats. In 2010, Christensen et al.\textsuperscript{42} mentioned that the tea infusions of \textit{S. officinalis} is effective against diabetes by reducing liver glucose production as well as rising the action of insulin.

The sage extract showed sign of protection against toxicants induced liver lesions and exhibited hepatoprotective effect. This antagonistic effect may refer to existence of the polyphenolic compounds which may scavenge free radicals\textsuperscript{63}. It might be added to the natural products which offer hepatic protection and its antioxidant potential mechanism suggesting that the extract of plant may be beneficial in preventing the oxidative stress induced damage.

Extracts of this plant species showed anti-obese effect and it is effective in reducing the body weight. This may refer to the inhibitory effect against the pancreatic lipase activity\textsuperscript{44}. The sage is effective in lowering plasma cholesterol, LDL, and triglycerides as well as increase HDL levels in lipidemic rats\textsuperscript{65}. It plays major role in prevention of cardiovascular diseases due to its effect in lowering the cholesterol level and its role in improvement of lipid profile, antioxidant defences and lymphocyte Hsp70 protein expression which may be responsible for the general health improving properties attributed to sage\textsuperscript{45}.

The \textit{in vitro} study showed that methanol extracts of 6 salvia species exhibited antiproliferative activity in human cancer cell lines. The previous studies suggested that there are great differences among the various species, and the results strengthen the evidence that the genus \textit{Salvia} may be considered as a natural antitumor agents\textsuperscript{46}.

The sage water extract showed a significant decrease in the induced oxidative damaged cells in rats and seems to have the ability to prevent growth of colorectal cancer cell\textsuperscript{47}. It is effective in inhibiting growth of some tumor cells. It showed a strong cytotoxic activity of the extract on human prostate carcinoma cells\textsuperscript{46}.

Xavier et al. (2008)\textsuperscript{49} suggested that sage extracts endorsed the use of sage on anticancer therapy/prevention. This may be due to its ability to inhibit the KRAS with a consequent down regulation of MAPK/ERK pathway and hence inhibit proliferation of HCT15 cells. This refers to presence of ursolic acid which effectively inhibits angiogenesis, invasion of tumor cells and metastasis and suppresses the lung colonization of B16 melanoma cells \textit{in vivo}\textsuperscript{50}.

The water sage extract showed radioprotective effect against irradiation. This was represented by lowering lipid peroxidation, protein carbonyl and NO in brain tissue and elevating the SOD and CAT enzymes activities and GSH contents when compared with irradiated rats\textsuperscript{51}.

\textit{S. officinalis} tincture showed antiinflammatory effects by reducing marrow acute phase response and NO synthesis. Although \textit{S. officinalis} tincture had a smaller inhibitory effect than diclofenac, it significantly reduced the total leukocyte and monocytes percentages and the activation of circulating phagocytes\textsuperscript{52}.

Presence of the organic compound, diterpene, is the major constituent which appears to be related to the anti-inflammatory properties of the plant. This is in addition to presence of compounds caryophyllene oxide and caryophyllene, both of which have displayed anti-inflammatory activity\textsuperscript{63}. Baracevic et al. (2001)\textsuperscript{54} showed that ursolic acid was the main component of different fractions of \textit{S. officinalis} L. chloroform extract.

The previous data obtained in this study showed that the crude extract of \textit{S. officinalis} at doses of 100 and 150 μg/kg was capable of reducing injuries caused as a result of absolute ethanol, suggesting a possible anti-ulcerogenic activity in rats\textsuperscript{55}.

The antioxidant effects of this extract have often been attributed to phenolic and monoterpenic compounds\textsuperscript{56}. Flavonoids which are considered as groups of the polyphenols\textsuperscript{57} and rosmarinic acid possess several modulatory effects, either inducing or decreasing the expression of SOD and CAT enzymes. Rosmarinic acid belongs to the predominant phenolic compound in sage\textsuperscript{58}. Its effect was attributed to the antioxidant properties through scavenging of reactive oxygen species\textsuperscript{59}. Sage extract has the ability to prevent GSH depletion by their main phenolic compounds, rosmarinic acid and luteolin-7-glucoside\textsuperscript{60}. Brandstetter et al. (2009)\textsuperscript{61} postulated that sage extract especially the methanolic extract) was able to induce the glutathione synthesis and hence increase basal GSH levels.

It is well know that the glutathione peroxidase system consists of several components, including GSH that effectively remove (hydrogen peroxide) and serves as a cofactor for glutathione transferase, which is responsible for removing the reactive molecules from the cells. The GSH undergoes detoxification process through the interaction directly with the ROS, as well as performing other critical activities in the cell.

Sage extract is characterized by its ability to increase effect on GSH content in brain tissues. Also, the enzymatic antioxidant defense system including SOD and CAT which can decompose superoxide and hydrogen peroxide in the cells are the main defense against oxidative injuries\textsuperscript{62}.

EL-Kholy et al. (2010)\textsuperscript{63} reposted during their studies that the different sage extracts possessed antioxidant constituents and antagonized Aluminum neurotoxicity. This might occur due to reducing the oxidative stress and improving the antioxidant status and particularly by inhibiting the acetylcholinesterase.

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\textsuperscript{UK J Pharm & Biosci, 2016: 4(5); 59}
activity, thus may improve memory and other brain cognitive activities.

3 Conclusion

Existence of the biologically active polyphenolic constituents which are characterized by presence of one or more aromatic rings with one or more hydroxyl groups, enable S. officinalis extracts to exert powerful antimicrobial, anti-cancer, antioxidant, anti-inflammatory and radioprotective activities.

4 Competing Interests

Authors have declared that no competing interests exist.

5 Author’s contributions

AME collected ideas and information from previous review articles. WMK write the manuscript. Both of them read and approved the final form of manuscript. WMK communicated with journal’s editor to publish the manuscript. AME carried out the corrections required.

6 References


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