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A review study of therapeutic effects of *Salvia officinalis* L

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ABSTRACT

Introduction:Salvia officinalis L.is a plant growing and cultivated in some parts of Iran. The leaves of Salvia officinalis L.(Lamiaceae) are used in Iranian folk medicine for their digestive, carminative, antispasmodic, sedative, analgesic, tonic and diuretic as well as for functional gastrointestinal disorders. The aim of this study is to overview its therapeutic effects than its nutritive and industrial effects. This review article was carried out by searching studies in PubMed, Medline, Web of Science, and Iran Medex databases .The initial search strategy identified about 158 references. In this study,113studies was accepted for further screening and met all our inclusion criteria (in English, full text, therapeutic effects of Salvia officinalis L. and dated mainly from the year 1980 to 2015).The search terms were "Salvia officinalis L.", "therapeutic properties", pharmacological effects. It is commonly used for its antioxidant, antimicrobial, anticancer and anti- tumor, anti-stress and anti-anxiolytic and antidepressant, anti-Alzheimer, anti-cardiovascular diseases, memory improving and concentration, anti-inflammatory. It was said to be good for insomnia and dyssomina. Salvia officinalis L.is widely used for therapeutic and non-therapeutic purposes that trigger its significant value. Various combinations and numerous medicinal properties of its extract, oil, and leaves demand further and more studies about the other useful and unknown properties of this multipurpose plant.

Key words: Sage; *Salvia officinalis* ,therapeutic effect, traditional medicine, pharmacognosy

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INTRODUCTION

Common sage (*Salvia officinalis* L.) (1)is an aromatic and medicinal plant well known for its pharmacological properties(2).*Salvia officinalis* (sage, also called garden sage, or common sage) is a perennial(3), evergreen subshrub(4), with woody stems, grayish leaves, and blue to purplish flowers. It is a member of the family Lamiaceae and is native to the Mediterranean region, though it has naturalized in many places throughout the world. It has a long history of medicinal and culinary use, and in modern times as an ornamental garden plant. The common name "sage" is also used for a number of related and unrelated species.*S. officinalis* has been used to help fertility .it was traditionally used as a diuretic, a local anesthetic for the skin, a styptic, and for other uses(5).

Chemical compound

The principal components in the sage oils were 1,8-cineole, camphor, *α*-thujone, *β*-thujone, borneol, and viridiflorol(6). The essential oil contains cineole, borneol, and thujone(7).The essential oils (EOs) extracted from the aerial parts of cultivated *Salvia officinalis* L. and the berries of *Schinus molle* L. are 1,8-cineole (33.27%), β-thujone

(18.40%), α-thujone (13.45%), borneol (7.39%) in *S. officinalis* oil and α-phellandrene (35.86%), β-phellandrene (29.3%), β-pinene (15.68%), p-cymene (5.43%) and α-pinene (5.22%) in *S. molle* oil.(8).its leaf contains tannic acid, oleic acid, ursonic acid, ursolic acid, carnosol, carnosic acid, fumaric acid,chlorogenic acid, caffeic acid, niacin, nicotinamide, flavones, flavonoid glycosides, and estrogenic substances (9).phenolic glycosides *cis*-*p*-coumaric acid 4-*O*-(2′-*O*-β-d-apiofuranosyl)-β-d-glucopyranoside and *trans*-*p*-coumaric acid 4-*O*-(2′-*O*-β-d-apiofuranosyl)-β-d-glucopyranoside were isolated and identified from *Salvia officinalis* together with 4-hydroxyacetophenone 4-*O*-(6′-*O*-β-d-apiofuranosyl)-β-d-glucopyranoside, luteolin 7-*O*-β-d-glucoside, 7- and 3′-*O*-β-d-glucuronide, 6-hydroxyluteolin 7-*O*-β-d-glucoside and 7-*O*-glucuronide, and 6,8-di-*C*-β-d-glucosylapigenin (vicenin-2). The luteolin glucuronides and vicenin-2 were identified as new sage constituents(9).volatile constituents is heterocyclic monoterpene 1,8-cineole (10, 11).The most abundant phenolic compounds present in the extracts were rosmarinic acid and luteolin-7-glucoside(12).One abietane diterpenoid, 12-*O*-methyl carnosol (2), was isolated from the leaves of sage (*Salvia officinalis* L.), together with 11 abietane diterpenoids, 3 apianane terpenoids, 1 anthraquinone, and 8 flavonoids. Antioxidant activity of these compounds along with 4 flavonoids isolated from thyme (*Thymus vulgaris* L.) .Carnosol, rosmanol, epirosmanol, isorosmanol, galdosol, and carnosic acid exhibited remarkably strong activity, which was comparable to that of α-tocopherol. The activity of miltirone, atuntzensin A, luteolin, 7-*O*-methyl luteolin, and eupafolin was comparable to that of butylated hydroxytoluene. The activity of these compounds was mainly due to the presence of *ortho*-dihydroxy groups(13).The phenolic diterpene carnosic acid appears to be the main substance for general oxidation leading to artifacts with*γ*-or δ-lactone structure in extracts of *Salvia officinalis* (14).The volatile and semi-volatile compounds of *S. officinalis* leaves infusion were polyphenol (2, 15).polar solvent extracts of *Salvia officinalis* was shown to contain Sagerinic acid, a novel cyclobutane and salvianolic acid K, derived from rosmarinic acid,3*β*,4a-diaryl-1a,2*β*-dicarboxylicacid diester(16)

MATERIALS AND METHODS

This review article was carried out by searching studies in PubMed, Medline, Web of Science, and IranMedex databases .The initial search strategy identified about 158 references. In this study, 113studies was accepted for further screening and met all our inclusion criteria [in English, full text, therapeutic effects of *Salvia officinalis L.*and dated mainly from the year 1980 to 2015].The search terms were "*Salvia officinalis* L.", "therapeutic properties",pharmacological effects.

Pharmacological effects

Anti-inflammatory activity

Salvia officinalis L. leaves, obtained from four plant populations of different origin, were investigated for their topical anti-inflammatory properties. Chemical and pharmacological investigation of sage revealed ursolic acid as the main component involved in its anti-inflammatory activity. The content of ursolic acid in sage and sage-based remedies for the topical treatment of inflammatory diseases is proposed as a parameter for quality control purposes.[1]

Anti-bacterial and antimicrobial activity

Antimicrobial activity

The essential oils and methanolic extracts of *Salvia cryptantha* and *Salvia multicaulis* were examined for their potential antimicrobial and radical scavenging activities. No, or slight, activity was observed when the polar and non-polar subfractions of the extracts were tested, whereas essential oils exhibited antimicrobial activity.the results indicate that the oils of *S. cryptantha* and *S. multicaulis* have the capacity to scavenge free radicals and to inhibit the growth of pathogenic microorganisms. Therefore they could be suitable for using as antimicrobial and antioxidative agents in the food industry.[17]

The essential oils of *Salvia officinalis* and *Salvia triloba* were analyzed . The essential oils of both species exhibited remarkable bacteriostatic and bactericidal activities against *Bacillus cereus*, *Bacillus megatherium, Bacillus subtilis, Aeromonas hydrophila, Aeromonas sobria*, and *Klebsiella oxytoca*.[18]

An extract from *Salvia officinalis* [Sage] leaves showed antimicrobial activity against vancomycin-resistant enterococci [VRE]. compounds also showed antimicrobial activity against *Streptococcus pneumoniae* and methicillin-resistant *Staphylococcus aureus* [MRSA]. These compounds showed bactericidal activity against VRE at least for 48 h in a dose-dependent manner [19]

Antioxidant activity

The essential oils of rosemary [*Rosmarinus officinalis* L.] and sage [*Salvia officinalis* L.] were and assayed for their antimicrobial and antioxidant activities. The most important antibacterial activity of both essential oils was expressed on *Escherichia coli*, *Salmonella typhi*, *S. enteritidis*, and *Shigella sonei*. antifungal activity and antioxidant activities[free radical scavenging capacity [RSC], together with the effect on lipid peroxidation] of essential oil of salvia was exhibited.[5] antioxidant activity of sage extract was evaluated. The most active compounds were found to be rosmarinic acid and luteolin-7-*O*-β-glucopyranoside. [3]

The antioxidant activities of the sage polyphenols, consisting of flavone glycosides and a range of rosmarinic acid derivatives, were evaluated for their capacity to scavenge DPPH and superoxide anion radicals and also to reduce Mo[VI] to Mo[V]. it was shown that The rosmarinic acid derivatives all showed potential antioxidant activity and their capacity to reduce Mo[VI] to Mo[V] and their superoxide radical scavenging activities.[2]

Antioxidant activity of this plant and thyme were evaluated and it was found that the antioxidant ativity of thyme is much higher than that of sage [13]

the antioxidant activity of methanolic extracts of oregano and sage samples was tested. The antioxidant activities of sage samples were, on average, higher than those of oregano samples. Some samples of sage had a very high antioxidant activity, with induction times more than 10-fold higher than that of oregano sample.[20]

The strong antioxidative activity of Rosmarinus officinalis and *Salvia officinalis* is caused by phenolic diterpenes. Extracts of these herbs are used as additives to stabilize fat and fat-containing foodstuffs against oxidation. [21]

Antioxidant potential of a traditional water infusion [tea] of common sage [*Salvia officinalis* L.] in vivo in mice and rats was examined. The replacement of water by sage tea for 14 days in the diet of rodents did not affect the body weight and food consumption and did not induce liver toxicity. thus,This study indicates that the compounds present in this sage preparation contain antioxidant activity improving the liver antioxidant potential.[22]

Methanolic and acetone extracts from organ [shoots and hairy roots] and undifferentiated [cell and callus] cultures of *Salvia officinalis* , as well as from shoots and roots of *in vitro* regenerated plants were evaluated for their antioxidant properties [scavenging of the free radicals, transition metal reduction and inhibition of lipid oxidation]. The concentrations of rosmarinic acid, diterpenoids [carnosic acid and carnosol] and total phenolic compounds in each extract were determined. The methanolic hairy root and root regenerated plant extracts possessed the strongest effects on reducing Mo and DPPH• radical scavenging.[23]

Antioxidative constituents of Rosmarinus officinalis and *Salvia officinalis* . Antioxidant activity of extracts under simultaneous storage and thermal stress depended directly on the concentration of phenolic diterpenes. [24]

The antioxidant activity [AA] of acetone oleoresins [AcO] and deodorised acetone extracts [DAE] of sage [*Salvia officinalis* L.], savory [*Satureja hortensis* L.] and borage [*Borago officinalis* L.] were tested . their effect was higher than that of the synthetic antioxidant butylated hydroxytoluene [0.02%]. The activity of sage and borage DAE was lower than that of AcO obtained from the same herb.[25]

Salvianolic acid L[a rosmarinic acid dimer, was isolated from *Salviaofficinalis*]showed strong free radical scavenging activities for DPPH and superoxide anion radicals.[26]

In vitro shoots of sage [*Salvia officinalis* L.] were established under four different cytokinin supplementations by culturing nodal segments excised from aseptically germinated seedlings. Rosmarinic acid and carnosol were the main compounds in all the antioxidant phenolic extracts. The increase in concentration of KIN decreased the accumulation of the most of phenolic diterpenes, particularly that of carnosol.[26]

The effectiveness of the extraction of antioxidative compounds from sage [*Salvia officinalis* L.] was evaluated by determining the capability of the extracts to scavenge the free radical DPPH• [1,1-diphenyl-2-picrylhydrazyl] *in vitro*. special attention was paid to rosmarinic and carnosic acids, carnosol and methyl carnosate..[27]

Alzheimer disease
Efficacy and safety of *Salvia officinalis* extract using a fixed dose [60 drops/day], in patients with mild to moderate Alzheimer's disease, over a 4-month period. The results of this study indicate the efficacy of *S. officinalis* extract in the management of mild to moderate Alzheimer's disease. Moreover, *S. officinalis* may well reduce agitation of patients but this needs to be confirmed.[28]

Hypoglycemic effect
In an animal study, hypoglycemic effect of essential oil and methanolic effect of sage leaves was investigated on healthy and streptozotocin-induced diabetic rats. And it was indicated that sage extract has hypoglycaemic effect on diabetic animals and the plant should be considered in future therapeutic researches.[29]

Anti-viral activity
Two new diterpenoids, safficinolide and sageone, which showed antiviral activity, were isolated from the aerial parts of *Salvia officinalis* . Their structures were established by a detailed spectroscopic analysis.[30]

Anti-anxiety activity
Salvia officinalis [sage] has previously been shown both to possess *in vitro* cholinesterase inhibiting properties, and to enhance mnemonic performance and improve mood in healthy young participants. The results confirm previous observations of the cholinesterase inhibiting properties of *S. officinalis*, and improved mood and cognitive performance following the administration of single doses to healthy young participants.[31]

An investigation of *Salvia officinalis* L. has led to the isolation of three new phenolic Compounds that were found to be moderately active as antioxidants in the DPPH test and metmyoglobin test. [32]

The antioxidant properties and total phenolic of different extracting solvents of thyme, sage, and marjoram were examined .results showed that thyme, sage, and marjoram have a potential use as natural antioxidants due to their significant antioxidant activity. HPLC analysis of methanolic extract showed the presence of: rosmarenic acid, methyl rosmarenate, caffeic acid, cinnamic acid, chlorogenic acid and quinic acid as phenolic acids, besides some flavonoids such as ferulic acid, apigenin, luteolin and quercetin.[33]

Anti-fungal activity
The action of *Salvia officinalis* L. essential oil, of its hydrocarbon and oxygenated fractions, and of its main components, α- and β-thujone, 1,8-cineole and camphor, were tested on a strain of *Botrytis cinerea* Pers. a chrysanthemum pathogen and compared with the action of two synthetic plant fungicides, iprodione and benomyl, on the same fungus. The essential oil, its oxygenated fraction and the camphor showed fungicidal activity in dose dependent manner [34]

Memory improving activity
In an animal study, the mnemogenic effect [cholinergic system on memory retention of passive avoidance learning] of sage leaves was investigated and It is concluded that the ethanolic extract of *Salvia officinalis* potentiated memory retention and also it has an interaction with muscarinic and nicotinic cholinergic systems that is involved in the memory retention process.[35]

Anti-cancer activity
In an in vivo study, the antiproliferative and proapoptotic effects of water extracts of *Salvia fruticosa* [SF] and *Salvia officinalis* [SO] against colon cancer were evaluated. Results show that SF, SO, and RA induce apoptosis in both cell lines, whereas cell proliferation was inhibited by the two sage extracts only in one of the types. The activity of sage extracts seems to be due, at least in part, to the inhibition of MAPK/ERK pathway.[36]

Potential side effects
The essential oil of sage is toxic and did not show protective effects against *t*-BHP-induced toxicity at conentrantion more than 200 nl/ml.[37]

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