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Research Article

Chemical Composition, Antioxidant and Anti-Inflammatory Properties of *Salvia Officinalis* Extract from Algeria

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ABSTRACT

Background: Due to its flavoring and seasoning properties, *Salvia officinalis* has been widely used in the preparation of many foods. In folk medicine in Asia and Latin America, it has been used for the treatment of various types of disorders, including seizures, ulcers, rheumatism, inflammation, dizziness, and high blood sugar. **Objective:** The purpose of this study is to determine the chemical composition by HPLC/UV, antioxidant activity and lipid peroxidation; thus the, the anti-inflammatory effect of the ethanolic extract of *Salvia officinalis* (EES) on certain homeostatic parameters, inflammatory biomarkers and antioxidant status in Wistar rats subjected to inflammation induced by carrageenan. **Method:** Male rats (n = 24) were exposed to inflammation of the peritoneal by carrageenan (200 µL: 2%) and treated for 5 days with ethanolic extract of *Salvia officinalis* (EES) in order to repair the damage caused by inflammation on homeostasis, TNF-α and PGE2. **Results:** The results of scavenging of DPPH and lipoperoxidation of the extract, showed an IC_{50} of 29.69 ± 1.32 and 46.17 ± 1.51 µg/mL, respectively. The identification of EEC by HPLC shows the presence of polyphenolic acids (salvianolic acid, rosmarinic acid, caffeic acid, ferulic acid) and many flavonoids (Cirsimaritin, Catechin, Acacetin, kaempferol, pinocembrine, quercetin). Salvia extract contains 221.08 ± 2.36 mg EAG/g and 80.54 ± 1.3 mg EQ/g dry extract. Compared to the control group, carrageenan induced a substantial decrease (P<0.05) in antioxidant enzymes and a highly significant increase (P<0.05) in homeostatic parameters (blood sugar, CRP and fibrinogen), biomarkers of inflammation (TNF-α and PGE2) and malondialdehyde levels. **Conclusion:** The administration of Salvia extract corrects this perturbation where there is an improvement in antioxidant enzymes and a decrease in biomarkers of inflammation. *Salvia officinalis* has been able to repair carrageenin-induced perturbations homeostasis and inflammation markers in Wistar rats.

Key words: *Salvia officinalis*, HPLC/UV, Lipoperoxydation, Biomarkers of inflammation, Oxydative stress.

INTRODUCTION

Medicinal plants are generally used for the prevention of several diseases or for the curative treatment. Antioxidant activity holds a prominent position among the properties underlying these virtues. Many medicinal plants contain many different types of phytochemicals which are the sources of natural antioxidants such as α-tocopherols, phenolic acids, flavonoids, and tannins. In addition to their antioxidant functions, these compounds have other biological properties, antimicrobial, anticancer and anti-inflammatory effects.[1] On the other hand, oxidative stress refers to the excessive production of reactive oxygen species (ROS) in cells and tissues, which may not be neutralized by the antioxidant method. The disorder in this protective mechanism may result in damage to cellular molecules such as DNA, proteins and lipids by increasing the chances of mutagenesis.[2]

Reactive oxygen species are normally produced in a limited quantity in the body and are important compounds involved in the regulation of processes involving the maintenance of cell homeostasis and functions such as signal transduction, gene expression and receptor activation.[3]

Hydroxyl radicals are the most destructive EROs of oxidative stress due to their intense reactivity resulting in velocity constants between 10^8 and 10^{10} mol-1.L.s-1.[4]

Over production of ROS, especially over a prolonged period of time, can damage cell structure and functions and induce somatic mutations and preneoplastic and neoplastic transformations.[5] Indeed, excessive production of ROS can cause irreversible damage to cells resulting in cell death through necrotic and apoptotic processes (Wang *et al.*, 2004).[6]

Excessive production of ROS can cause tissue damage that can lead to inflammatory process.[7] Various inflammatory stimuli such as natural or artificial chemicals have been reported to initiate the inflammatory process leading to the synthesis and secretion of pro-inflammatory cytokines.[8,9]

The activation of nuclear-orkappa B factor/active protein-1 (NF-κB/AP-1) and the production of tumor necrosis factor alpha (TNF-κ) playing a

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critical role in the inflammatory process leading to several chronic diseases.[10]

In addition, Elinav[11] showed that the inflammatory response is associated with the release of various inflammatory mediators, cytokines and with an oxidative stress-induced nitroso-redox imbalance. Among these generations of COX-2, IL-6, TNF-α and NO induce the expression of adhesion molecules and the sequestration of leukocytes from the bloodstream to the site of inflammation causing tissue damage.

However, phytochemicals, such as polyphenols, can modulate inflammatory processes.[10] Polyphenols are the abundant antioxidants of many food materials.[12] Polyphenols are secondary plant metabolites involved in the defensive system, including protection from ultraviolet rays and pathogenic agents.[13] Polyphenols have anti-inflammatory and antibiotic properties, and can activate the Nrf2 transcription factor in addition. Nrf2 plays a key role in cell protection against oxidative stress and inflammation.[14]

Among these plants; officinal sage (*Salvia officinalis L.*), belonging to the labiate family according to Maatoug[15], is made up of small shrubs with thin windy leaves, with a characteristic camphoric smell. It is an aromatic and medicinal plant that is generally used either naturally or as an extract or as an essential oil. In addition to a traditional use (family food and popular medicine), this plant is used by the perfumery and cosmetology industries, by the food industry and finally by the pharmaceutical industry.

It is necessary to consume this plant in moderation. For example, regulations in some countries limit the possibilities of using sage because of the existence of chemical components that can cause accidents when too high doses of this product are ingested. But the existence of interesting properties makes that, despite the existence of toxic components, sage and its extracts are attributed to many medicinal virtues according to Stary and Jirasek,[16]; Catione,[17] ; Biere,[18]: antiseptic, antispasmodic, ca1lmante, cephalique, digestive, febrifuge. The Latin name clearly demonstrates the importance of sage in the traditional pharmacopoeia.

The purpose of this study was to assess the antioxidant activity and anti-inflammatory power of sage.

MATERIALS AND METHODS

Plant materials

The leaves of *Salvia officinalis* were the subject of this study. They were collected in February 2017, in the commune of Mohammadia (W. Mascara), located in the west of Algeria, 80 km south-east of Oran, 35 km north of Mascara, 40 km from Mostaganem and 57 km from Relizane.

Chemicals and reagents

The TFA, EtOH, acetonitrile, formic acid, $AlCl_3$, Folin-Ciocalteu, 2,2-diphényl-1-picrylhydrazyle (DPPH), gallic acid, ascorbic acid, quercetin, Na_2CO_3, were obtained from Sigma-Aldrich (St Louis, MO, USA).

Preparation of *Salvia officinalis* extract

10 g of *Saliva officinalis* leaves were cleaned, cut and then homogenized using a mixer (Moulinex). They were then extracted with 100 mL of 80% ethanol in a hermetically sealed glass container for 72 hours at room temperature in the dark. Filtration is performed on Whatman N°1 filter paper, and the solvent has been recovered from the filtrate by evaporation in a HANVAPOR type rotavapor, at a temperature of 40 °C. The extract obtained is called extract ethanolic *Salvia officinalis* (EES) and it was stored at +4 °C in a dark glass bottle until use.[19]

HPLC/UV identification and quantification of phenolic compounds in *Saliva officinalis* extract

High performance liquid chromatography (Agilent 1100) was carried out on the ethanolic extract of *Salvia officinalis* (EES) in order to identify its different constituents by separating them according to their elution rates on an Agilent 120EC poroshell column (100 mm x 2.1 mm, 2.7 µm), using mobile phases: water/TFA/formic acid (99: 0.25: 0.75) (A) and acetonitrile (B). Elution occurred at a flow rate of 0.6 mL/min with an aliquot of 10 µL and a temperature of 55°C. Using a gradient process (t/min, percentage B) as follows: (0, 0), (1, 10), (2, 12.5), (3, 15), (9, 80), (10, 100), (11, 100), (14, 0) with 5 min. He recorded chromatograms at 270 and 320 nm. They reported chromatograms at 270 and 320 nm.

The sample was prepared by diluting the EES with 1: 100 (v/v) methanol. The components of *Salvia officinalis* were identified by comparing their retention times and UV spectra with different phenolic standards (trans-cinnamic acid, gallic acid, benzoic acid, ferulic acid, m-coumaric acid, caffeic acid, rosmarinic acid and ellagic acid), flavonoids (catechin, hesperidin, thymol, galangin, tectochrysin, pinocembrin, acacetin, rutin, chrysin, apigenin, kaempferol and quercetin) and other organic compounds (ascorbic acid and menthol). The standards were dissolved in methanol to obtain stock solutions at a rate of 1 mg/mL. These phenolic compounds were identified using calibration curves of the different standards expressed in mg per 1 g of salvia.

Antioxidant activity *in vitro* of *Salvia officinalis*

Determination of total phenols

Total polyphenols were quantified according to the analytical method of Singleton[20] using Folin Ciocalteu's reagent. Mix 0.5 mL of the ethanolic extract of *Salvia officinalis* with 0.5 mL of distilled water and 0.5 mL of folin ciocalteu. After 03 min, 0.5 ml of 10% sodium carbonate (Na_2CO_3) is added. Leave the reaction medium to react for 1 hour at room temperature, and then read the absorbance at 760 nm. The calibration curve is made with gallic acid, using the same dosage measurement.

Determination of flavonoïds

The content of flavonoids in the EES extract was measured according to the experimental protocol of Woisky and Salatino.[21] 1 mL of salvia extract is mixed with 1 mL of 2% aluminum trichloride. The absorbance is measured at 430 nm after 30 min incubation at room temperature. The calibration curve was plotted using quercetin.

DPPH Radical Scavenging Assay

The antioxidant activity of the EES extract was calculated using the stable 2,2-diphenyl 1-pycrilhydrazile (DPPH) radical as defined by Arnous.[22] The preparation of the samples consists of mixing 0.025 mL of ethanolic extract of *Salvia officinalis* at different concentrations (0.5, 1, 5, 10 and 50 µg/mL) with 0.975 mL of DPPH (60 µM), incubating for 30 min under light protection and reading the absorbance at 517 nm.

The absorbance results obtained were converted into the rate of anti-free radical power (% RSA or Radical Scavenging Activity) of DPPH according to the equation:

$$\%RSA= [(Abs_{control} – Abs_{E})/ Abs_{contrôle} \text{ x } 100]$$

Lipid peroxidation

Mixed 100 µL of EES (5–100 µg / mL) with 100 µL tris-HCl buffer (10 mM, pH 7.4). After 1 hour of incubation at 37 ° C, added 100 µL of thiobarbituric acid, then incubate the reaction mixture at 100 °C for 1 h and read the absorbance using spectrophotometry at 532 nm. The malondialdehyde curve was used to analyze the results expressed as nmol MDA/mg protein.[23]

Anti-inflammatory activity *in vitro*

Anti-Hyaluronidase Activity

With a few modifications, the inhibition rate of hyaluronidase was calculated according to the method defined by Silva.[24]. Mixed 50 µL of ethanolic extract of *Salvia officinalis* EES (5, 10, 20, 50 and 100 mg/mL) with 50 µL hyaluronidase enzyme (350 units) and incubate at 37 °C for 20 minutes. Then, to activate the enzyme, 1,25 µL of calcium chloride was added. 0.5 mL of hyaluronic acid sodium salt was added after incubating the reaction medium at 37 ° C for 20 minutes. 0.1 mL of potassium tetraborate was added after incubation at 37 ° C for 40 minutes and the mixture was incubated for 3 minutes in a boiling water bath. In order to avoid the reaction, the mixture was put at 6 ° C and then 3mL of p-dimethylaminobenzaldehyde was added. The incubation was conducted for 20 min at 37 ° C.

Finally, at 585 nm, the absorbance was measured. They did all the tests three times.

Antioxidant and anti-inflammatory activity *in vivo*

Animals

Twenty-four male Wistar rats weighing between 100 and 150 g were used in this experiment. The rats were provided by the Algerian Pasteur Institute. The Protocol is in conformity with the recommendations of the National Institute of Health (NIH-USA).

Upon receipt, the rats were randomly placed into 4 experimental groups in metabolic cages for an adaptation period of 2 weeks at room temperature and a photoperiod of 12/12 h. Rats have free access to food (kibble from the animal feed production company, Bouzaréa, Algiers) and water. All rats have access to water and food.

Acute carrageenan-induced inflammatory reaction in the peritoneal cavity of rats

After the adaptation period, first and second group rats (G1 and G2) received 1 mL of physiological saline daily orally, while group 3 and 4 (G2 and G3) animals received 1 mL of 250 mg/kg/day ethanol extract of *Saliva officinalis* (EES) orally.

On the 5th day, thirty minutes after treatment, the rats in the groups (G2 and G3) received an injection of 200 µL of carrageenan (2%) intraperitoneally (i.p) in order to induce inflammation.

Two hours after induction of inflammation; the rats were kept under mild chloroform anesthesia before being sacrificed.

Blood is collected by cardiac puncture in dry tubes and heparin or EDTA tubes. A dissection has been made on the rats; their peritoins are carefully separated, inspected, rinsed with physiological water and then preserved in PBS for prostaglandin determination.

Biochemical studies

The albumin and blood sugar assay are performed by the colorimetric method (Kit Biosystems). Fibrinogen is measured by performing the functional chronometric method using titrated calcium thrombin (100 NIH units/mL) containing a heparin inhibitor (fibriprest Automate).

Erythrocytes antioxidant enzymes activities

Lipid peroxidation scavenging (malondialdehyde MDA) was performed on erythrocytes according to the protocol of Yagi.[23] The enzymatic activity of catalase is determined in the erythrocyte according to the method of Lück[25] and Aebi[26] which consists of a spectrophotometric analysis of the rate of decomposition of hydrogen peroxide. Superoxide dismutase (SOD) activity is measured according to the method of Elstner.[27] The principle is based on the chemical reaction that generates the superoxide ion (O_2^-) from molecular oxygen in the presence of EDTA, $MnCl_2$ and mercaptoethanol. The activity of glutathione peroxidase (GSH-Px) of erythrocytes was determined according to the method described by Paglia and Valentine.[28] The principle of the test is based on the conversion of $NADPH^+ H^+$ to $NADP^+$ as a result of a series of reactions.

Biomarkers of inflammation

The ELISA kit (Thermo Fisher Scientific, USA) was used to assess the amount of TNF-α present in peritoneal fluid. Another ELISA Prostaglandin E2 ELISA package (Abcam Explore More, UK) was used to test PGE2 in peritoneal fluid.

Statistics

Analysis was performed by SigmaStat software (SPSS, 3.0, SPSS, Inc., Chicago, IL). Data were presented as mean ± standard deviation and were assessed by one-way ANOVA, with Dunnett's post hoc test. Row ANOVA analysis with Dunn's post hoc test was used where appropriate.

RESULTS

EES chemical composition

Table 1 and Figure 1 displays the phenolic acid and flavonoid content of *Salvia officinalis*. Salvianolic acid (6.27 mg/g at 4.58 min) and Rosmarinic acid (7.85 mg/g at 2.38 min) are the main phenolics acids contained, while catechin is the predominant flavonoïds (5.96 mg/g at 0.42 min) and quercetin (4.75 mg/g at 3.89 min).

In vitro antioxidant activity

Total polyphenols and flavonoïds

The determination of total polyphenols and flavonoids shows that the Ethanol *Salvia officinalis* Extract (EES) contains 221.08 ± 2.36 mg EAG/g and 80.54 ± 1.3 mg EQ/g respectively, as shown in Table 2.

Antioxidant activity (DPPH) assay and lipoperoxydation

The anti-free radical activity of EES (ethanolic extract of *Salvia officinalis*) is 86% for the concentration 100 µg/mL, with an IC_{50} of 29.69 ± 1.32 µg/mL (Table 2). The inhibitory concentration IC_{50} of antioxidant capacity via the TBARS test is 46.17 ± 1.51 µg/mL (Table 2).

Hyaluronidase inhibition

From our results, it is observed that the inhibitory activity of hyaluronidase increases with the increase in the concentrations of *Salvia officinalis* extract (EES) (IC_{50} value of 21.86 ± 0.29 mg/mL). The percent inhibition was 92% at a salvia concentration of 100 mg/mL (Figure 2).

In vivo anti-inflammatory effects of *Salvia officinalis*

Biochemical findings

In the light of our results (Table 3), it is observed that carrageenan caused a significant increase ($P < 0.05$) in glycemia of + 70% compared to the rats of the negative control group (G1). On the other hand, the rats of G4 (which were administered with 250 mg/kg of EEC and then injected with 200 µL of carrageenan), showed a significant decrease in blood sugar levels by 47% compared to G2. In the G3 group (which received only the extract ethanolic of *Salvia officinalis*), administration of EES to rats for 15 days resulted in no change in blood sugar levels compared to the control group.

Carrageenan-induced inflammation is followed by a very large ($P < 0.05$) increase in CRP of +10 mg/L in the G2 group of animals. This

Table 1: Composition of extract ethanolic of *Salvia officinalis* (EES) by HPLC/UV (mg/g).

Peak number	Compounds	Amount (mg/ g EES)	Retention time (min)
1	Catechin	5,96	0,42
2	Cirsimaritin	4,38	2,38
3	Luteolin	3,4	3,7
4	Quercetin	4,75	3,89
5	hesperidin	2,71	4,02
6	Acacetin	4,09	4,58
7	Rutin	3,52	4,71
8	Kaempferol	4,72	5,25
9	Pinocembrin	3,12	5,73
10	Apigenin	1,9	6,73
11	Apigenin acetylglucoside	1,82	6,89
12	Chrysin	2,68	7,26
13	Thymol	2,38	7,37
14	Hispidulin	3,84	7,85
15	Gallic acid	1,41	0,42
16	Carnosic acid	2,49	2,13
17	Rosmarinic acid	7,85	2,38
18	Ferrulic acid	3,58	3,75
19	ascorbic acid	1,8	3,89
20	Salvianolic acid	6,27	4,58
21	caffeic acid	3,62	5,25
22	Trans cinnamic	1,36	5,66
23	Sagerinic acid	1,29	7,85

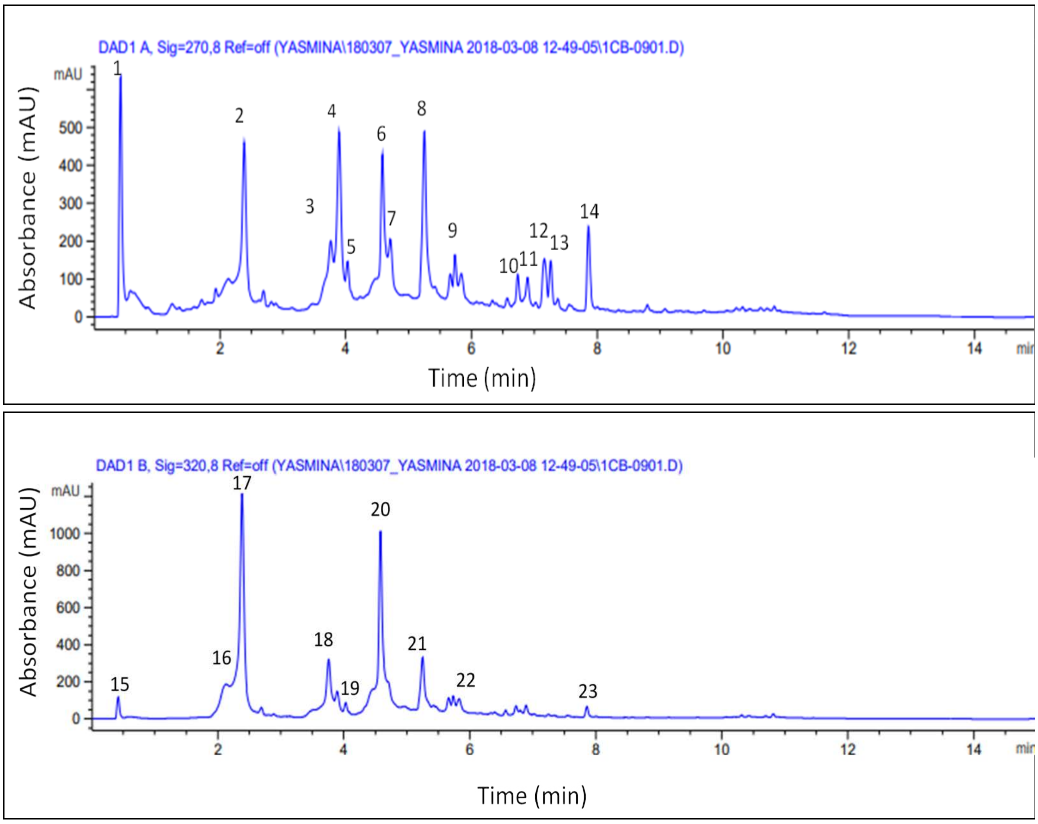

Figure 1: Chromatograms by HPLC/UV analysis of EES at a wavelength of 270 (a) and 320 nm (b): 1. Catechin; 2. Cirsimaritin; 3. Luteolin; 4. Quercetin; 5. hesperidin; 6. Acacetin; 7. Rutin; 8. Kaempferol; 9. Pinocembrin; 10. Apigenin; 11. Apigenin acetylglucoside; 12. Chrysin; 13. Thymol; 14. Hispidulin; 15. Gallic acid; 16. Carnosic acid; 17. Rosmarinic acid; 18. Ferrulic acid; 19. Ascorbic acid; 20. Salvianolic acid; 21. Caffeic acid; 22. Trans cinnamic; 23. Segerinic acid.

Table 2: Content of total phenolic and flavonoic compounds in ethanolic extract of *Salvia officinalis*.

	Phenolics compounds		Antioxidant activity	
Ethanolic extract of *Salvia officinalis*	Polyphenols (mg EAG/g of salvia)	Flavonoids (mg EQ/g of salvia)	IC_{50} DPPH (µg/mL)	IC_{50} TBARS (µg/mL)
	221.08 ± 2.36	80.54 ± 1.3	29.69 ±1.32	46.17 ± 1.51

The values are expressed as mean ± SD (n=3).

Table 3: Biological parameters of the experimental groups of rats.

Parameter	Experimental groups			
	G1	G2	G3	G4
Blood sugar	1.9 ± 0.15	4.36 ± 0.18	1.87 ± 0.12**	2.28 ± 0.11*
Albumin (g/L)	47.16 ± 0.95*	18.16 ± 2.55*	48.7 ± 1.11*	31.06 ± 2.01**
Fibrinogen (g/L)	2.43 ± 0.27**	7.68 ± 0.69**	2.62 ± 0.21*	3.47 ± 0.42*
CRP (mg/L)	2.66 ± 0.68	12.66 ± 2.01*	5.33 ± 0.25*	7.66 ± 0.68**

The values are expressed as mean ± SD (n=5).
*Significant difference from the control group ($p < 0.05$). **Significant difference from the carrageenan inflammation group ($p < 0.05$).

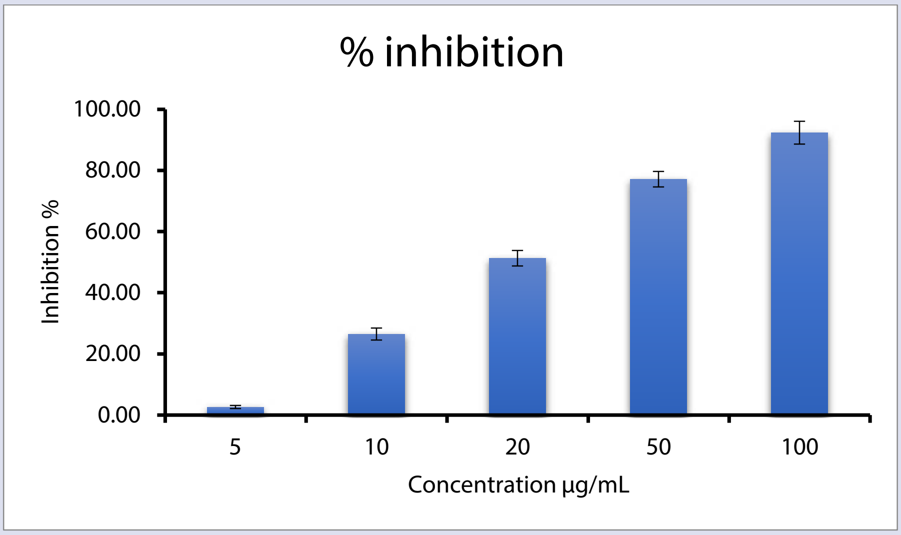

Figure 2: Inhibition of hyaluronidase (%) activity by ethanol extract of *Salvia officinalis* (EES) for each concentration. The values are expressed as mean ± SD (n=3).

amount was effectively reduced by 250 mg / kg EES (G3) + 7.33 mg/L compared to the group G1 (table 3). The administration of EES in combination with carrageenan in the G4 group showed a very significant decrease (P < 0.05) in CRP (+7.33 g / L) compared to the group G2. The albuminemia is reduced by - 29 and - 16.1 g/L in groups G2 (received an injection of carrageenan) and G4 (received 250 mg/Kg of EES and 200 µL of carrageenan) compared to the control (G1); whereas it is not significantly (p> 0.01) different in the control rats (47.16 g/L) and those having received only salvia (48.7 g/L) (Table 3). Compared to the G1 control group, a significant increase in the fibrinogen level was marked in the G2 rats of +5.25 g / L, while a slight increase in the G3 (treated with 250 mg/kg EES) was recorded. Although, the G4 rats given the extract and the carrageenan at the same time, their serum fibrinogen levels were corrected by + 82% compared to the G2 group (Table 3).

Oxidative stress status

From our results, it is observed that the rats of group G2 (which received an injection of 200 µL of carrageenan) show a high plasma concentration of MDA of up to 7.31 mM / L compared to the control group where we noted a rate up to 2.44 mM / L (Table 4). In the G3 group, administration of salvia alone resulted in a significant decrease in this rate (-52%) compared to the control group (G1). In the G4 group (rats treated with salvia and carrageenan at the same time), the level of plasma MDA (4.21 mM / L) was reduced by 2 times the value of that of the control group (G1). The enzymatic activity of catalase in rats in the G2 group was significantly decreased compared to rats in the control group (-105.36 U/mg Hb). This reduction in catalase activity indicates oxidative stress caused by carrageenan exposure of rats. Compared with the rats in the control group (G1), salvia increased catalase activity in the rats in group 3 (+15.77 U / mg Hb). A significant increase (P <0.05) in catalase activity was noted in the rats of the group G4 which received EES in combination with carrageenan (+ 79%) compared to the rats of the G2 group. Compared to the enzyme activity of rats in the control group, the decreased SOD and GPx enzyme activity of rats in the G2 group was-22.22 U/cg Hb and -96.33 U/g Hb, respectively (Table 4).

Inflammation markers

According to the results reported in Table 5, the inflammation of the peritoneum induced by carrageenan is accompanied by a highly significant increase (+1121 pg / mL) (P <0.05) in the level of prostaglandin E2 (PGE2) in animals of the group (G2) compared with the control group (G1).

Table 4: Anti-oxidant enzyme activity in the plasma of the experimental groups of rats.

Parameter	Experimental groups			
	G1	G2	G3	G4
MDA (mmol/L)	2.44 ± 0.21	7.31 ± 0.5**	3.46 ±0.33**	4.21 ± 0.33*
SOD (U/cg Hb)	33.61 ± 1.87*	11.39 ± 1.32*	39.11± 2.33**	26.73 ± 0.91**
CAT (U/mg Hb)	140.16 ± 8.2*	34.8 ± 3.07*	155.93 ± 6.72**	95.9 ± 3.54*
GPx (U/g Hb)	160.46 ± 6.65*	64.16 ± 2.59*	178 ± 5.24*	105.7 ± 3.89**

The values are expressed as mean ± SD (n=5).
*Significant difference from the control group ($p < 0.05$). **Significant difference from the carrageenan inflammation group ($p < 0.05$).

Table 5: Concentrations of prostaglandin E2 (pg/mL) and TNF-α (pg/mL) in peritoneal exudates of rats for the tested groups.

Parameter	Experimental groups			
	G1	G2	G3	G4
PGE2	221 ±17.8	1342 ±22.8*	316 ±17.4**	467 ±23**
TNF-α (pg/mL)	2375 ± 145*	7954 ± 241**	2268 ± 166*	4322 ± 255**

The values are expressed as mean ± SD (n=5).
*Significant difference from the control group ($p < 0.05$). **Significant difference from the carrageenan inflammation group ($p < 0.05$).

Pretreatment of the rats with 250 mg/kg extract ethanolic of *Salvia officinalis* led to a significant decrease (P <0.05) prostaglandins PGE2 with an 85% decrease compared to the G2 group (the rats which received only 200 μL of carrageenan).

As shown in Table 5, TNF-alpha levels in the peritoneal fluid increased significantly compared to the control group (G1:2375 pg/mL) after injection of carrageenan (G2:7954 pg/mL). The administration of extract ethanolic of *Salvia officinalis* (EES) at a dose of 250 mg / kg to rats in group G4 resulted in a significant decrease in the concentration of TNF-α by 54% compared to group 2 (rats received carrageenan injection).

DISCUSSION

The gradient of the HPLC analysis has been required to separate as many flavonoids and phenolic acids as possible in a short time.

Zimmermanna[29] identified by HPLC/MS/MS, that besides rosmarinic acid and luteolin-O-glucoside, sage contains other phenolic acids such as Salvianolic acid, Methydihydrojasmonic acid, Chlorogenic acid, caffeic acid, syringic, rosmarin, salvianolic K and salvianolic I, and methyl rosmarinate. He presence of luteolin-3-glucuronide, as well as other flavone glycosides, in sage was also confirmed by Cvetkovikj.[30]

Some other phenolic compounds have also been found in sage extract, such as chlorogenic acid, isorhamnetine-luteolin, apigenin-7-O-glucoside, caffeic acid, homoplantaginin and apigenin-acetylglucoside, which accounted for 49.11% of the total peak area, according to the study by Yuanyuan.[31]

In accordance with previous reports, our results show that sage varies considerably depending on the composition of the solvent and the results are consistent with previous studies which have shown that the nature of the solvent exerts a great power on the phenolic extraction capacities in many species.[32,33]

Moreover, this result was consistent with previous reports suggesting that a binary solvent system (ethanol/water) is more efficient than a mono-solvent system (water or pure ethanol) in the extraction of phenolic compounds in terms of their relative polarity.[34,35]

The results of their work, Durling[36] concur with previous studies which observed that total polyphenols increased during a shorter extraction period, while increasing the extraction time potentially increases the loss of solvent by evaporation, while suggesting that an estimated extraction time does not exceed 3 h.

Our results are in agreement with those of Kianbakht[37], who found a total flavonoid content that was 912.03 mg EQ/g while, the total phenolic content of the extract was 738.59 mg EAG/g. Matkowski[38] showed that *Salvia officinalis* reveals a total polyphenol content of 62.2 mg EAG/g of salvia.

Whereas, Hamrouni[39] reported that *Salvia officinalis* had very low phanolic compound and flavonoid levels than ours, respectively, 2.337 mg EAG/g and 0.923 mg EQ /g.

Differences in plant variety, time, temperature, solvent, equivalent phenolic acid and method of extraction can result from these differences.[40,41]

In fact, antioxidant activity may be due to different mechanisms, such as prevention of chain initiation, peroxide decomposition, prevention of continuous hydrogen abstraction, free radical trapping, reduction capacity and binding of transition metal ion catalysts.[42]

In various chronic pathologies, such as cancer and cardiovascular diseases, among others, free radicals involved in the lipid peroxidation process are known to play a major role.[43] The DPPH• is considered to be a model of a stable lipophilic radical. Lipid autoxidation initiated a chain reaction in lipophilic radicals. Antioxidants react with DPPH•, reducing a number of DPPH• molecules equal to the number of their available hydroxyl groups.[44] (Xu et al., 2005).

The antiradicalar scavenging (RSA) of the DPPH radical observed by Annamalai[45] increases as the microwave power and infrared temperature increase, while it decreases when the oven drying temperature increases. The effect of carnosol entrapment of radicals is comparable to that of α-tocopherol.[46,47] The superoxide trapping activity of rosmarinic acid derivatives is 15 to 20 times higher than that of trolox; a water-soluble synthetic vitamin E. Arici[48] supported the hypothesis by proving that the radicals and molecules produced form as a result of exposure to radiation. These free radicals can react with O_2 in the long term and cause the formation of hydroperoxides, which create alcohols, aldehydes, aldehyde esters and hydrocarbons.

Martins[49] recorded an IC_{50} value for inhibiting anti-free radical activity RSA for methanolic sage extract of 32.97 μg/mL. Otherwise, Albano[50] report a more moderate percentage inhibition of RSA with an IC_{50} of 2.8 μg/mL in an aqueous extract of *Salvia officinalis*. This difference in value is due to the chemical composition of *Salvia officinalis*, the place of harvest and much more the climate.[51]

In addition, the presence of rosmarinic acid also contributes to the activity detected, hence Cuvelier[52] provided a correlation between antioxidant efficacy and sage composition, indicating that carnosol, rosmarinic acid and carnosic acid had the greatest antioxidant activities among its constituents. Although, some flavonoids are potent antioxidants, the flavonoids identified made a rather low contribution to the total antioxidant capacity of the extracts due to their low abundance. In addition to rosmarinic acid, other flavonoids of *S. officinalis*, in particular quercetin and rutin, have strong antioxidant activities.[53]

Sadeghnia[54] revealed that rutin reversed by hexachlorobutadiene induces an increase in lipid peroxidation and depletion of thiol content in the kidney. Zhang[55] found that sage had excellent antioxidant capacity and that its addition to Chinese sausage effectively inhibited protein oxidation, as indicated by the TBARS value which was around 10 μg/mL lower.

A decrease in serum concentration of total proteins may be a sign of chronic hepatopathy but also of a nutritional deficiency in protein, anorexia, poor assimilation, kidney loss, effusion, hemorrhage, hyperhydration, or burns as indicated by Dietz and Wiesner.[56] Our results showed that *Salvia officinalis* increases the level of total proteins, which confirms that it has an anti inflammatory effect. Whereas fibrogen is a soluble protein synthesized by the liver, it is a marker of inflammation.[57]

Transferrin is the plasma protein that transports iron into the body, and is reduced in inflammatory states.[58] In our work, the decrease in transferrin is an index of inflammation as it decreases in rats injected by carrageenan and increases in rats treated with EES.

In addition, Mansourabadi[59] reported that flavonoids from *S. officinalis* extracts reduce inflammation in the mouse carrageenan model and induce an analgesic effect in a dose-dependent manner. This is due to flavonoids and terpenes, the molecules most likely to lead to anti-inflammatory activities.[53,60,61]

Although the anti-inflammatory action of ursolic and rosmarinic acid from *Salvia officinalis* is twice as powerful as that of indomethacin.[61]

Rathee[62] noted that anti-inflammatory activity is attributed to flavonoids and phenolic acids. Our *Salvia officinalis* extract is rich in compounds such as caffeic acid, gallic acid and flavonoids such as Salvigenin, terpenes and tannins.[63,64]

Flavonoids, as confirmed by Bahmani[65], have effects on opioid receptors and alpha-adrenergic receptors that can inhibit enzymes involved in inflammation and pain. In addition, flavonoids work in inflamed tissue by inhibiting cyclooxygenase, so they can prevent the formation of prostaglandins.

According to Medzhitov[66], the induction of inflammation by acetic acid promotes the peritoneal release of inflammatory mediators which in turn stimulates the increase in vascular permeability with leakage of plasma proteins as well as the migration of leukocytes to the blood peritoneal cavity.

In acute inflammation, the C-reactive protein, also known as CRP, is a glucoprotein that increases very quickly in the blood.[67] Furthermore, prostaglandins are one of the main mediators of inflammation and pain. Indeed, it is involved in acute inflammation, inflammatory pain and also in the development of chronic inflammation. On the other hand, PGE2 plays an important role in the protection of the gastric mucosa, in the maintenance of renal homeostasis and in the fever phenomenon.[68]

Increased levels of TNF-α were identified in the inflammatory groups. *Salvia officinalis* extract decreased this rate by more than 57%.[69] Inflammation plays an important role in the pathophysiology of many diseases and can cause oxidative stress damage.

The generation of large quantities of free radicals is also associated with inflammation. Transcription factors (e.g., NF-κB) that facilitate the production of pro-inflammatory cytokines (e.g., IL-6) can be stimulated by oxidative stress. In this context, antioxidants have been shown to suppress IL-6 and TNF-alpha by macrophages[70] and to inhibit the expression of cyclooxygenase-2 and inducible nitric oxide synthase[71], as well as to enhance anti-inflammatory IL-10 secretion.[70]

Kolac[69] showed that the levels of MDA in erythrocytes of inflammatory rats (induced by lipopolysaccharide) were found to be significantly higher than those of groups treated with *Salvia officinalis* extract. This last group (which received Salvia extract) showed higher activity of superoxide dismutase, catalase and glutathione peroxidase compared to the inflammatory group.[69]

CONCLUSION

The purpose of our study was to demonstrate the antioxidant and anti-inflammatory impact of the ethanolic extract of *Salvia officinalis* (EES), an important source of polyphenols and flavonoids. The EES extract has been shown to have a high antioxidant and inflammation suppressant capacity due to its richness in phenolic compounds.

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CONFLICTS OF INTEREST

We wish to confirm that there are no known conflicts of interest associated with this publication.

ABBREVIATIONS

CAT: Catalase; CRP; C Reactive Protein; DPPH: 2,2-Diphenyl-1-Picrylhydrazyl; IC_{50}: Inhibitory Concentration 50; EAG: Gallic Acid Equivalent; GSH-Px: glutathione peroxidase; HPLC/UV: High Performance Liquid Chromatography/Ultraviolet; IL-1 β: Interleukin-1 β; IL-6: Interleukin-6; MDA: Malondialdehyde; PBS: *Phosphate-buffered saline*; PGE 2: Prostaglandin E2; EQ: Quercetin Equivalent; SOD: Superoxide dismutase; TBARS: Thiobarbituric Acid Reactive Substances; TNF-α: Tumor Necrosis Factor-α.

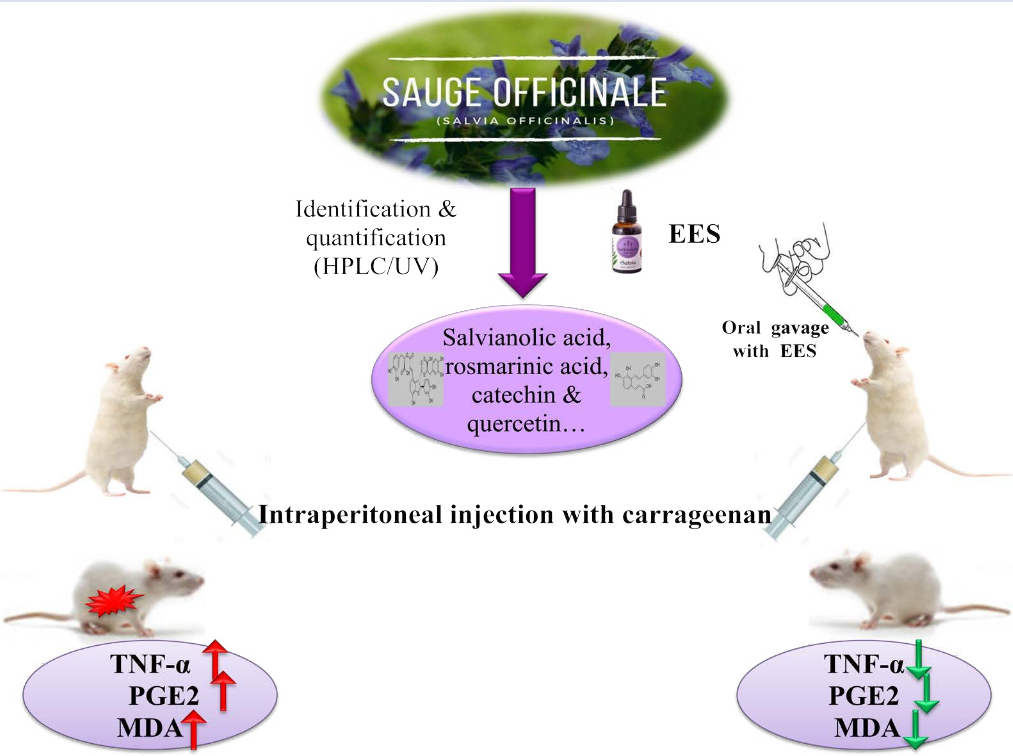
REFERENCES

1. Lee JY, Hwang WI, Lim ST. Antioxidant and anticancer activities of organic extracts from Platycodon grandiflorum A. De Candolle roots. J of Ethnopharm. 2004; 93(2-3): 409-415.
2. Durackova Z. Some current insights into oxidative stress. *Physiological Research*. 2010; 59(4): 459-469.
3. Kumar S, Pandey AK. Free radicals: health implications and their mitigation by herbals. British Journal of Medicine and Medical Research. 2015; 7(6): 438-457.
4. Cadet J, Delatour T, Douki T, Gasparutto D, Pouget JP, Ravanat JL, Sauvaigo S. Hydroxyl radicals and DNA base damage. Mutat Res. 1999; 424(1-2):9-21.
5. Chang CH, Yu FY, Wu TS, Wang LT, Liu BH. Mycotoxin citrinin induced cell cycle G2/M arrest and numerical chromosomal aberration associated with disruption of microtubule formation in human cells. *Toxicol Sci*. 2011; 119(1): 84-92, 2011.
6. Wang C, Schuller Levis GB, Lee EB, Levis WR, Lee DW, Kim BS, Park SY, Park E. Platycodin D and D3 isolated fromthe root of Platycodon grandiflorum modulate the production of nitric oxide and secretion of TNF-*α* in activated RAW 264.7 cells. *International Immunopharmacology*. 2004; 4(8): 1039-1049.
7. Willcox JK, Ash SL, Catignani GL. Antioxidants and prevention of chronic disease. Critical Reviews in Food Science and Nutrition. 2004; 44(4): 275-295.
8. Berlett BS Stadtman ER. Protein oxidation in aging, disease, and oxidative stress. J of Biol Chem. 1997; 272(33): 20313-20316.

9. Salzanoa S, Checconia P, Hanschmannc EM, Horst Lillig C, Bowler LD, Chan P, Vaudry D, Mengozzi M, Coppo L, Sacre S, Atkuri KR, Sahaf B, Herzenberg LA, Herzenberg LA, Mullen L, Ghezzi P. Linkage of inflammation and oxidative stress via release of glutathionylated peroxiredoxin-2,which acts as a danger signal. Proceeding of National Academy of Sciences of United States of America. 2014; 111(33): 12157-12162.
10. Kim YS, Young MR, Bobe G, Colburn NH, Milner JA. Bioactive food components, inflammatory targets, and cancer prevention. Cancer Prev Res. 2009; 2(3): 200-208.
11. Elinav E, Nowarski R, Thaiss CA, Hu B, Jin C, Flavell RA. Inflammation induced cancer: crosstalk between tumours, immune cells and microorganisms. Nat Rev Cancer. 2013; 13(11): 759-771.
12. Manach C, Scalbert A, Morand C, Rémésy C, Jiménez L. Polyphenols: food sources and bioavailability. The American J of Clin Nutr. 2004; 79(5): 727-747.
13. Pandey KB, Rizvi SI. Plant polyphenols as dietary antioxidants in human health and disease. Oxidative Medicine and Cellular Longevity. 2009; 2(5): 270-278.
14. Cardozo LFMF, Pedruzzi LM, Stenvinkel P, Stockler-Pinto MB, Daleprane JB, Leite Jr M, Mafra D. Nutritional strategies to modulate inflammation and oxidative stress pathways via activation of the master antioxidant switch Nrf2. Biochimie. 2013; 95(8): 1525-1533.
15. Maatoug H. Nos plantes médicinales. Lexique clinique des plantes médicinales non toxiques employées en Tunisie, ed isbn, p. 109-116; 1990.
16. Stary F, Jirasek V. Herbs. Hamlyn Publ. London, 1977.
17. Catione P, Marotti M, Toderi G, Tétényi P. Cultivazione della piante medicinali e aromatiche, ed Patron, Bologna, p. 253-263; 1986.
18. Beier RC. Natural pesticides and bioactive components in food. Rev Env Contam Toxicol. 1990, 113: 47-137.
19. Hasanein P, Felehgari Z, Emamjomeh A. Preventive effects of *Salvia officinalis L.* against learning and memory deficit induced by diabetes in rats: Possible hypoglycaemic and antioxidant mechanisms. Neurosci Lett. 2016; 622: 72-77.
20. Singleton VL, Orthofer R, Lamuela-Raventos RM. Analysis of total phenols and other oxidation substrates and antioxidants by means of Folin-Ciocalteu reagent. Methods Enzymol. 1999; 299: 152-178.
21. Woisky RG, Salatino A. Analysis of Propolis: Some Parameters and Procedures for Chemical Quality Control. Journal of Apicultural Research. 1998; 37 (2): 99-105.
22. Arnous A, Makris DP, Kefalas P. Correlation of pigment and flavanol content with antioxidant properties in selected aged regional wines from Greece. J Food Compos Anal. 2002; 15 (6): 655-665.
23. Yagi K. A simple fluorometric assay for lipoperoxide in blood plasma. Biochem Med. 1976; 15 (2): 212-216.
24. Silva JC, Rodrigues S, Feas X, Estevinho LM. Antimicrobial activity, phenolic profile and role in the inflammation of propolis. Food and Chem Toxic. 2012; 50(5): 1790-1795.
25. Luck H. Catalase. 2nd Ed. In: Bergmeyer HU, Editor. Methods of Enzymatic Analysis. Academic Press, London; 1965.
26. Aebi H. Catalase. 2nd Ed. In: Bergmeyer HU, Gawehn, K, Editors. Methods of enzymatic analysis V2: Verlag Chemie: Academic Press, Weinheim; 1974.
27. Elstner EF, Youngman RJ, Obwald W. Superoxyde dismutase in methods of enzymatic analysis. 3rd Ed. Bergmeyer H, Editor. Method of Enzymatic analysis. Weinheim: Verlag Chemie. GmbH; 1983.
28. Paglia DE, Valentine WN. Studies on the quantitative and qualitative characterization of erythrocyte glutathione peroxydase. J of Laboratory and Clin Med. 1967; 70: 158-169.
29. Zimmermann BF, Walch SG, Tinzoh LN, Stühlinger W, Lachenmeier DW. Rapid UHPLC determination of polyphenols in aqueous infusions of *Salvia officinalis L.* (sage tea). J of Chromatogr B. 2011; 879: 2459-2464.
30. Cvetkovikj I, Stefkov G, Acevska J., Stanoeva JP, Karapandzova M, Stefova M, Dimitrovska A, Kulevanova S. Polyphenolic characterization and chromatographic methods for fast assessment of culinary Salvia species from South East Europe. J of Chromatogr A. 2013; 1282: 38-45.
31. Li L, Liu H, Han Q, Kong B, Liu Q. Cooperative antioxidative effects of zein hydrolysates with sage (*Salvia officinalis*) extract in a liposome system. Food Chemistry. 2017; 222: 74-83.
32. Akowuah GA, Ismail Z, Norhayati I, Sadikun A. The effects of different extraction solvents of varying polarities on polyphenols of Orthosiphon stamineus and evaluation of the free radical-scavenging activity. Food Chem.2005; 93: (2) 311-317.
33. Turkmen N, Sari F, Velioglu YS. Effects of extraction solvents on concentration and antioxidant activity of black and black mate tea polyphenols determined by ferrous tartrate and Folin-Ciocalteu methods. Food Chem.2006; 99: (4) 835-841.
34. Wang J, Sun B, Cao Y, Tian Y, Li X. Optimisation of ultrasound-assisted extraction of phenolic compounds from wheat bran. Food Chem.2008; 106: (2) 804-810.
35. Zhang ZS, Li D, Wang LJ, Ozkan N, Chen XD, Mao ZH, Yang HZ. Optimization of ethanol-water extraction of lignans from flaxseed. Sep Purif Technol. 2007; 57: (1) 17-24.
36. Durling NE, Catchpole OJ, Grey JB, Webby RF, Mitchell KA, Foo LY, Perry NB. Extraction of phenolics and essential oil from dried sage (*Salvia officinalis*) using ethanol water mixtures. Food Chem. 2007; 101: (4)1417-1424.
37. Kianbakht S, Hashem Dabaghianb F. Improved glycemic control and lipid profile in hyperlipidemic type 2 diabetic patients consuming *Salvia officinalis L.* leaf extract: A randomized placebo. Controlled clinical trial. Compl Ther in Med. 2013; 21: (4)441-446.
38. Matkowski A, Zielinska S, Oszmia nski J, Lamer-Zarawska E. Antioxidant activity of extracts from leaves and roots of Salvia miltiorrhiza Bunge, S. przewalskii Maxim., and S. verticillata L. Biores Techn. 2008; 99(16): 7892-7896.
39. Hamrouni-Sellami I Rahali FZ, Bettaieb Rebey I, Bourgou S, Limam F, Marzouk B. Total Phenolics, Flavonoids, and Antioxidant Activity of Sage (*Salvia officinalis L.*) Plants as Affected by Different Drying Methods. Food Bioprocess Technol. 2013; 6: 806-817.
40. Hinneburg I, Damien Dorman HJ, Hiltunen R. Antioxidant activities of extracts from selected culinary herbs and spices. Food Chem. 2006; 97(1), 122-129.
41. Pizzale L, Bortolomeazzi R, Vichi S, Überegger E, Conte LS. Antioxidant activity of sage (*Salvia officinalis* and *S fruticosa*) and oregano (*Origanum onites* and *O indercedens*) extracts related to their phenolic compound content. J of the Sci of Food and Agric. 2002; 82(14): 1645-1651.
42. Mao LC, Pan X, Que F, Fang XH. Antioxidant properties of water and ethanol extracts from hot air-dried and freeze dried daylily flowers. European Food Research and Technology. 2006; 222: (3-4) 236-241.
43. Dorman HJD, Peltoketo A, Hiltunen R, Tikkanen MJ. Characterisation of the antioxidant properties of de-odourised aqueous extracts from selected Lamiaceae herbs. Food Chem. 2003; 83: (2) 255-262.
44. Xu J, Chen S, Hu Q. Antioxidant activity of brown pigment and extracts from black sesame seed (Sesamum indicum L.). J of Food Chem. 2005; 91 (1): 79-83.
45. Annamalai A. Effect of drying treatment on the contents of antioxidants in Cardiospermum halicacabum Linn. Inter J of Pharm and Biol Sci. 2011; 2 (1): 304-313.
46. Dianat M, Esmaeiliziadeh M, Badavi M, Samarbafzadeh A, Naghizadeh B. Cardiac protective effects of crocin on hemodynamic parameters and infarct size in compare vitamin E after ischemia reperfusion in isolated rat heart. Planta Med. 2014; 80: 393-398.
47. Miura K, Kikuzaki H, Nakatani N. Antioxidant activity of chemical components from sage (*Salvia officinalis L.*) and thyme (Thymus vulgaris L.) measured by the oil stability index method. J of Agric Food Chem. 2002; 50 (7):1845-1851.
48. Arici M, Arslan FA, Gecgel U. Effect of gamma radiation on microbiological and oil properties of black cumin (Nigella sativa L.). Grasas y Aceites. 2007; 58 (4): 339-343.
49. Martins N, Barros L, Santos-Buelga C, Henriques M, Silva S, Ferreira ICFR. Evaluation of bioactive properties and phenolic compounds in different extracts prepared from *Salvia officinalis L.* Food Chem. 2015; 170: 378-385.

50. Albano SM, Miguel MG. Biological activities of extracts of plants grown in Portugal. Ind Crops and Prod. 2011; 33 (2): 338-343.
51. Akcan T, Estevez M, Serdaroglu M. Antioxidant protection of cooked meatballs during frozen storage by whey protein edible films with phytochemicals from *Laurus nobilis L.* and *Salvia officinalis*. LWT - Food Sci and Tech. 2017; 77: 323-331.
52. Cuvelier ME, Richard H, Berset C. Antioxidative activity and phenolic composition of pilot-plant and commercial extracts of sage and rosemary. JAOCS. 1996; 73 (5): 645-652.
53. Azevedo MI, Pereira AF, Nogueira RB, Rolim FE, Brito GAC, Wong DVT, Lima-Júnior RCP, Ribeiro RDA, Vale ML. The antioxidant effects of the flavonoids rutin and quercetin inhibit oxaliplatin-induced chronic painful peripheral neuropathy. Mol Pain. 2013; 9: 53.
54. Sadeghnia HR, Yousefsani BS, Rashidfar M, Boroushaki MT, Assadpour E, Ghorbani A. Protective effect of rutin on hexachlorobutadiene-induced nephrotoxicity. Ren Fail. 2013; 35: 1151-1155.
55. Zhang L, Lin YH, Leng XJ, Huang M, Zhou GH. Effect of sage (*Salvia officinalis*) on the oxidative stability of Chinese-style sausage during refrigerated storage. Meat Sci. 2013; 95 (2): 145-150.
56. Dietz O, Wiesner E. Haematology and biochemistry of normal mice and the significance of pathologic variation. In: Diseases of the mice. Part1, S. Karger, Basel. p 28-31; 1984.
57. Louisot P. Catabolisme des protéines et métabolisme des amino-acides. I: Biochimie générale et médicale, structurale, métabolique sémiologique. Villeurbane, Simep, p702-750 ; 1983.
58. Wish JB. Assessing Iron Status: Beyond Serum Ferritin and Transferrin Saturation. Clin J Am Soc Nephrol. 2006; 1: S4-S8
59. Mansourabadi AM, Sadeghi HM, Razavi N, Rezvani E. Anti-inflammatory and analgesic properties of salvigenin, *Salvia officinalis* flavonoid extracted. Adv Herb Med. 2015; 2 (1): 31e41.
60. Rodrigues MRA, Kanazawa LKS, Neves TLM, Silva CFD, Horst H, Pizzolatti MG, Santos ARS, Baggio CH, Werner MFP. Antinociceptive and anti-inflammatory potential of extract and isolated compounds from the leaves of *Salvia officinalis* in mice. J of Ethnophar. 2012; 139 (2): 519-526.
61. Baricevic D, Sosa S, Della Loggia R, Tubaro A, Simonovska B, Krasna A, Zupancic A. Topical anti-inflammatory activity of *Salvia officinalis L.* leaves: the relevance of ursolic acid. J Ethnopharmacol. 2001; 75 (2-3): 125-132.
62. Rathee P, Chaudhary H, Rathee S, Rathee D, Kumar V, Kohli K. Mechanism of action of flavonoids as anti-inflammatory agents: a review. Inflamm Allergy Drug Targets. 2009; 8(3): 229-35.
63. Lu Y, Yeap Foo L. Antioxidant activities of polyphenols from sage (*Salvia officinalis*). Food Chem. 2001; 75 (2): 197-202.
64. Ollanketo M, Peltoketo A, Hartonen K, Hiltunen R, Riekkola ML. Extraction of sage (*Salvia officinalis L.*) by pressurized hot water and conventional methods: antioxidant activity of the extracts. Eur Food Res Technol. 2002; 215(2): 158-63.
65. Bahmani M, Shirzad H, Majlesi M, Shahinfard N, Rafieian-Kopaei M. A review study on analgesic applications of Iranian medicinal plants. Asian Pac J Trop Med. 2014; 7(S1): S43-S53.
66. Medzhitov R. Origin and physiological roles of inflammation. Nature. 2008; 454 (7203): 428-435.
67. Borghini T, Vernez L, Kesseler D. Protéine C réactive (CRP) et Vitesse de sédimentation (VS). CSCQ. 2013.
68. Blain H, Jouzeau JY, Netter P, Jeandel C. Les anti-inflammatoire non steroidiens inhibiteurs séléctifs de la cyclooxygénase 2. Intérêt et perspectives .La revue de médecine interne. 2000 ; 21(11): 978-988.
69. Kolac UK, Ustuner MC, Tekin N, Ustuner D, Colak E, Entok E. The anti-inflammatory and antioxidant effects of *Salvia officinalis* on lipopolysaccharide induced inflammation in rats. J of Med Food. 2017; 20 (12): 1193-1200.
70. Mueller M, Hobiger S, Jungbauer A. Anti-inflammatory activity from extracts from fruits, herbs and spicies. Food Chem. 2010; 122 (4): 987-996.
71. Gaspar A, Craciunescu O, Trif M, Moisei M, Moldovan, L. Antioxidant and anti-inflammatory properties of active compounds from *Arnica montana* L. Rom. Biotechnol Lett. 2014; 19 (3): 9353-9365.

GRAPHICAL ABSTRACT



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