Research Article

Acute Oral Toxicity and Neurobehavioral Effects of *Salvia officinalis* Essential Oil in Female Wistar Rats

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Abstract | In recent years, Salvia *officinalis* has been a subject of intensive studies to document its traditional use and to find new biological effects. Numerous studies have been carried out in this contest and most of them were interested in Salvia *officinalis* extract' effects and not many explored the biological activities of Salvia *officinalis* essential oil, especially the ones related to the central nervous system. The Purpose of this study is to investigate the acute toxicity of *salvia officinalis* essential oil in female Wistar rats, and to explore the antidepressant-like and anxiolytic-like effects and memory enhancing of the safe dose of this essential oil. In this experiment, *salvia officinalis* essential oil was administered once by oral gavage to four groups of female Wistar rats (n=6) at three different doses; 1000, 2000 and 3000 mg/kg. During 14 days after dosing, a follow-up was carried out for the mortality, food and water consumption, body weight changing and clinical signs. Biochemical parameters and organ weight were also examined. The behavior of rats was evaluated at the end of the experiment for anxiety-like and depression-like and memory. Accordingly, treatment with salvia *officinalis* essential oil at a dose of 2000 mg/kg showed no mortality or clinical signs, nor any changes in body, organ weights or biochemical parameters, except for mortality induced in one female rat treated with 2000 mg/kg. Furthermore, the LD50 (50% lethal dose) was determined at 3000 mg/kg. Based on these findings, the no observed adverse effect level of *salvia officinalis* essential oil was established to be 1000 mg/kg. Evaluation of the effect of this therapeutic dose revealed a clear anxiolytic and antidepressant actions and improved memory functioning in female Wistar rats. In conclusion, *salvia officinalis* essential oil produce neuroprotective activity in female rats.

Keywords | Herbal medicine, Acute toxicity, *Salvia officinalis*, Anxiety, Depression, Memory, Rats, Phytotherapy

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INTRODUCTION

According to the World Health Organisation's estimate, the primary health care needs of 80% of the population in some developing countries is covered by the traditional medicine, Asia, Latin America and Africa, especially in rural areas due to the proximity and accessibility of this type of care, the low purchasing power of families, and the lack of access to modern medicine for these populations (WHO, 2013) of which we find the Moroccan population using phytotherapy for their diseases (Fatiha et al., 2017; Ajjoun et al., 2022).

Medicinal plants represent an interesting source of a massive variety of bioactive molecules, which reported to be responsible for eliciting such therapeutic effects (Jahani

et al., 2019). In addition, various herbal medicines are known as active in the central nervous system, and they can have an effect on several neurological disorders such as epilepsy, anxiety or depression, unresponsive to standard treatments (Hasanein et al., 2017; Carrillo-Mora et al., 2023; Garg et al., 2023). Yet, the evaluation of toxicity in animals is essential to prove its safety for clinical use. Thus, experiments are presently being expanded in this sense.

Salvia officinalis (*S. officinalis)* is considered a prominent plant containing beneficial essential oil (Hasanein et al., 2017; Rhaimi et al., 2022). Due to its biological properties: anti-inflammatory, antibacterial, cytotoxic, antimutagenic and antioxidant activities, *S. officinalis* has been widely used in the treatment of certain diseases such as hyperglycemia, dizziness, ulcers, gout, tremor, diarrhea, paralysis, and rheumatism (Ghorbani and Esmaeilizadeh, 2017; Hasanein et al., 2017; Ashkani-Esfahani et al., 2021; Ezema et al., 2022; Mot et al., 2022; Rhaimi et al., 2022). Furthermore, this plant is traditionally noted for memory enhancing and boosting 'head and brain' tasks (Lopresti, 2017). Recently, *S. officinalis* has been a subject of thorough studies to find new neurobiological effects.

Despite extensive bioactivity studies on *S. officinalis* plant and its constituents, studies on the toxicological profile of the *S. officinalis* essential oil is lacking in the literature. In addition, there is no experimental evidence on its effect on affective and cognitive behaviors. Thus, underscoring the need for this work which has two main goals: (1) To investigate the acute toxicity of *salvia officinalis* essential oil following to a single doses exposure in female Wistar rats. (2) To explore the antidepressant, anxiolytic and memory enhancing effects of the safe dose of this essential oil.

MATERIALS AND METHODS

Plant material

The plant material was collected in the province of Kenitra (Morocco) (Figure 1) and left to dry in the shade. After drying, the plant material was stored in the shade until it was used (Rhaimi et al., 2022).

Extraction of the *S. officinalis* essential oil

The plant leaves were subjected to hydrodistillation with the Clevenger apparatus (Fagbemi et al., 2021). The distillation process was performed for 3 h, and the obtained essential oil was collected, dehydrated and stored at (+4 °C) in the dark before analysis (Rhaimi et al., 2022).

Experimental animals

This experimentation is executed on 30 adults female Wistar rats, 3 months old and raised in the pet house of the Department of Life Sciences, Faculty of Sciences of Kenitra, Ibn Tofail University. The experimental protocol is accomplished in line with the Organization for Economic Co-operation and Development (OECD) requirements. Accordingly, each rat weight is chosen to be in reach of 20% of the average weight of all the animals used in this study. The animals are distributed in cages, lined with a bedding composed of wood chips which is renewed every two days, with a temperature of 20-25 °C, lighting and ventilation are controlled. The animals have free access to food and water (standard diet). To familiarize with the living conditions for at least five days before the experiment, the animals were kept in cages after being individually identified by a mark. To avoid possible stress, the animals are always handled in the same time intervals. The experimental procedures were carried out in accordance with the National Institutes of Health Guide for the Care and Use of Laboratory Animals and approved by the Animal Ethics Committee (Local Institutional Research Committee).

Figure 1: *Salvia officinalis* plant.

Experimental design

The female rats were divided into four groups of 6 rats (n=6), as following:

Groups	Treatments
Normal control	Normal saline 2 ml/160 g body weight
1000 mg/kg group	*S. officinalis* essential oil at the dose of 1000 mg/kg
2000 mg/kg group	*S. officinalis* essential oil at the dose of 2000 mg/kg
3000 mg/kg group	*S. officinalis* essential oil at the dose of 3000 mg/kg

The essential oil of *S. officinalis* was administered to all animals by oral gavage (OECD, 2002).

Detected clinical signs and body weight

Clinical signs were recorded based on the Functional Observational Battery at least twice a day. These include changes in water and food intake and mortality. In addition, body weights were measured every day during the 14 days after dosing.

Neurobehavioral tests

Anxiety-like measurement

Open field test (OFT): The OFT is a widely used model of anxiety-related behavior developed to evaluate emotionality in rodents (Carola et al., 2002). The test was constructed in white plywood (100 x 100 cm) surrounded by 40 cm high walls. It was divided into 25 squares (20 × 20 cm); (9 central and 16 peripheral). During the light period, the animal behavior was recorded for 10 minutes after being placed in the middle of the apparatus. The next parameters were measured: The number of total tiles (central and peripheral) visited (NTS), as a measure of locomotion. The number of central tiles visited (NRC), and the time spent in the central area (TCA) as indices of anxiety, since the augmentation in these parameters can be interpreted as anxiolytic. The apparatus was cleansed with 70% ethanol after each trial to remove any odors left by other rats.

Elevated cross maze test (EPM)

The EPM is a *accredited* test that measures anxiety in rats (Naranjo-rodriguez et al., 2000). The labyrinth consists of a cross-shaped platform; 1 m high above the ground, with 2 open arms (50×10 cm) and 2 closed arms (50×10×40 cm). Rats are placed in the maze, fronting an open arm. The open arms and the elevation of the maze are a source of anxiety. The time spent in the open arms (TOA) and the number of entries into the open arms (EOA) was measured for 5 min as indicators of anxiety status. Anxiety reduction is defined by an increase in TOA and EOA. An entry is defined when both of the rat's forepaws are on the arm. The apparatus was cleansed with 70% ethanol after each trial to remove all traces (defecation and urine) of the previous animals.

Measurement of the depression-like

Forced swimming test (FST)

The FST or Porsolt test, is frequently used to examine depressive behavior (Porsolt et al., 1978). It consists of a cylinder with the height of 50 cm, 30 cm in the diameter and containing 27 cm of water (22°C) forbidding the rats from escaping. The animals were put in the water individually and the test swimming was recorded for 5 min in the absence of the experimenter. The water in the cylinder was changed after each test. The parameter measured was the immobility time (TIM).

Cognitive assessment

Y-maze test

The working memory condition in rats was evaluated by calculating the % of alternation in the Y-maze test as formerly described (Sierksma et al., 2014). It consists of three similar lanes (branches) (45 × 12 × 35 cm), arranged at an angle of 120° to each other. In the present study, rats were placed in one of the three lanes, with their heads directed towards the point of intersection of the three lanes, and were then left for 8 minutes to explore freely. The % of alternation was determined by the following equation: (Number of alternations/ (Number of visits – 2)) × 100.

Object recognition test (ORT)

The ORT is considered as an important protocol to study learning and memory in rodents (Bevins and Besheer, 2006). The experiment was performed in a cubic box (40 cm^3), where the rats were put individually in the middle allowing them to explore and adapt themselves with the two identical objects for 5 min. Twenty-four hours later; the test trial was conducted when a new object was put in the place of one of the two familiar objects of a different color (the new object) for the same rats to explore for 5 min. Trials were filmed in the absence of the experimenter to quantify interaction time. The objects and the box were cleansed with 70% ethanol after each trial to get rid of all previous animals' traces.

The recognition index (% RI) was calculated as follows: [The total time spent exploring the novel object/ (The total time spent exploring the novel object + The total time spent exploring the familiar object)] x 100. Short-term recognition memory deficits are reflected by a decrease in the recognition index.

Biochemical assays

Blood samples were collected into plain tubes and centrifuged at 2500 rpm for 15 min to obtain the serum of experimental rats. The serum samples were further biochemically analyzed to determine the concentrations of glucose (Lott and Turner, 1975) and HDL cholesterol (Alya et al., 2015).

Relative organs weight

On day 14 of the experiment, all rats were anaesthetized after 12 hours. Blood was collected in dry tubes. The analyses were performed on the serum recovered from the blood after centrifugation at 3000 rpm for 10 minutes. The selected subjects were weighed and sacrificed, and the organs (liver, kidney, heart and brain) were removed for weighing.

Statistical analysis

IBM's SPSS version 23 was used for all statistical analysis

(IBM Corp., Armonk, NY, United States). Body weight, food and water intake, organ weight and serum biochemistry data were statistically analyzed using ANOVA (One-way). The behavioral data were subjected to Student's t test and differences between means were determined by Duncan test at ($p < 0.05$). The values were expressed as mean±SEM.

RESULTS

Acute toxicity of *Salvia officinalis*

Mortality and clinical signs

In female rats, no S. *officinalis* essential oil treatment-related mortalities were observed at the dose of 1000 mg/kg (Table 1). All female rats (6/6; 100%) survived during the 14-day experimental period. The administration of 2000 mg/kg caused the death of a single batch rat. While the administration of S. *officinalis* essential oil at the dose of 3000 mg/kg induce the death of one-half of the rats (3/6; 50%). The results obtained could show that the lethal dose of the studied extract is 3000 mg/kg. While the no observable toxic effect level (NOAEL) and therapeutic dose was observed in rats receiving 1000 mg/kg.

Table 1: Mortality and clinical signs observed in rats exposed with *S. officinalis* essential oil during the acute toxicity study.

Parameters	Control	*S. officinalis* essential oil		
		1000 mg/kg	2000 mg/kg	3000 mg/kg
Mortality	0/6	0/6	1/6	3/6
Clinical signs behavior	N	N	N	N
Posture	N	N	N	AN
Scratching	N	N	N	P
Appearance of hair	N	N	N	N
Aggressiveness	N	N	N	A
Paralysis	N	N	N	P
Sedation	N	N	N	N
Drowsiness	N	N	N	P
Trembling	N	N	N	P
Asphyxiation	N	N	N	P

N: normal, AN: abnormal, P: presence, A: aggressive.

In terms of clinical signs, no abnormal clinical signs were observed in animals treated with *S. officinalis* essential oil at doses of 1000 and 2000 mg/kg during the observation period. While, a various abnormal clinical signs in the rats treated with the dose of 3000 mg/kg were observed (aggressiveness, paralysis, drowsiness, trembling and asphyxiation).

Body weight

While comparing body weight in all dosing groups tested with that of vehicle control in all dose levels during the 14-day experimental period, no meaningful changes were detected ($p > 0.05$) (Figure 2).

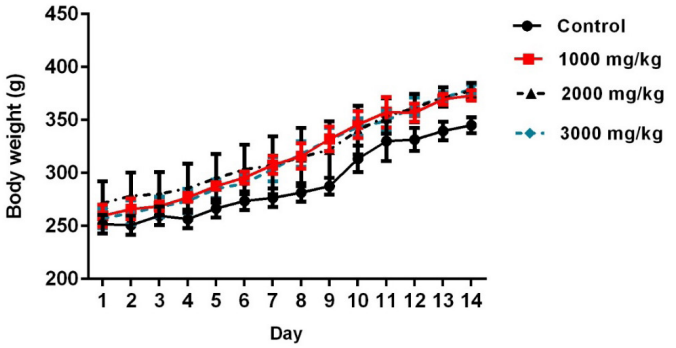

Figure 2: Changes on the body weights during 14 days of observation in male rats after single oral treatment of *S. officinalis* essential oil.

Food and water intake

All female rats treated with *S. officinalis* essential oil at various doses (1000, 2000 and 3000 mg/kg) show no significant differences in mean food consumption or water intake while comparing with the control group ($p > 0.05$) (Figures 3a and 3b).

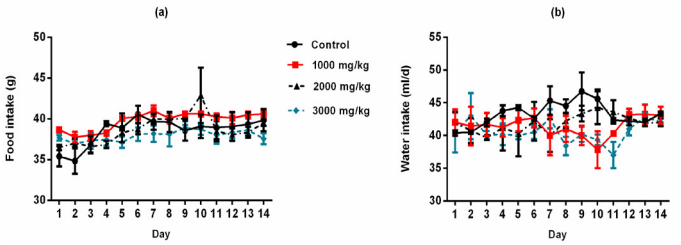

Figure 3: Food consumption expressed in g/d (a) and Water intake expressed in ml/d (b) of female rats orally administered with *S. officinalis* essential oil.

Biochemical parameters

No significant change in HDL cholesterol nor blood glucose were observed in treated rats comparing to control group ($p > 0.05$) (Table 2).

Table 2: Serum biochemical parameters (mean ± SEM) of Wistar rats in acute oral toxicity study of *S. officinalis* essential oil.

Parameter/ Group	Control	S. *officinalis* essential oil		
		1000 mg/kg	2000 mg/kg	3000 mg/kg
GLU (g\l)	0.82±0.20	1.02±0.22	0.90±0.39	0.98±0.61
HDL (g\l)	1.27±0.40	1.45±0.41	1.29±0.29	1.52±0.63

Values represent the mean ± SEM for n = 6.

Organs weight

Regarding the weights of the organs removed after the sacrifice of the *S. officinalis* essential oil treated rats and the control rats, no meaningful changes were found between the different experimental groups ($p > 0.05$) (Table 3).

Table 3: The relative organs weights (mean±SEM) of Wistar rats in acute oral toxicity of *S. officinalis* essential oil.

Organ/ Group	Control	S. *officinalis* essential oil		
		1000 mg/kg	2000 mg/kg	3000 mg/kg
Liver	10.03±0.09	09.12±0.28	10.50±0.19	09.81±0.10
Heart	01.25±0.12	01.24±0.08	01.26±0.08	01.55±0.08
Kidneys	02.10±0.04	02.12±0.03	02.11±0.04	02.10±0.04
Brain	01.20±0.08	01.61±0.05	01.71±0.06	01.64±0.02

Values represent the mean ± SEM for n = 6.

Behavioral tests

Effect of *S. officinalis* essential oil on the levels of anxiety-like behavior measured in the OFT

Figure 4 reveal the significant increased of the TCA (a) and NRC (b) in female Wistar rats due to *S. officinalis* essential oil ($p < 0.01$). On the contrary, locomotor activity was unaffected by S. *officinalis* essential oil ($p > 0.05$). This reflects the insignificant effect of the studied essential oil on the locomotor activity of the tested rats.

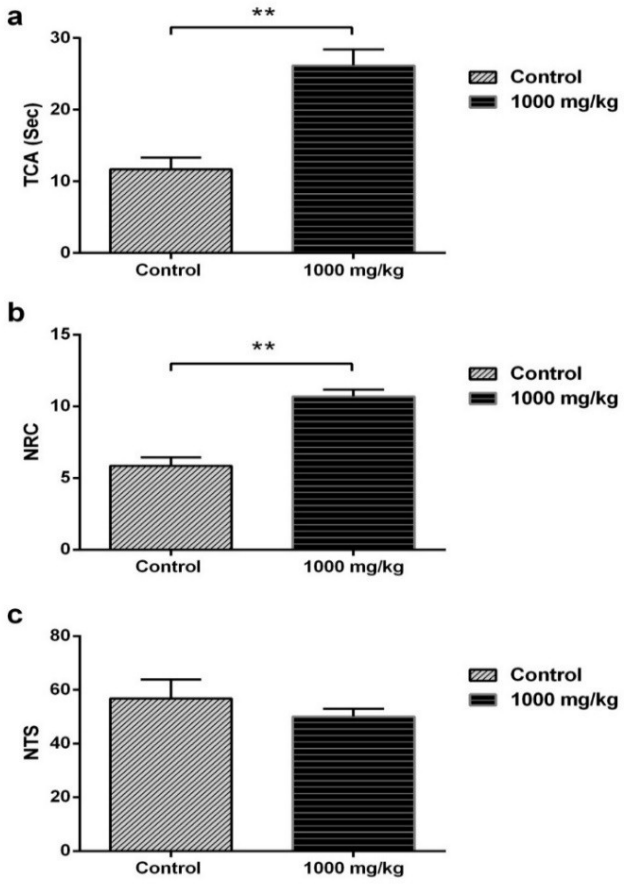

Figure 4: (a) Total amount time spent in the center (TCA). **(b)** Number of returns into the center area of the arena in the open-field behavior apparatus (NRC). **(c)** Number of total squares (NTS) in the open field test in female rats after the administration of 1000 mg/kg of *S. officinalis* essential oil. Data are represented as mean ± S.E.M. *p < 0.05 vs. control group.

S. officinalis essential oil' effect on the levels of anxiety-like behavior measured in the EPM

Figure 5 show the levels of anxiety in the rats evaluated and confirmed by the EPM test. The TOA and TEA parameters were significantly increased in case of *S. officinalis* essential oil-treated female rats when compared with control rats ($p < 0.01$), suggesting the anxiolytic effect of the test article.

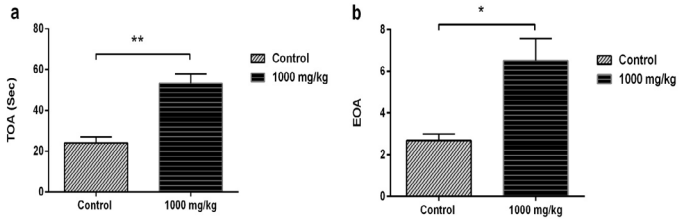

Figure 5: (a) Total amount of time spent in open arms (TOA). **(b)** Number of entries in open arms (EOA) in the EPM test in female rats after the administration of 1000 mg/kg of *S. officinalis* essential oil. Data are represented as mean ± S.E.M. *p < 0.05 vs. control group.

S. officinalis essential oil effects on depressive-like performances evaluated by the FST

Based on student t analysis, the duration of immobility in the FST in female rats was significantly decreased when administrating *S. officinalis* essential oil ($p < 0.001$) (Figure 6).

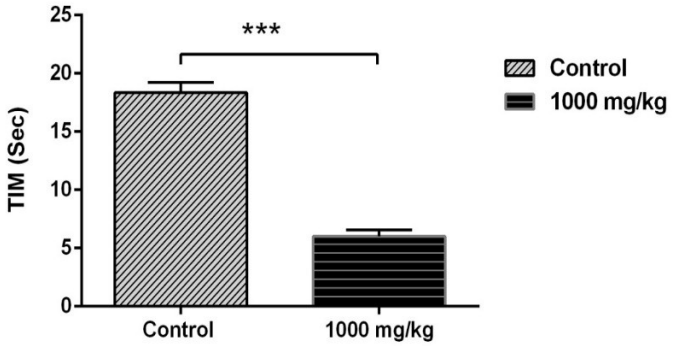

Figure 6: Immobility time expressed in seconds (Sec) (TIM), in the forced swimming test in female rats after the administration of 1000 mg/kg of *S. officinalis* essential oil. Data are represented as mean ± S.E.M. *p < 0.05 vs. control group.

S. officinalis essential oil effects on memory

Y-maze test

Statistical analysis shows a significant increase in % alternation in the rats of the 1000 mg/kg group compared to the control group ($p < 0.01$) (Figure 7).

ORT

Recognition performance was evaluated by ORT test and was showed in Figure 8. *S. officinalis* essential oil could improve the recognition index non significantly better than control group ($p > 0.05$).

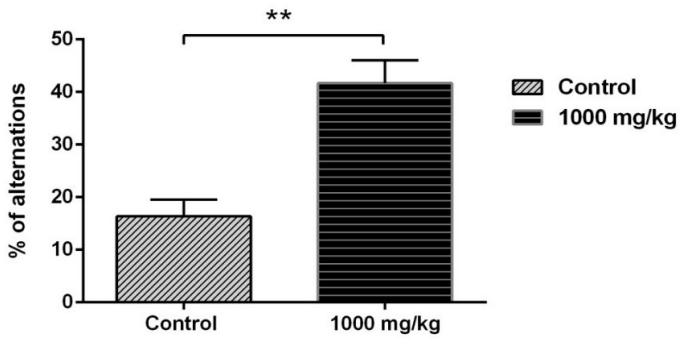

Figure 7: Effect of oral administration of S. *officinalis* essential oil (1000 mg/kg) on spontaneous alternation percentage measured in Y-maze. Data are represented as mean ± S.E.M. *p < 0.05 vs. control group.

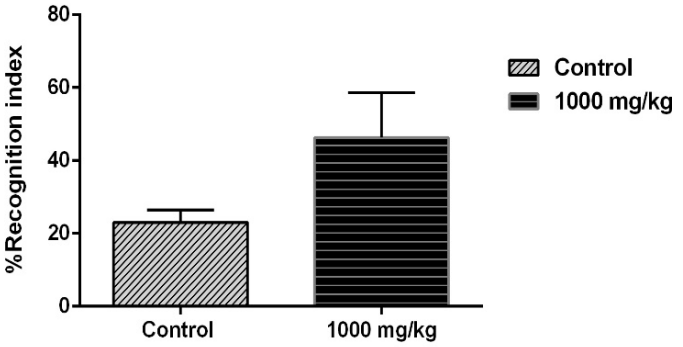

Figure 8: Effects of *S. officinalis* essential oil (1000 mg/kg) on recognition memory measured in the object recognition test. Data are represented as mean ± S.E.M. *p < 0.05 vs. control group.

DISCUSSION

The purpose of the present study was to evaluate the acute toxicity of *S. officinalis* essential oil on the female Wistar rat as a part of the safety test, and to clear up the anxiolytic, antidepressant and memory enhancing effects of the safe dose. The test substances were once orally administered to female rats at dose levels of 3000, 2000 and 1000 mg/kg.

Because no *S. officinalis* essential oil treatment related mortalities neither sign of behavioural changes or toxicity signs were detected throughout 14 days of observation period at the dose of 1000 mg/kg in female rats in the present experiment, the NOAEL (the safe dose) was determined to be 1000 mg/kg. Additionally, the administration of *S. officinalis* essential oil at the dose of 3000 mg/kg causes some clinical signs of toxicity (paralysis, drowsiness, trembling, asphyxiation) and the death of 50% of the rats. This is an indication that the LD50 value is estimated to be 3000 mg/kg. The rate of mortality increased in a dose-dependent manner. According to OECD (OECD, 2002), the LD50 value indicates that the *S. officinalis* essential oil, administered orally, is considered as safe and non-toxic. These results agreed with other studies of using different concentration of *S. officinalis* extracts. For example, a recent study on acute toxicity by Maliki et al. (2021) reported that the aqueous extracts of *S. officinalis* appear to be generally safe at a dose level of 2000 mg/kg, and the LD50 was estimated to be >2000 mg/kg (Maliki et al., 2021). In another study, ethanolic S. *officinalis* leaf extract administered orally in female rats was considered not toxic at the maximum dose of 2000 mg/kg (Sabry et al., 2022). In this work, the LD50 of *S. officinalis* essential oil is higher when compared to a previously published lethal dose of this plant, which can be attributed to the difference in extraction method and to the purity of the extracted sample.

The safety of herbal products implies the determination of rodents food and water consumption (Kurtz and Feeney, 2019). In this study, regardless of the dose used, *S. officinalis* essential oil administration induced no significant changes in feed intake and water consumption, which proves the safety of using this essential oil. Furthermore, to assess the health status of experimental animals, the body weight parameter can be used (Wang et al., 2019). Daily body weights recorded on this work showed no meaningful changes were detected in all dosing groups tested compared to control. This could be an indicator to the health sustaining benefit of *S. officinalis* essential oil in stabilizing their vital parameters.

The relative organ weight in toxicology study is also an important indicator of the harmful effect of the tested compound (Lazic et al., 2020). Noticeably, there was no substantial alteration in relative organ (liver, heart, kidneys and brain) treated rats weight compared to control group, implying that the essential oil did not appear to cause any damaging on the rats organs. This finding is in agreement with the results of the previous *in-vivo* study (Maliki et al., 2021). Additionally, the data were consistent with normal serum biochemistry of all treated rats in acute toxicity experiment. Serum biochemical parameters are also included in testing the toxicity of medicinal plants (Fazliana et al., 2008). Collectively, all the results suggested that *S. officinalis* essential oil administration did not provoke systemic toxicity in rats.

In the present study, *S. officinalis* essential oil administration (1000 mg/kg) has shown a significant anxiolytic effect in the OFT end EPM in rats. Our findings are in line with the work and observation of Choukairi *et al.* that the administration of *S. officinalis* Leaves extracts induce an anxiolytic effect in adult rats (Choukairi et al., 2019). Moreover, according to our information, this is the first experiment revealing the antidepressant effects of *S. officinalis* essential oil. This finding is congruent with the results obtained by Kennedy DO when he tested the effects of *S. officinalis* leafs extracts on the modulation of

mood performance in 30 healthy participants (Kennedy et al., 2006). In addition, according to the results attained in the study of Maliki and coworkers., the aqueous extracts of *S. officinalis* reduced the time of immobility of animals in FST, reflecting an antidepressant activity of the extract (Maliki et al., 2021). The results obtained are probably due to synergistic action of several constituents present in the test article. In this direction, it has been demonstrated that several compounds from S. *officinalis* such as the rosmarinic acid and phenolic acids, possess anxiolytic and antidepressant-like activities (Hasanein et al., 2017). Importantly, it has been reveled in a neuropharmacological analysis that these substances could no influence the uptake of monoamines to synaptosomes or mitochondrial monoamine oxidase activity in the mouse brain, suggesting that they provoke their anxiolytic and antidepressant-like actions via other mechanisms (Lopresti, 2017). Furthermore, considering this fact that oxidative stress is linked to the etiology of behavioral disorders (Lamtai et al., 2020, 2022), the antioxidant activity of S. *officinalis* essential oil might be one of the possible mechanisms of action in the observed effect. Salvia plants and their individual chemicals including rosmarinic acid, carnosol and carnosic acid, possess strong radical scavenging activity (Ghorbani and Esmaeilizadeh, 2017). In the study of Oboh and Henle (2009), the aqueous extracts of *S. officinalis* leaf protect the brain from oxidative stress, which is attributed to the antioxidant effect of the high total phenol and vitamin C content of the leaf. However, further experiments need to be realized to confirm this hypothesis.

Y-maze and OR tests were applied to evaluate the cognitive-enhancing activities of *S. officinalis* essential oil in Wistar rats. Our data have shown that the oral administration of the essential oil at the dose of 1000 mg/kg could enhance the memory performance in all female rats. This finding is in agreement with the results of the previous in-vivo study conducted by (Hasanein et al., 2016; Ayoub et al., 2022). who reported that *S. officinalis* has cognitive- and memory-enhancing effects in rats. Also, the extract of this plant has previously been shown to have cognitive performance benefits in both healthy older and younger adults (Edwards et al., 2021). Generally, *in vitro* and animal experiments have demonstrated that several compounds found in Salvia plants can change some biological mechanisms linked to cognition performance including their actions on oxidative stress and cholinergic activity. For example, in the study of Ayoub et al. (2022), the memory enhancing effect of Salvia was accompanied to amelioration in oxidative stress markers and acetylcholinesterase activity in rat. In another work, it has been reported that *S. officinalis* extract lowered acetylcholinesterase activity in mice (Smach et al., 2015). These studies and others proposed that due to the antioxidant and acetylcholin esterase inhibitory activities of *S. officinalis* constituents especially the rosmarinic acid, improvement in the cognitive function seems plausible (Hasanein and Mahtaj, 2015; Hasanein et al., 2017; Ayoub et al., 2022).

CONCLUSIONS AND RECOMMENDATIONS

The current experimental data taken demonstrate the safety of acute oral administration of *S. officinalis* essential oil in female Wistar rats, and for the first time, we reported that the safe dose of this essential oil (1000 mg/kg) possesses a clear anxiolytic and antidepressant properties and memory enhancing effects.

After these favorable results being reported, a study of toxicity and neurobehavioral effects of *S. officinalis* essential oil in male Wistar rats must be executed to create larger data that used both male and female rats to understand sex differences. In addition, further studies are needed to investigate the effects of *S. officinalis* essential oil on liver and kidney function and histology in rats. And why not looking into discovering the exact mechanism involved in the observed effects.

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Abbreviations

S. officinalis: *Salvia officinalis*; OECD: Organization for Economic Co-operation and Development; OFT: Open Field Test; NTS: The number of total tiles visited; NRC: The number of central tiles visited; TCA: the time spent in the central area; EPM: Elevated Cross Maze Test; TOA: The time spent in the open arms; EOA: the number of entries into the open arms; FST: Forced Swimming Test; TIM: Immobility time; ORT: Object Recognition Test; RI: The recognition index; HDL: high-density lipoprotein; NOAEL: non observed adverse effect level; LD50: *Lethal Dose.*

NOVELTY STATEMENT

The novelty of this study is investigating the acute toxicity of S. Officinalis essential oil in female Wistar and exploring the antidepressant-like and anxiolytic-like effects and memory enhancing of the safe dose of this essential oil.

AUTHOR'S CONTRIBUTION

All authors contributed equally to the manuscript.

Conflict of interest

The authors have declared no conflict of interest.

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