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Original article

Histopathological and Biochemical Toxicity of *Cymbopogon schoenanthus* Essential Oil in Female Mice

Elahe Fathifar[1], Zahra Mousavi[2*], Tayebeh Rastegar[3], Jinous Asgarpanah[4]

[1]Faculty of Pharmacy and Pharmaceutical Sciences, Tehran Medical Sciences, Islamic Azad University, Tehran, IR Iran (IAUMS).
[2]Department of Pharmacology and Toxicology, Faculty of Pharmacy and Pharmaceutical sciences, Tehran Medical Sciences, Islamic Azad University, Tehran, IR Iran (IAUMS).
[3]Department of Anatomy, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran.
[4]Department of Pharmacognosy, Faculty of Pharmacy and Pharmaceutical Sciences, Tehran Medical Sciences, Islamic Azad University, Tehran, IR Iran (IAUMS).

Abstract

Background and objectives: The species of *Cymbopogon* are generally used for different pharmacological effects. No histopathological study has been conducted on the plant's toxicity so far. Thus, the acute and repeated toxicity of *Cymbopogon* essential oil were investigated. **Methods:** The essential oil from aerial parts of *Cymbopogon schoenanthus* was administered in mice by gavage in both acute and repeated models. The animals were then divided into control and test groups. In the acute toxicity, 2000 mg/kg *C. schoenanthus* essential oil was administered in mice. Death rate, toxic symptoms, body weight, and abnormal behaviors were also observed for 14 days. In the repeated toxicity, *C. schoenanthus* essential oil (10, 100, and 200 mg/kg) was daily administered for a 4-week period. On the 28thday, all animals were sacrificed and their blood and tissue samples were prepared. Moreover, clinical, biochemical, and histopathological changes were compared to the control group.
Results: No mortality was noticed in the acute test; therefore, the oral LD_{50} value was determined to be greater than 2000 mg/kg in the female mice. In the repeated test, the animals were given *C. schoenanthus* essential oil, which consequently showed no mortality and toxic symptoms. The repeated administration of *C. schoenanthus* essential oil had a variation on glucose, urea, Na^+, and K^+ levels. Moreover, the terminal necropsies revealed low toxic effects on the liver. **Conclusion:** The results indicate that the oral acute toxicity of *C. schoenanthus* essential oil in mice was of a low order with LD_{50} being more than 2000 mg/kg. Additionally, slight tissue damage to liver was observed when it was administered sub-chronically at the dose of 200 mg/kg.

Keywords: acute toxicity; *Cymbopogon schoenanthus*; mice; subchronic toxicity

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Introduction

The genus *Cymbopogon* belongs to Poaceae family, which comprises of about 180 species, sub-species, varieties, and sub-varieties. Because of their scent that is similar to lemon, this genus has some species cultivated as culinary and medicinal herbs. *Cymbopogon* species and their essential oils, commonly known as lemongrass, are used in foods, drugs, cosmetics, perfumery industry, and soap products [1].

Cymbopogon schoenanthus is one of the native species to western parts of Asia, especially Saudi Arabia. It is commonly known as camel grass and is imported and widely distributed in Iranian local markets. *Cymbopogon schoenanthus*, which is

*Corresponding author: moosavi.z@iaups.ac.ir

traditionally well known, is widely used as an antispasmodic, anti-malarial, and anti-helminthic agent and also as a protection against fever and intestinal ailment problems [2]. Furthermore, it is considered as an effective renal antispasmodic and diuretic agent [3], and has been shown to possess sedative, digestive, and anti-parasitic properties [4]. It has also been revealed that *C. schoenanthus* could be used as an anti-fungal and anti-inflammatory agent to prevent and treat acute inflammatory skin conditions [5]. It can also be used as an anti-abortive, anti-convulsive or laxative, anti-rheumatic, asthmatic, and antipyretic agent [6]. *Cymbopogon schoenanthus* is used for the treatment of colds, epilepsy, and abdominal cramps and pains as well as in culinary and perfume industries [7]. The oil extracted from the plant has a strong aroma and great medicinal value [3]. In a previous study, the anti-inflammatory effect of *C. schoenanthus* essential oil was investigated using several tests in experimental animals [8].

There are few studies on the toxicity of *C. schoenanthus* and other species of *Cymbopogon.* The data obtained from a study performed on the acute toxicity of C. *schoenanthus* revealed its safety after oral, eye, and dermal administrations [9]. The acute oral toxicity of *C. citrates Stapf*. was examined at a dose of 5000 mg/kg in rats using the limited test dose of the Up and Down Procedures [10]. Fandohone et al. studied the acute and sub-acute toxicities as well as gastric tolerances of *C. citratus, Ocimum gratissimum,* and *Ocimum basilicum* oils in rat for 14 consecutive days. Thereafter, a dose-dependent effect of the tested oils was observed during the study. The oils administered at doses higher than 1500 mg/kg body weight generally caused significant functional damages to stomach and liver of rats [11].

Despite the widespread local use of lemongrass, there are few controlled toxicological studies confirming its efficacy and safety in a long-term treatment. Accordingly, this can be due to the reason that sub-acute and repeated dose toxicity's data are required to verify the two above-mentioned objectives [12]. Therefore, the aim of the current study was to investigate the toxicological profile of *C. schoenanthus* essential oil after acute or repeated oral treatment in female mice, by mainly focusing on biochemical and histopathological endpoints.

Materials and Methods

Ethical considerations

All procedures were carried out in terms of the local guidelines for the care of laboratory animals of Faculty of Pharmacy, Pharmaceutical Sciences Branch, Islamic Azad University (IAUPS), Iran. (ethical approval number: IR.IAU.PS.REC.1397.137).

Chemicals

Formalin and ethanol (Merck, Germany) were used in this study.

Plant material

Cymbopogon schoenanthus was obtained from a local market in Kerman, Iran (2019). The plant was identified by our academic staff of Pharmacognosy Department, Dr. Kazemivash and the voucher specimens were kept under No. AUPF-1626 at the herbarium of Faculty of Pharmacy, Islamic Azad University of Medical Sciences, Tehran, Iran (Figure 1).

Figure 1. Image for herbarium picture of *Cymbopogon schoenanthus*

Essential oil preparation

The aerial parts of the plant were dried and then subjected to hydrodistillation in a Clevenger-type apparatus for 3 h. The oil was collected, dried with anhydrous Na_2SO_4, and transferred to a clean glass vial and finally kept at -18℃ until biological and analytical tests.

Essential oil analysis

Cymbopogon schoenanthus (aerial parts) essential oil (CSEO) analysis was performed on an HP-6890 gas chromatograph (GC) equipped with an FID and a DB-5 capillary column of 30 m × 0.25 mm with 0.25 µm film thicknesses. The temperature program was between 60° and 240°C at 4°C/min. The carrier gas N_2 had at a flow of 2.0 mL/min and the temperatures of the injector port and detector were set at 250°C and 300°C, respectively. The obtained samples were injected by splitting with a ratio of 1:10. Analysis of GC/MS was performed on a Hewlett-Packard 6890/5972 system with a DB-5 capillary column (30 m × 0.25 mm; 0.25 µm film thickness). The operating conditions were the same conditions as described earlier, except for the carrier gas, which changed to He. The mass spectra were taken at 70 eV. The range of scan mass was from 40 to 400 m/z at a sampling rate of 1.0 scan(s). Quantitative data were obtained from electronic integration of FID peak areas. The oil components were identified by their retention time and indices, relativity to C_9-C_{28} n-alkanes, computer matching with WILEY275.L library, and also by comparing their mass spectra with the data mentioned in the literature [13,14].

Animals

Female Mice (25-35 g) were bought from Tehran University of Medical Sciences, Tehran, Iran. The experiments were conducted between 9:00 a.m. and 15:00 p.m. with normal room light (12 h light/dark cycles) and at room temperature (22 ± 1°C).

Acute toxicity study

Acute toxicity was evaluated in terms of the guideline No. 423 of OECD [15]. Six female mice (3control and 3 tests) were used and the essential oil dose was determined as 2000 mg/kg body weight. The control group was given sweet almond oil (2000 mg/kg) . The animals in both groups were followed up for general behavior changes (i.e., appearance of feces, urine color, sensitivity to sound and touch, mobility, aggression, convulsions, ataxia, hypo activity, and ventilation disorders) during the first 4 hours, and daily thereafter, for a total of 14 days. Physical examinations including hair coat, mucus membrane/eye/skin color, body temperature, respiratory rate, lacrimation, salivation amount, eye prominence, food consumption, water intake and body weight were checked up to 14 days.

Sub-chronic toxicity study

Sub-chronic oral toxicity test was performed in terms of the OECD guideline No. 407 [16,17] with a little modification. The female mice were divided into two groups as control (sweet almond oil, 200 mg/kg) and test (*C.schoenanthus* essential oil), each one consisting of three animals. The test group was daily treated with oral administration of the essential oil at doses of 10, 100, and 200 mg/kg for a 28-day period. In addition, the control group was treated with sweet almond oil for 28 days. Behavioral parameters, body weight, food consumption, and water intake were recorded during the experimental period. Blood samples and main organs were collected on the 28th day of the experiment to perform biochemical assays and pathological studies [17].

Biochemical assays

At the end of the sub-chronic toxicity experiments, the animals were deprived of food for 12 h and then sacrificed. Afterward, their heart blood was collected into dry tubes and centrifuged at 3000g for 15 min at 4 °C. Subsequently, the serum was sent to the lab for biochemical analyses of glucose, SGOT (AST), SGPT (ALT), urea, creatinine, and electrolytes.

Histopathology study

The animals were euthanized 28 days post-treatment, the harvested tissues (liver, heart, kidney, pancreas, intestine, ovary, and stomach) were fixed in 10% neutral buffered formalin (NBF, PH. 7.26) for 48 h, then processed, and finally embedded in paraffin. Thereafter, the 5 µm thick sections were prepared and stained with heamtoxylin and eosin (H&E). The histological slides were evaluated by an independent reviewer using light microscopy (Olympus BX51; Olympus, Tokyo, Japan). Any changes such as acute and chronic inflammatory responses, fatty change, coagulative necrosis, and hemorrhage were assessed in different samples.

Statistical analysis

The data were expressed as mean ± SEM. The statistical significance was determined using one- and two-way analysis of variance followed by the Tukey as the post-test, using Graphpad Prism 8 software. The differences were considered as statistically significant when $p<0.05$.

Results and Discussion

The composition percentage of the identified compounds was calculated relatively and from the GC peaks areas with no correction factors (Table 1). The main components of *C. schoenanthus* essential oil collected from different regions worldwide, were compared with the studied *C. schoenanthus* essential oil composition (Table 2).

At the dose of 2000 mg/kg, *C.schoenanthus* essential oil showed no adverse effect on the behavioral responses of the experimental animals during 14 days of observation. Physical observations also indicated no signs of change in the skin, fur, eyes mucous membrane, behavioral patterns, tremors, salivation, and diarrhea of the animals. In addition, no mortality was reported at the tested dose (2000 mg/kg) in the acute test, and the body weight did not change ($p>0.05$) (Figure 2A).

Daily oral administration of *C.schoenanthus* essential oil at the doses of 10, 100, and 200 mg/kg for 28 days induced no obvious symptom of toxicity in mice. Moreover, no deaths or obvious clinical signs were found in the test group throughout the experimental period. Physical observations of the treated animals throughout the study revealed no signs of toxicity in their skin, fur, eyes, and mucus membrane or in their behavioral patterns, including diarrhea, tremors, salivation, sleep, and coma. Notably, similar to the acute test, no changes were noticed in the body weight of the mice after the oral administration of the essential oil (10, 100, and 200 mg/kg) in sub-chronic test ($p>0.05$) (Figure 2B). In acute toxicity test, the animals' food consumption was significantly different ($p<0.0001$) between the control and the test group on the 2nd, 7th, and 14th days of the experiment (Figure 3A). Similarly, in the sub-chronic toxicity test, the food consumption was significantly different between the control and the test group at doses of 10 mg/kg (days 2, 7, 14, and 21: $p<0.0001$; and day 28: $p=0.0034$), 100 mg/kg (days 14, 21, and 28: $p<0.0001$), and 200 mg/kg (days 7, 14, 21, and 28: $p<0.0001$) (Figure 3B).

Water intake level significantly varied in both control and test groups (2000 mg/kg) on the 2nd ($p=0.0015$), 7th ($p<0.0001$), and 14th ($p<0.0001$) days of the experiment in acute test (Figure 4A).

In sub-chronic test, water intake level was significantly greater (10, 100, and 200 mg/kg) in the test group compared to the control group on all days of the experiment ($p<0.0001$) (Figure 4B).

Table 1. GC-MS analysis of the essential oil of *Cymbopogon schoenanthus* in the aerial parts

Compound[a]	KI[b]	KI[c]	Percentage
1. Tricyclene	919	921	0.2
2. α-Pinene	939	937	0.3
3. Camphene	953	949	0.7
4. 1,3,5-Cycloheptatriene, 3,7,7-trimethyl	-	973	1.1
5. 4-Carene	1001	998	2.4
6. α-Phellandrene	1005	1004	1.0
7. α-Terpinene	1018	1021	0.5
8. ρ-Cymene	1026	1024	0.9
9. β-Phellandrene	1031	1033	2.8
10. Linalool	1098	1095	0.2
11. **ρ-Mentha-2-ene-1-ol**	1140	1143	14.3
10. **β-Terpineol**	1159	1152	10.1
11. Borneol	1165	1167	0.3
12. ρ-Mentha-1,5-diene-8-ol	1170	1172	0.6
13. ρ-Cymenol	1183	1180	0.1
14. α-Terpineol	1189	1191	0.2
15. Piperitone	1282	1278	2.5
16. β-Elemene	1375	1374	0.3
17. β-Selinene	1485	1482	0.2
18. β-Agarofuran	1504	1510	0.2
19. δ-Cadinene	1524	1522	0.5
20. **Elemol**	1547	1550	24.1
21. Caryophyllene oxide	1581	1578	0.2
22. γ-Eudesmol	1630	1628	3.0
23. Dihydro-*cis*-α-copaene	-	1637	7.8
24. Torreyol	1645	1641	0.5
25. **β-Eudesmol**	1649	1651	12.0
Total			87.0

[a]Compounds listed in order of elution; [b]KI (Kovats index) measured relative to *n*-alkanes (C_9-C_{28}) on the non-polar DB-5 column under condition listed in the Materials and Methods section; [c]KI, (Kovats index) from literature.

Table 2. The main components of *Cymbopogon schoenanthus* essential oil collected from different regions in the world comparing with those of the studied CSEO (>10%)

Compounds	A (%)	B (%)	C (%)	D (%)	E (%)	F (%)
Elemol	24.1	-	-	-	-	10.8
ρ-Mentha-2-ene-1-ol	14.3	-	-	-	-	-
E-Eudesmol	12.0	-	-	-	-	11.5
β-Terpineol	10.1	-	16.2	-	-	-
Piperitone	-	42.0	-	71.5	-	14.6
cis-Sabinene hydrate	-	-	10.0	-	-	-
Guaiol	-	-	20.4	-	-	-
Hinesol	-		10.6	-	-	-
α-Terpineol	-	-	-	-	11.0	-
Limonene	-	-	-		27.3	-
β-Phellandrene	-	-	-	-	16.3	-
δ-Terpinene	-	-	-	-	21.2	-
Cyclohexan methanol	-	-	-	-	-	11.6
β-Elemene	-	-	-	-	-	11.6

A: *Cymbopogon schoenanthus*; B: *Cymbopogon schoenanthus* collected from Burkina Faso [18]; C: *Cymbopogon schoenanthus* collected from Algeria [19]; D: *Cymbopogon schoenanthus* collected from Sudan [20]; E: *Cymbopogon schoenanthus* collected from Tunisia [21]; F: *Cymbopogon schoenanthus* collected from Saudi Arabia [3]

In terms of the animal organs weight, significant differences were observed in the control and test groups, but only in terms of the liver weight/body weight index. At the dose of 10 mg/kg, this index was significantly lower ($p=0.0453$) and at the doses of 100 mg/kg ($p=0.0057$) and 200 mg/kg ($p=0.0326$), it was significantly more than the control group. Other organs showed no significant fluctuation in this parameter (Figure 5). The effects of sub-chronic administration of *Cymbopogon schoenanthus* essential oil on some biochemical parameters are presented in Table 3.There were some significant differences in terms of glucose level at doses of 100 and 200 mg/kg ($p<0.05$) in the test group compared with the control group. There were also significant differences in urea level at doses of 10 ($p<0.05$), 100 ($p<0.01$), and 200 mg/kg ($p<0.01$) in the test group compared with the control group.

Plasma electrolyte level showed some variations and sodium ion was significantly more at doses of 100 and 200 mg/kg ($p<0.05$) in the test group compared to the control group. In addition, potassium ions were significantly less at dose of 200 mg/kg ($p<0.05$) in the test group. No changes were noticed in other biochemical parameters of the mice, including calcium ion, creatinine, SGOT, and SGPT after oral administration of the essential oil at all doses in sub-chronic test and control groups.

The images of hematoxylin and eosin-stained organs of the mice with a special diet (different doses of the essential oil) are shown in Figure 6. Histopathological evaluation of the animals' heart, pancreas, intestine, stomach, and kidney showed normal organs' structures at all treatment doses 28 days post-treatment (Figure 6). Histopathological evaluation of the liver treated with doses of 10 and 100 mg/kg revealed a normal structure, as well; however, at the dose of 200 mg/kg, some changes such as moderate fatty changes, vacuolization, ballooning degeneration and infiltration of kidney inflammatory cells, and the disruption of portal triad structures were noticed (Figure 6).

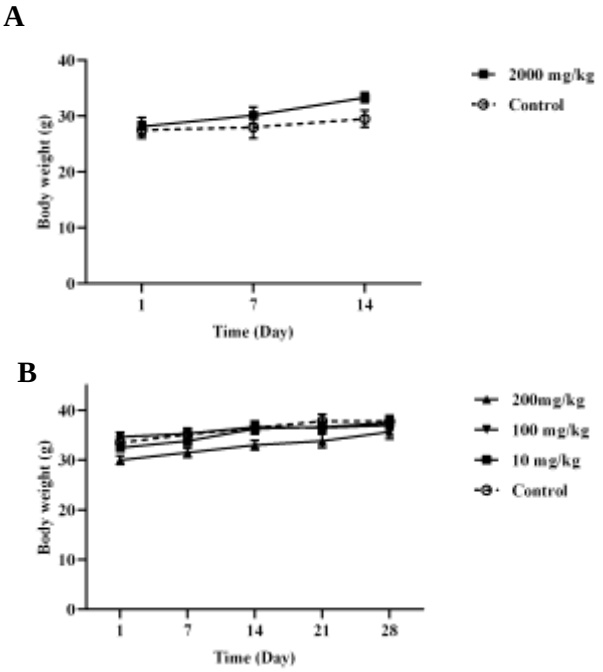

Figure 2. Effects of the acute oral toxicity (A) and sub-chronic oral toxicity (B) of *Cymbopogon schoenanthus* essential oil on the change of body weight in female mice

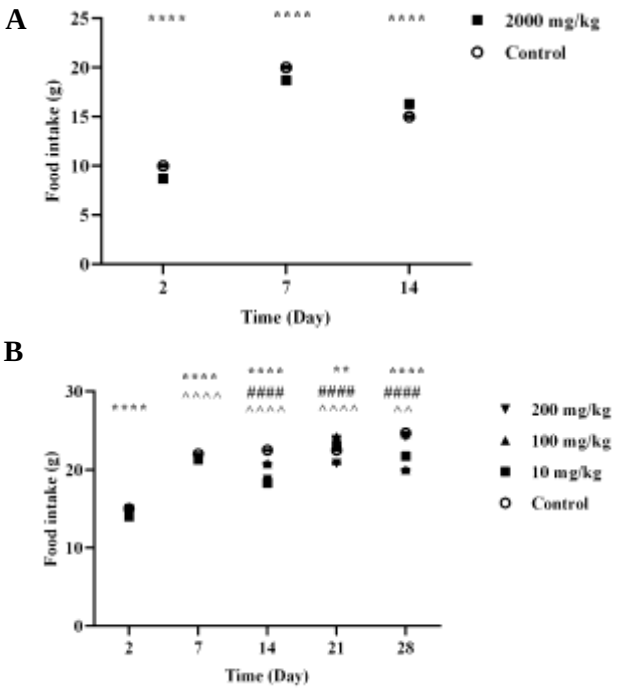

Figure 3. Effects of the acute oral toxicity (A) and sub-chronic oral toxicity (B) of *Cymbopogon schoenanthus* essential oil on the food intake; **p<0.01, ****p<0.0001 compared 10 mg/kg to the control; ##p<0.01, ####p<0.0001 compared 20 mg/kg to the control; and ^^p<0.01, ^^^^p<0.0001 compared 200 mg/kg to the control

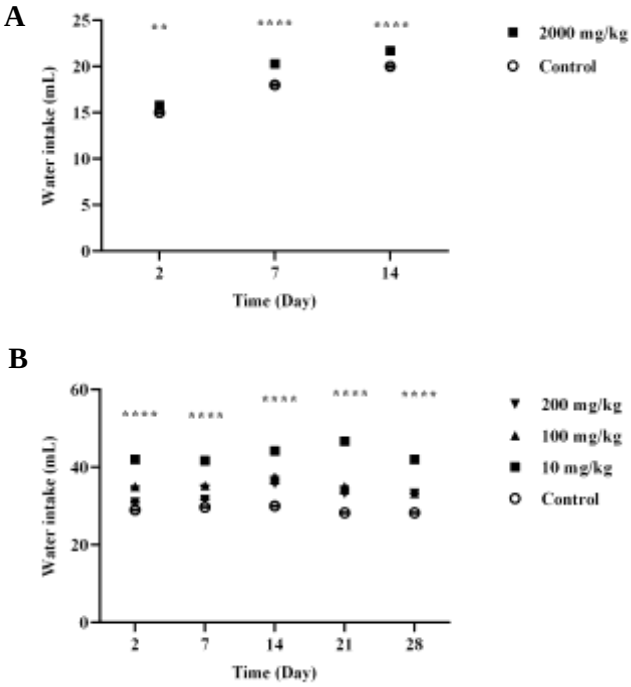

Figure 4. Effects of the acute oral toxicity (A) and sub-chronic oral toxicity of *Cymbopogon schoenanthus* essential oil on the water intake; **p<0.01, ****p<0.0001 compared to the control group; (B) **** p<0.0001 compared to the control group

Table 3. Effects of *Cymbopogon schoenanthus* essential oil on biochemical parameters in the sub-chronic toxicity in female mice

Serum biochemical parameters /Groups	Control	10 mg/kg	100 mg/kg	200 mg/kg
Blood sugar	245.0± 13.6	220.0 ± 13.2	175.7 ± 22.5 *	170.7 ± 2.9 *
SGOT (AST)	199.3 ± 49.5	199.7 ± 17.2	211.0 ± 10.4	295.7 ± 15.3
SGPT (ALT)	90.0 ± 30.5	61.3 ± 9.1#	59.0 ± 0.6#	59.7 ± 12.4
Urea	64.3 ± 5.8	47.7 ± 1.8 *	48.7 ± 0.9 *	42.3 ± 0.3 **
Creatinine	0.52 ± 0.00	0.50 ± 0.01	0.52 ± 0.00	0.52 ± 0.00
Ca^{2+}	11.03 ± 0.3	11.07 ± 0.2	10.83± 0.2	10.50 ± 0.2
Na^{+}	145.3 ± 0.3	147.7 ± 1.3	150.3 ± 0.3 **	151.0 ± 0.5 **
K^{+}	11.80± 1.3	10.20 ± 0.6	11.3 ± 0.1	8.5 ± 0.3 *

Cymbopogon schoenanthus essential oil was administrated at sub-chronic oral doses (10, 100, and 200 mg/kg/day over28 days). The serum biochemical parameters were measured at the end of the experimental period. Data are expressed as mean ± SEM; n=3; *p<0.05, **p<0.01 compared to the control group and # p<0.05 compared to the test group 200 mg/kg

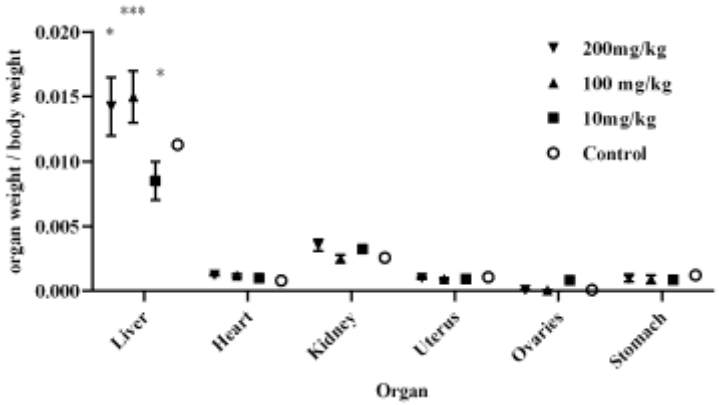

Figure 5. Effects of sub-chronic oral toxicity of *Cymbopogon.schoenanthus* essential oil on the organ weight to body weight index; *P<0.05, ***P<0.001 compared to the control group

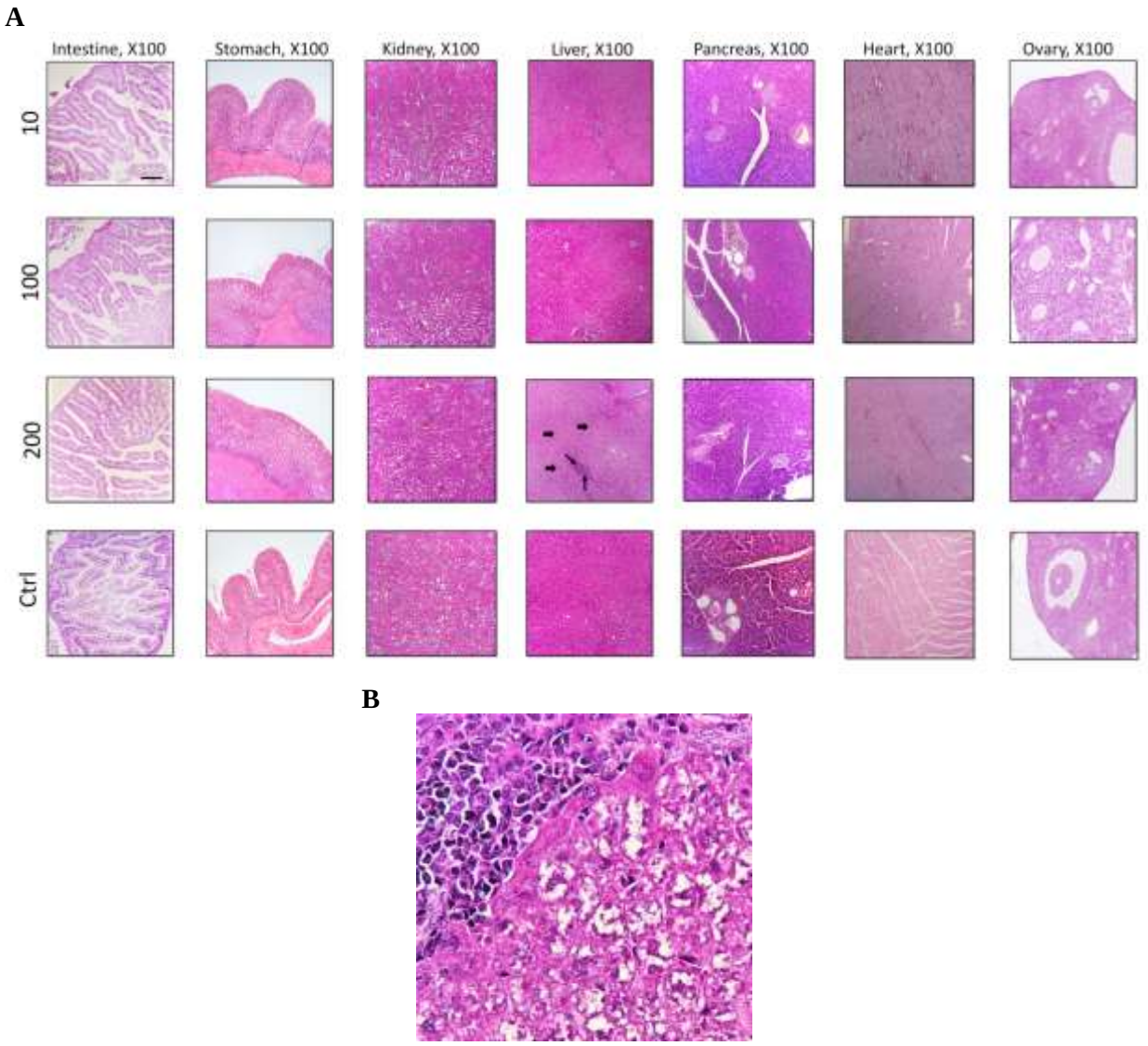

Figure 6. (A) Histopathologic sections of the intestine, stomach, kidney, liver, pancreas, and heart of the experimental groups; H&E stain (×100); thin arrows: mononuclear inflammatory cells; thick arrows: degeneration of hepatocytes (fatty change); (B) histopathologic sections of the liver (×400)

The main objective of the present study was to examine the acute and repeated oral toxicity of the *C. schoenanthus* essential oil, which is a complex mixture of terpenes, in female mice. The essential oil used in the current study contained 25 identified components, of which elemol (24.1%), para-mentha-2-ene-1-ol (14.3%), beta-eudesmol (12%), and beta-terpineol (10%) are known as the main ones.

The results showed that the administrated acute and sub-chronic doses of *C. schoenanthus* essential oil caused no mortality; however, the repeated administration of the essential oil changed glucose, urea, Na^+, and K^+ levels and also demonstrated few toxic effects on liver, as the main organ.

Cymbopogon schoenanthus is commonly used for its potent therapeutic effects in Iranian traditional medicine. The present study undertook and succeeded to demonstrate the plant's safety profile in both models of toxicity assessment. Given that no death and signs of toxicity were observed in the first 24 h following the administration of *C. schoenanthus* essential oil at the dose of 2000 mg/kg, the essence can be classified as the Category 4 material in terms of Globally Harmonized System of Classification and Labeling of Chemicals [22]. The criteria for Category 4 were intended to enable the identification of substances with slightly toxic hazard. The *C. schoenanthus* essential oil was anticipated to have an LD_{50} higher than 2000

mg/kg, which is not hazardous in acute doses in mice. In acute toxicity study, although no changes were observed in the body weight, physic, and behavioral patterns of the animals, there were some changes in the food and water intakes.

The results of the present study are consistent with previous findings confirming the absence of abnormal signs and symptoms in experimental animals treated with the essential oil of *C. schoenanthus* as well as the other *Cymbopogon* species like *C. citrates* [9,23]. Ilboudo et al. in their study showed that the essential oils of C. *schoenanthus* presented no extensive toxic effect in mice; since its oral LD_{50} was at 5000 mg/kg [9]. Costa et al. have also reported that the essential oils of C. *citrates* had no severe toxic effect in mice, because its oral LD_{50} was around 3500 mg/kg [23].

No changes were found in the body weight, physical conditions, and behavioral patterns of the animals in the repeated toxicity experiment; however, some changes were noticed in food and water intakes of the test and control groups. The blood glucose level was significantly less in the treated female mice (100 and 200 mg/kg) compared to the control group. Although the mechanism(s) by which the essential oil induced hypoglycemic effects was not the focus of the present study, they may be occurred due to the increased insulin synthesis and secretion and/or the increased peripheral glucose utilization; however, further studies are required to validate this assumption. Regarding the hypoglycemic activity of *C. schoenanthus* essential oil in normal mice, studying its anti-diabetic effects and mechanisms in animals is recommended. Correspondingly, in line with that, Adeneye and Ajagbonna reported the hypoglycemic and hypolipidemic effects of the single daily oral dose (500 mg/kg) of *C. citrates* Stapf. aqueous extract on normal male rats during 42 days of treatment [10].

The blood urea nitrogen level was significantly less in the test groups (treated with all doses) compared to the control group. It is worth mentioning that the low BUN levels could be due to liver damage; however, further studies are needed to clarify the causes.

The repeated administration of the essential oil caused some changes in Na^+ and K^+ levels as hypernatremia and hypokalemia. The former one is always resulted from a negative water balance when the water intake is lower than its urinary excretion. Regarding that in current study, the test groups of animals ingested enough free water, and according to the pathological findings and the kidney damage, electrolyte disturbances can be probably due to kidney tissue damage. However, the *C. schoenanthus* essential oil showed no effect on other biochemical parameters.

Observations during the experiment revealed some clinical signs of toxicity such as food consumption and water intake. Also, a steady increase in the body weight was observed in both groups of the treated and control animals. In female mice treated with the dose of 200 mg/kg, the decrease in the body weight was slight during the first 28 days. Costa et al. in their study reported a significant decrease at the dose of 500 mg/kg during the first, third, and fourth weeks of the experiment [23]. Body weight loss is an important marker of gross toxicity or interference with absorption of nutrients [15]. In this regard, the consumptions of plant extracts [24] and essential oils in experimental animals [9] showed inducing body weight loss.

Microscopic examination of vital organs such as heart, liver, kidney, stomach, intestine, and spleen of the treated animals showed that *C. schoenanthus* essential oil induced pathological changes in liver. In contrast, Ilboudo et al. reported no changes in macroscopic appearance of vital organs such as heart, lung, liver, kidney, and spleen of the treated animals [9].

Consistent with the current study, the *C. citrus* essential oil induced no abnormalities in serum levels of aspartate aminotransferase, alkaline phosphatase, gamma-glutamyl transferase (GGT), albumin, creatinine, and total protein or triglycerides of mice. However, a significant reduction was reported in terms of total serum cholesterol level at the dose of 100 mg/kg for 21 days [23]. Other toxicity tests of *C. schoenanthus* essential oil revealed that the essential oil had no irritating effects on the eyes and skin in animal models [9].

Conclusion

The findings of the present study demonstrated that the essential oil of *C. schoenanthus* was practically nontoxic with an LD_{50} greater than 2000 mg/kg. However, the repeated administration of *C. schoenanthus* at a relatively lower dose over a 28-day period induced hypoglycemia, hyper uremia, hypernatremia, and liver organ damages in mice. At the dose of 10

mg/kg, there were no significant changes in biochemical parameters and histological analyses. Thus, it would be prudent to use *C. schoenanthus*at at lower doses to limit its adverse effects.

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Author contributions

Zahra Mousavi designed the experiments and prepared and edited the manuscript; Jinous Asgarpanah contributed to perform the essential oil analysis; Tayebeh Rastegar contributed in histopathological study and analysis; Elahe Fathifar prepared the plant essential oil and performed the animal handling and experimentation

Declaration of interest

The authors declare that there is no conflict of interest. The authors alone are responsible for the accuracy and integrity of the paper content.

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Abbreviations

CSEO: *Cymbopogon schoenanthus* essential oil; LD_{50}: lethal dose, 50%; SGOT: serum glutamic-oxaloacetic transaminase; AST: aspartate amino transferase; ALT: alanine amino transferase; SGPT: serum glutamic-pyruvic transaminase; GGT: gamma-glutamyl transferase; GC: gas chromatograph; GC-MS: gas chromatograph-mass spectrometry