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ORIGINAL ARTICLE

Evaluation of the immunomodulatory, antioxidant, and histopathological effects of *Cymbopogon schoenanthus* essential oil extract on kidney and spleen in BALB/C Mice

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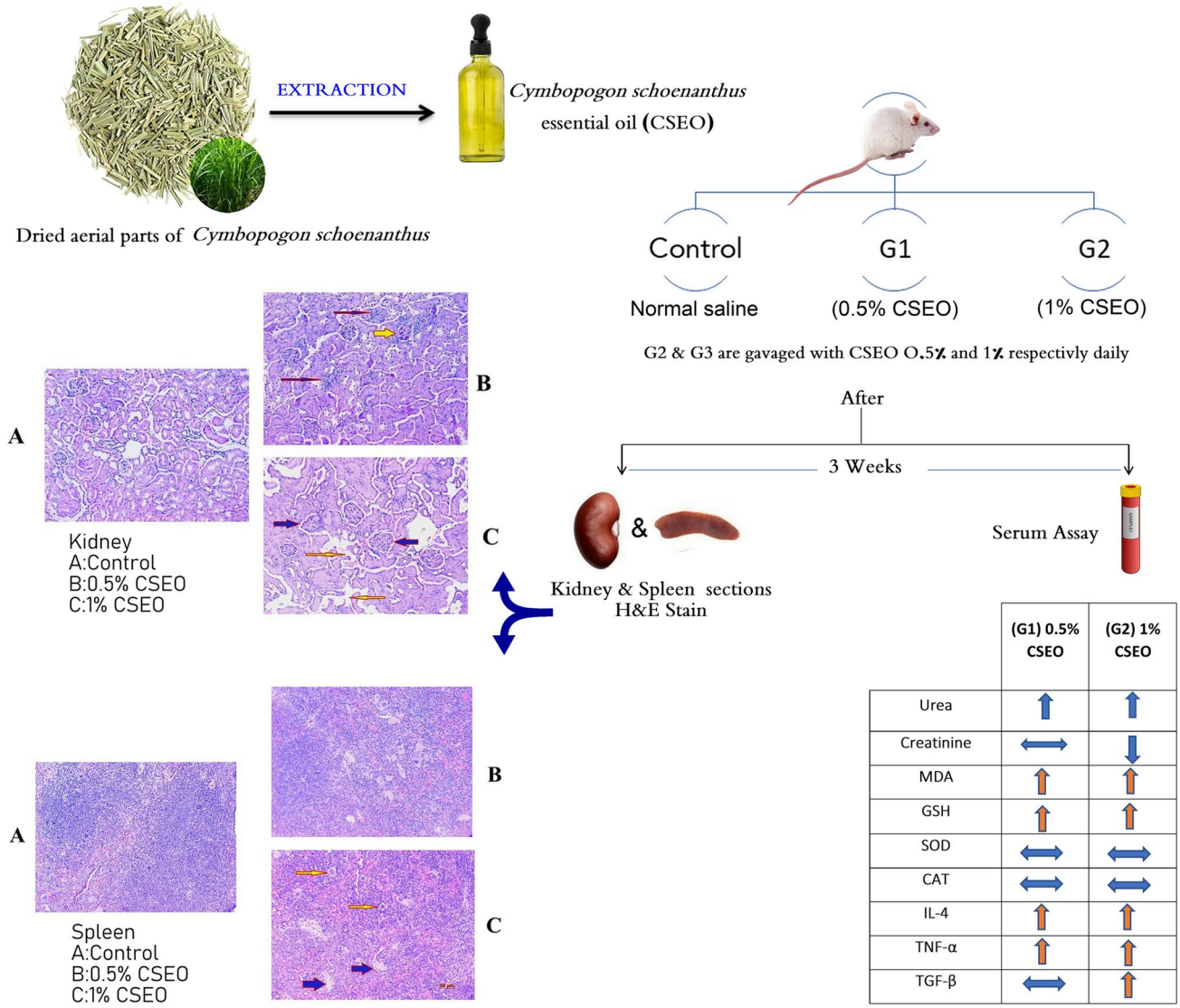
Abstract

This study aimed to evaluate the impact of *C. schoenanthus* essential oil (CSEO) on the immune system, antioxidant balance, and histological changes in the kidney and spleen of female BALB/C mice. The chemical composition of CSEO was analyzed using GC-MS. Twenty-nine compounds were identified, representing 99.04% of the total detected. The main components were Piperitone (47.93%), Elemol (11.91%), 2-Carene (10.69%), β-eudesmol (7.67%), α-eudesmol (5.12%), and γ-eudesmol (4.24%). For bioassay, the mice were divided into three groups: control, 0.5% CSEO (G1), and 1% CSEO (G2). The effects of CSEO on various markers, including malondialdehyde (MDA), glutathione (GSH), superoxide dismutase (SOD), catalase (CAT), urea, creatinine, and cytokines (IL-4, TNF-α, and TGF-β1), were evaluated. Additionally, kidney and spleen histopathological examinations were conducted. The treatment groups showed a significant increase in IL-4, TNF-α, and TGF-β1 levels compared to the control group, except for G1, which showed a non-significant decrease in TGF-β1 levels. Group 2 exhibited a significant increase in MDA levels compared to the control group, while group 1 had a nonsignificant increase. Both treatments showed a significant increase in GSH levels, while SOD and CAT levels showed a non-significant increase in G2 and a non-significant decrease in G1. Urea levels showed a non-significant increase, while creatinine levels were significantly decreased in G2 and non-significantly decreased in G1 compared to the control group. The histopathological examinations revealed congested red pulp with activated hematopoiesis and focal fibrosis in spleen sections of both G1 and G2. The study suggests that medicinal herbs such as CSEO need to be used with caution, and their effects should be evaluated carefully, especially in terms of dose-dependent effects. The results indicate that high doses of CSEO may increase the levels of some cytokines and antioxidants and have harmful effects on kidney architecture, congested red pulp, and fibrosis with increased hematopoiesis. Therefore, the random use of medicinal herbs may have harmful effects and needs to be carefully controlled to ensure safe use.

Keywords *Cymbopogon schoenanthus* · Essential oil · Chemical composition · Cytokines · Dose dependent · Histopathology · Blood chemistry · Nephrotoxicity

Extended author information available on the last page of the article

Graphical abstract



Abbreviations

CAT	Catalase
CKD	Chronic kidney disease
CS	*Cymbopogon schoenanthus*
CSEO	*Cymbopogon schoenanthus* Essential oil
FSGS	Focal segmental glomerulosclerosis
GC–MS	Chemical analysis by gas chromatography–mass spectrometry
GSH	Glutathione
H&E	Haematoxylin and Eosin
IL-1	Interleukin1
IL-2	Interleukin 2
IL-4	Interleukin 4
IL-10	Interleukin 10
MDA	Malondialdehyde
SOD	Superoxide dismutase
SSH	Salt-sensitive hypertension
TGF-β1	Transforming growth factor- β1
TNFR1	Tumor necrosis factor receptor 1
TNFR2	Tumor necrosis factor receptor 2
TNF-α	Tumor necrosis

1 Introduction

The kidney is a vital organ that performs several functions in the body. Nephrotoxicity is one of the most common kidney complications that can occur due to exposure to an extrinsic

or intrinsic toxicant, necessitating the acquisition of appropriate treatments. Natural cures have recently gotten much attention because they have fewer negative effects than most conventional pharmaceuticals.

Cymbopogon schoenanthus (L.) Spreng is an odorous grass that grows in large colonies of independent tufts based on a rhizomatous stock. *C. schoenanthus* (L.) Spreng., common name lemon-grass or Camel-grass, is an aromatic herb known in Egypt as "Halfa Barr" or "Halfabr," in Saudi Arabia as "Izkhir or Athkhar" [1], in Algeria, as "Lemmad" [2], common in the North and West tropical Africa, and Arabian Peninsula [3]. According to Zahra et al. [4], it was shown that Cymbopogon sp. possesses properties that exhibit anti-inflammatory, antibacterial, antioxidant, and anticancer activity. Lemongrass, *Cymbopogon schoenanthus* (CS), has a long history of use in Egyptian folk medicine as a diuretic and antispasmodic for the kidneys [5]. *C. schoenanthus* has been conventionally utilized for multiple purposes, such as healing dromedary wounds, serving as an aphrodisiac, aiding in digestion, alleviating intestinal spasms, and treating anorexia, as reported by various studies conducted by Jayaprakasha et al. [6], Khadri et al. [3], and Wang et al. [7]. The grass is used for snake bites in North Ghana and Togo, and its leaves, crushed with a little water, are used as an embrocation in Ghana for body aches [3]. In addition, *C. schoenanthus* is used to cure ailments such as common colds, epilepsy, stomach cramps, and various types of pain, as well as in culinary and fragrance products, as noted by Takaisi-Kikuni et al. [8]. Pavlović et al. [9] found that these oils possess potent spasmolytic properties, while Wang et al. [7] discovered their antitrypanosomal effects. Additionally, Ketoh et al. [10] demonstrated their antimicrobial properties, Hellali et al. [11] identified their antioxidant and anticholinesterase activity, and Aous et al. [12] and Khadri et al. [13] reported their insecticidal effects. Furthermore, Gomes et al. [14] found evidence of their anti-inflammatory effects, and Katiki et al. [15] demonstrated their antihelmintic activity. *C. schoenanthus* extract doses were safe in rats' blood biochemical parameters, lipid profiles, and liver and kidney tissues. They might be utilized to reduce or eliminate formalin hazards [5]. Regarding cytotoxic effects, there is limited scientific evidence on the specific cytotoxic properties of *Cymbopogon schoenanthus*. However, cytotoxicity refers to the quality of being toxic to cells, which implies that a substance may be capable of killing or inhibiting the growth of cells. In the context of medicinal plants, this term is often associated with potential anticancer activity. A few studies have investigated the potential cytotoxic effects of Cymbopogon species, such as *Cymbopogon citratus* (lemongrass). Some of these studies indicate that certain compounds found in these plants may have cytotoxic effects on different cancer cell lines. However, it is important to note that these results are preliminary and should be interpreted with caution. To determine the cytotoxic effects of *Cymbopogon schoenanthus* specifically, more research is needed. *In vitro* and *in vivo* studies should be conducted to identify the active compounds responsible for cytotoxic activity and to evaluate their potential therapeutic applications in the treatment of cancer or other diseases characterized by uncontrolled cell growth.

In conclusion, while some Cymbopogon species have shown potential cytotoxic effects, the specific cytotoxic properties of *Cymbopogon schoenanthus* remain understudied. Further research is necessary to uncover the potential therapeutic applications of this plant in the context of cytotoxicity.

As the prediction of side effects is a regulatory necessity before the effective use of a new product as a medicine or pesticide constituent is allowed. As a result, we aimed to see how *C. schoenanthus* essential oil extract affected the immune system, antioxidant balance, and histological impacts, particularly on kidney and spleen structure. The chemical composition of the essential oil of *C. schoenanthus* was also investigated.

2 Materials and methods

2.1 Plant material and essential oil extraction

The aerial part of *C. schoenanthus* was collected from Wadi Allaqi in southern Egypt. The plant identification was determined by comparing it to a specimen with a known identification in Cairo's National Research Center's herbarium (Egypt). The shade-dried aerial parts (100 g) were cut into small pieces. The essential oil was obtained by hydrodistillation for 3 h using Clevenger-type equipment. The average of the three replicates was used to compute the essential oil yield. This oil was dried over anhydrous sodium sulfate and kept at 4 °C until analysis. Chemical analysis by gas chromatography–mass spectrometry (GC–MS) system (Agilent Technologies) was carried out with gas chromatograph (7890B) and mass spectrometer detector (5977A) at Central Laboratories Network, National Research Centre, Cairo, Egypt. The GC was equipped with an HP-5MS column (30 m × 0.25 mm internal diameter and 0.25 µm film thickness). Analyses were carried out using helium as the carrier gas at a flow rate of 1.0 ml/min at a split ratio of 10:1, injection volume of 1 µl and the following temperature program: 40 °C for 1 min, rising at 4 °C /min to 150 °C and held for 6 min; rising at 4 °C/min to 210 °C and held for 1 min. The injector and detector were held at 280 °C and 220 °C, respectively. Mass spectra were obtained by electron ionization (EI) at 70 eV; using a spectral range of m/z

40–550 and solvent delay of 3.7 min. Different constituents were identified by comparing the spectrum fragmentation pattern with those stored in Wiley and NIST Mass Spectral Library data.

2.2 Animals and experimental design

Thirty female BALB/C mice were used in the study. Mice were obtained from the Medical Research Centre at the Faculty of Medicine, Jazan, KSA. Mice were kept in cages under hygienic conditions with light/dark cycles of 12 h at 25 °C, fed on standard rodent chow and supplied with water. The animals were kept in a 12 h light/ 12 h dark cycle at a comfortable temperature (20 ± 4 °C) and relative humidity (65% ± 10%). The animals had ad libitum access to food and water. The mice were separated into three groups, each with ten mice. For three weeks, the control group was gavaged with 1 ml saline daily, while the second and third groups were administered orally daily with 0.5% and 1% of CSEO extract, respectively. All tests were carried out by the rules of Jazan University's institutional animal ethics committee in Jazan, Saudi Arabia.

2.3 Biochemical studies

Both antioxidants and cytokines were analyzed using ELISA technique according to Erel, [16] and each parameter was analyzed using specific ELISA Kit. While Serum creatinine and urea levels were measured colorimetrically using diagnostic kits (BioVision, USA). Urea was determined as carried out by Fawcett and Scott [17]. Serum creatinine was determined according to the method of Perrone [18].

2.3.1 Antioxidant parameters

2.3.1.1 MDA Using Abbexa Malondialdehyde (MDA) ELISA kit Cat. No. abx150359.

2.3.1.2 GSH Using MyBioSource Glutathione (GSH) ELISA Kit Cat. No. MBS261448.

2.3.1.3 SOD Using Abbexa Superoxide Dismutase (SOD) ELISA Kit Cat. No. abx258686.

2.3.1.4 CAT Using mybiosource Catalase (CAT) ELISA kit (Competitive ELISA) Cat. No.: MBS726781.

2.3.1.5 Urea Using BioVision colorimetric assay kit Cat. No. K375.

2.3.1.6 Creatinine Using BioVision colorimetric assay kit Cat. No. K625.

2.3.2 Immunoassay

2.3.2.1 IL-4 IL-4 ELISA Kit from Invitrogen (Cat. No. BMS628, USA).

2.3.2.2 TNF-α TNF-ELISA Kit, we used Invitrogen Kit Cat. No. KRC3011, USA.

2.3.2.3 TGF-β1 Using the CUSABIO CSB-E04727r Transforming Growth Factor **β1,** ELISA Kit.

2.4 Histological investigation

Different groups' kidney and spleen tissues were collected, fixed in 10% formalin, embedded in paraffin wax, and sectioned using a rotary microtome (HESTION, M3000) Then, using a light compound microscope (Nikon Eclipse E200 Trinocular Microscope with Nikon Microscope Camera {Nikon DS-Fi1 High-Definition Color Camera], the sections were stained with hematoxylin and eosin (H&E).

2.5 Statistical analysis

The data were analyzed by ANOVA using the SPSS 19 software package for Windows. The dissimilarities between the groups were evaluated. The data are expressed as the means ± SDs. The least significant (LSD) test was used to compare the groups. The statistical significance was set at $P < 0.05$.

3 Results

3.1 Identification of essential oil constituents

The essential oil of shade-dried aerial parts of *Cymbopogon schoenanthus* was obtained by hydrodistillation in 1.45% as pale yellow with a characteristic odor. Analysis of the essential oil by GC/MS resulted in 29 volatile components identified in the Table 1 and Figs. (1 and 2), accounting 99.04% of the total oil detected. Resulted data showed that the oil contains Piperitone (47.93%), Elemol (11.91%), (+)-2-Carene (10.69%), *β*-Eudesmol (7.67%), *α*-Eudesmol (5.12%), and *γ*-Eudesmol (4.24%) as main components. Oxygenated monoterpenoids (52.25%), Oxygenated sesquiterpenoids (30.95%), and monoterpene hydrocarbons (14.0%) were the prominent common classes.

3.2 Biochemical parameters

The treated group no. (2), administered with 1% *Cymbopogon schoenanthus* essential oil extract, showed a significant

Table 1 The chemical compounds identified from the essential oil of *C. schoenanthus*

	RT	Compound name	M.F	Area %
1	7.931	*α*-Pinene	$C_{10}H_{16}$	0.12
2	9.149	3,7,7-Trimethyl-1,3,5-cycloheptatriene	$C_{10}H_{14}$	0.29
3	9.86	2,3-Dehydro-1,8-cineole	$C_{10}H_{16}O$	0.15
4	10.21	2-Carene	$C_{10}H_{16}$	10.69
5	10.326	*γ*-Terpinene	$C_{10}H_{16}$	0.12
6	10.763	*α* -Terpinene	$C_{10}H_{16}$	0.1
7	11.043	*m*-Cymol	$C_{10}H_{14}$	0.26
8	11.183	D-Limonene	$C_{10}H_{16}$	2.42
9	14.523	*trans-p*-menth-2-en-1-ol	$C_{10}H_{18}O$	1.09
10	16.207	3-Acetoxy-4-(1-hydroxy-1-methylethyl)-1-methyl-cyclohexene	$C_{12}H_{20}O_3$	0.44
11	16.516	Terpinen-4-ol	$C_{10}H_{18}O$	0.19
12	16.936	*p*-Cymen-8-ol	$C_{10}H_{14}O$	0.38
13	17.034	*α*-Terpineol	$C_{10}H_{18}O$	1.77
14	17.169	*Cis*-(-)-p-Menth-1-en-3-ol	$C_{10}H_{18}O$	0.36
15	17.676	*trans*-(-)-p-Menth-1-en-3-ol	$C_{10}H_{18}O$	0.38
16	19.442	Piperitone	$C_{10}H_{16}O$	47.93
17	22.409	*α*-Terpinyl acetate	$C_{12}H_{20}O_2$	0.36
18	23.779	*β*-Elemene	$C_{15}H_{24}$	0.34
19	24.618	Caryophyllene	$C_{15}H_{24}$	0.23
20	26.693	*β*-Selinene	$C_{15}H_{24}$	0.1
21	27.544	*γ*-Cadinene	$C_{15}H_{24}$	0.16
22	27.824	*δ*-Cadinene	$C_{15}H_{24}$	0.41
23	28.658	Elemol	$C_{15}H_{26}O$	11.91
24	29.648	Caryophyllene oxide	$C_{15}H_{24}O$	0.3
25	31.426	*γ*-Eudesmol	$C_{15}H_{26}O$	4.24
26	31.817	*τ*-Cadinol	$C_{15}H_{26}O$	1.06
27	32.196	*β*-Eudesmol	$C_{15}H_{26}O$	7.67
28	32.324	*α*-Eudesmol	$C_{15}H_{26}O$	5.12
29	32.505	Selin-7(11)-en-4-ol	$C_{15}H_{26}O$	0.45
		Monoterpene hydrocarbons		14
		Oxygenated monoterpenoids		52.25
		Monoterpene ester		0.8
		Sesquiterpene hydrocarbons		1.24
		Oxygenated sesquiterpenoids		30.75
		Total identified		99.04

Rt Retention time in seconds, *M.F* Molecular formula of the identified compound

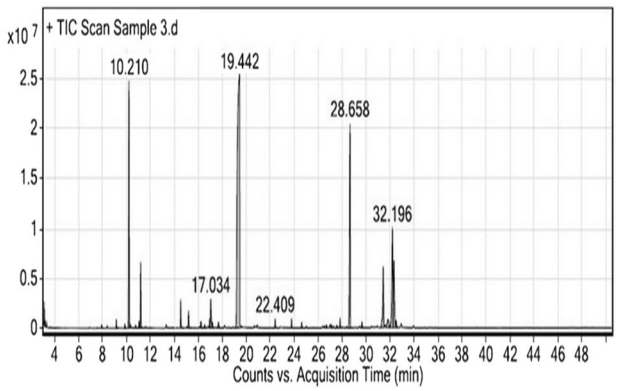


Fig. 1 GC–MS analysis of the essential oil extract from *C. schoenanthus*

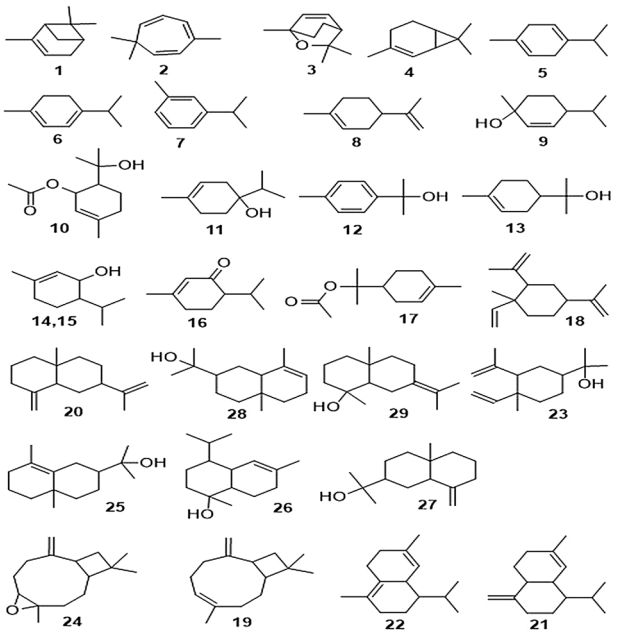


Fig. 2 The structure of the identified components from the essential oil of *C. schoenanthus*

increase in MDA levels compared to a control group with a 56.81% percent of change, while group no. (1), which was administered orally with 0.5% of *C. schoenanthus* extract, exhibited a non-significant increase with a 20.6% percentage of change. In contrast, the glutathione (GSH) levels significantly increased in both treated groups, with percentages of change of 28.75% and 37.83%, respectively. However, SOD and CAT levels showed a non-significant increase in the group no. (2), with a percentage of change of 7.54% and 6.9%, respectively, and a non-significant decrease in the group no. (1), with percentages of change − 10.11% and − 1.51%, respectively, Table 2 and Fig. 3.

3.3 Immunoassay

Both treatments with *C. schoenanthus* essential oil extract exhibited a significant elevation in IL-4, TNF-α, and TGF-β1 except the treatment with 0.5% of the extract showed a non-significant decrease in TGF-β1 levels comparing them with that of control: Table 3 and Fig. 4.

Table 2 Effect of *C. schoenanthus* essential oil extract on different antioxidant enzymes

	Control	G1	G2
MDA nm/mg	25.98 ± 1.3	31.33* ± 3.21	40.74* ± 1.47
% of change		20.6%	56.81%
GSH U/mg	12 ± 1.45	15.45* ± 1.08	16.54* ± 1.42
% of change		28.75%	37.83%
SOD U/ml	10.48 ± 1.09	9.42 ± 1.04	11.27 ± 0.96
% of change		− 10.11%	7.54%
CAT U/mg	103.64 ± 9.27	102.08 ± 3.41	110.76 ± 3.12
% of change		− 1.51%	6.9%

*Significant as compared to control group

3.4 Kidney functions

Treatment with both concentrations of *C. schoenanthus* essential oil extract revealed a non-significant increase in urea concentration in blood serum with percentages of change of 25.87% and 15.9%, respectively. While creatinine concentration was significantly decreased with 1% concentration and a non-significant decrease with the percentage of change of 10.45% in the first group (0.5%) compared with the control group. Table 4 and Fig. 5.

3.5 Histopathological features in kidneys and spleens

Table 5 and Figs. 6 and 7 represents a photomicrograph of kidneys and spleen of treated mice groups (G1& G2) with 0.5% and 1% of *C. schoenanthus* leaves extract, respectively, as compared to the control group. The kidney's histopathological architecture indicated differences between the treated groups and the control group. Specifically, in group 2, the glomeruli had focal sclerosis with an abnormal size, while in group 1, there was congested cellularity with an abnormal size. However, the number of glomeruli in both groups was normal when compared to the control group. Furthermore, cloudy swellings were observed in the kidney tubules of both groups (1 and 2), with group 2 showing focal inflammation in the interstitium and group 1 displaying edema.

Regarding the spleen structure, group 2 exhibited congested red pulp and fibrosis, while group 1 had congested

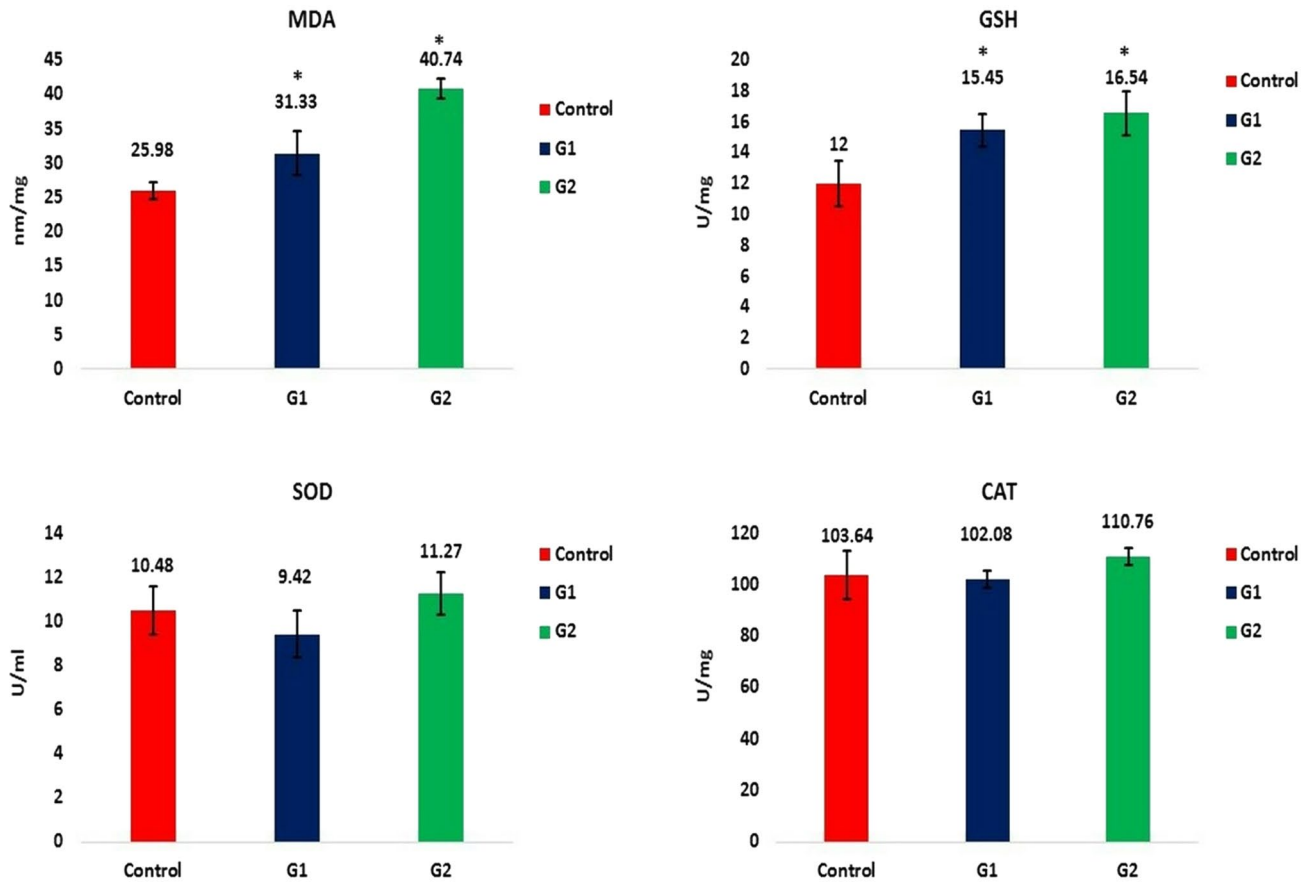


Fig. 3 Effect of *C. schoenanthus* essential oil extract on different antioxidant enzymes

Table 3 Effect of *C. schoenanthus* essential oil extract on some serum cytokines

	Control	G1	G2
IL-4 pg/ml	186.71 ± 6.16	314.43* ± 28.48	327.67* ± 27.68
% of change		68.41%	75.5%
TNF-α pg/ml	219.43 ± 5.77	369.71* ± 20.16	329.01* ± 35.78
% of change		68.5%	49.94%
TGF- β1 pg/ml	212.27 ± 11.1	204.05 ± 17.93	237.81* ± 19.65
% of change		− 3.87%	12.03%

*Significant as compared to control group

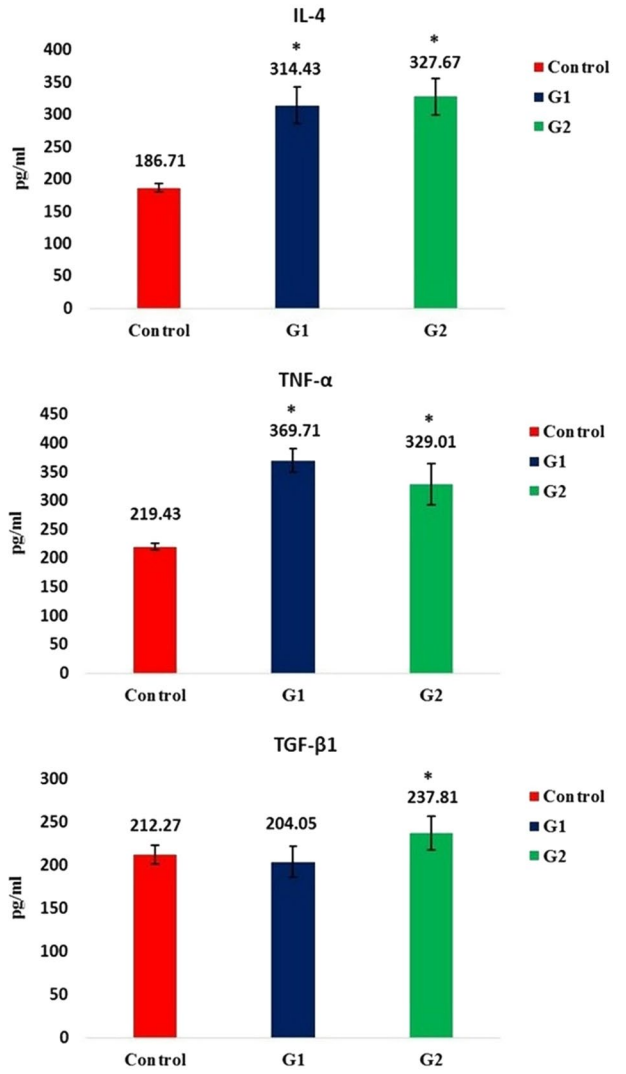


Fig. 4 Effect of *C. schoenanthus* essential oil extract on some serum cytokines

red pulp without fibrosis. Additionally, an investigation of the spleen revealed an activated hematopoietic condition in both treated groups compared to the control group.

Table 4 Effect of *C. schoenanthus* essential oil extract on kidney functions

	Control	G1	G2
Urea mg/dl	24.85 ± 4.25	31.28 ± 6.66	28.8 ± 5.92
% of change		25.87%	15.9%
Creatinine mg/dl	0.67 ± 0.1	0.6 ± 0.17	0.36* ± 0.1
% of change		− 10.45%	− 46.27%

*Significant as compared to control group

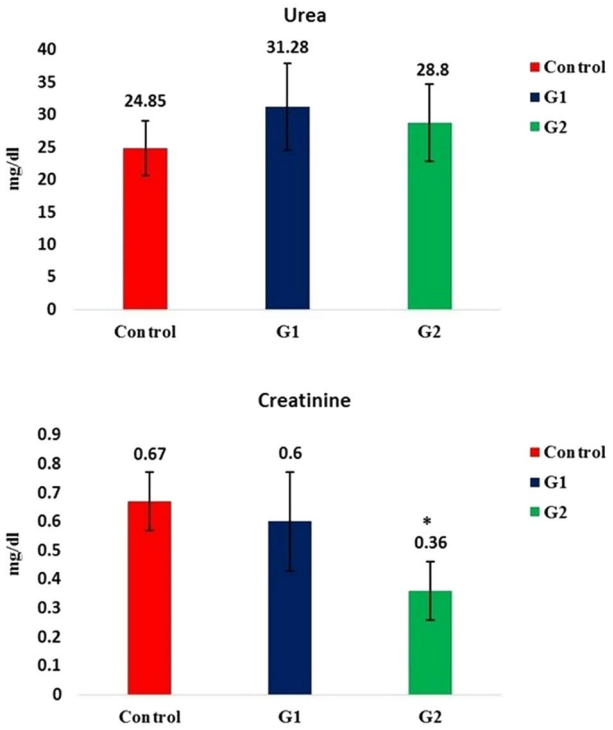


Fig. 5 Effect of *C. schoenanthus* essential oil extract on kidney functions

4 Discussion

This study aims to evaluate the toxicity and safe use of *Cymbopogon schoenanthus* essential oil (CSEO) while using it as a drug for renal spasms. The results presented in Table 4 showed renal function estimations in the different animal groups indicating a non-significant increase in blood urea in both treated groups G1&G2 compared to the control group with percentages of change (25.87% & 15.9%), respectively. These results are ineffective in inducing a toxic effect on the kidney. This result is consistent with Ahmed et al. [19], who clarified that the high blood urea nitrogen levels and serum creatinine concentrations indicate renal insult rather than liver damage. While the obtained results showed a significant decrease in serum creatinine in G2 received

Table 5 Histopathological features in kidneys and spleens of control and *C. schoenanthus* treated mice

Group	Kidney					Spleen	
	Glomeruli			Tubules	Interstitium	Architecture	Hematopoiesis
	Number	Size	Cellularity				
Control	N	N	N	N	N	N	N
1% *C. schoenanthus*	N	±N	Focal sclerosis	Cloudy swelling	Focal inflammation	Congested red pulp & Fibrosis	+
0.5% *C. schoenanthus*	N	I	congested	Cloudy swelling	Edema	Congested red pulp	+

I Increase, *N* Normal

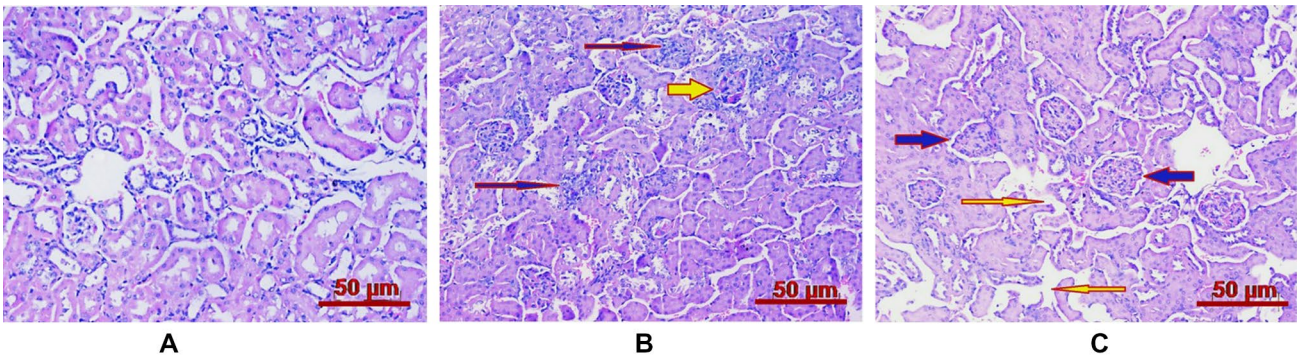


Fig. 6 **A** Section in kidney of control mice revealed normal histopathological structure of glomeruli, tubules and interstitium (H&E stain, X200). **B** Section in kidney of mice receiving 1% *C. schoenanthus* essential oil extract revealed focal infiltration of the interstitium by mononuclear inflammatory cells (thin blue arrows), cloudy swelling of the tubal epithelial cells and focal glomerular sclerosis (short yellow arrow) (H&E stain, X200). **C** Section in kidney of mice receiving 0.5% *C. schoenanthus* essential oil extract revealed focal interstitial edema (thin yellow arrows), cloudy swelling of the tubal epithelial cells and focal glomerular hypertrophy (thick blue arrows) (H&E stain, X200)

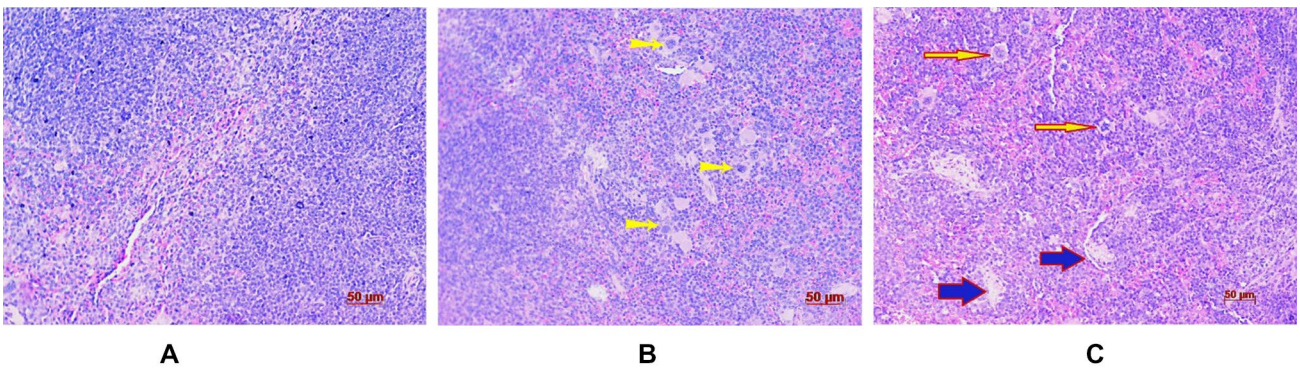


Fig. 7 **A** Section in a spleen of control mice, showing the normal histopathological structure (H&E stain, X200). **B** Section in a spleen of mice receiving 0.5% *C. schoenanthus* essential oil extract, showing the mildly congested red pulp with activated hematopoiesis (yellow arrow) (H&E stain, X200). **C** Section in a spleen of mice receiving 1% *C. schoenanthus* essential oil extract, showing the congested red pulp with activated hematopoeisis (thin yellow arrows) and focal fibrosis (thick blue arrows) (H&E stain, X200)

1% of (CSEO), and G1 received 0.5% CSEO, displayed a slight and non-significant reduction with percentages of change (− 46.27%; − 10.45%) respectively, as compared to the control group. But histopathological examinations of the kidney in different groups Fig. 6 showed focal interstitial edema, cloudy swelling of the tubal epithelial cells,

and focal glomerular hypertrophy in mice receiving 0.5% *C. schoenanthus* essential oil; also, mice group receiving 1% *C. schoenanthus* extract revealed focal infiltration of the interstitium by mononuclear inflammatory cells, cloudy swelling of the tubal epithelial cells and focal glomerular sclerosis, these changes may be caused due to the overdose of *Cymbopogon schoenanthus* essential oil.

GC–MS analysis of CSEO showed that it is composed of (29) volatile components listed in the Table 1 and Figs. 1 and 2. The oxygenated monoterpene hydrocarbon Piperitone, the major component, increases nitrofurantoin susceptibility in members of the family *Enterobacteriaceae* [20]. 2-Carene [12] and Elemol [1] are represented by very closely percent with previous literature [1, 12]. The percentage of each β-Eudesmol, and γ-Eudesmol (7.67, and 4.24%) agree with the data from Hashim et al., [1] (8.5 and 4.2%).

The current study's findings indicated in Table 3 and Fig. 4 revealed that the mice groups (G1&G2) given (CESO) had a highly significant increase in serum IL-4, with percentages of change reaching (68.41% and 75.5%, respectively) when compared to the control group. Also, compared to the control group, serum Tumor necrosis factor alpha (TNF- α) levels in mice treatment groups (G1&G2) revealed a considerable increase, with percentage changes of 68.5 percent and 49.94 percent, respectively. Furthermore, our findings show that serum Transforming Growth Factor- β1 (TGF- β1) levels in (G1) are non-significantly lower (-3.87%) than in the control group. In contrast, mice given 1% *Cymbopogon schoenanthus* essential oil in G2 had a considerable rise, with a percent change (12.03%) compared to the control group. According to the phytochemical studies, the anti-inflammatory benefits of *C. schoenanthus* essential oil may be related to its piperitone content. Several investigations have found that plants enriched with piperitone exhibit anti-inflammatory properties, suggesting they could be used as an anti-inflammatory medication candidate [21]. According to Golestaneh et al., [22], *C. schoenanthus* essential oil has physiologically active components with considerable anti-inflammatory potential. Several investigations, according to Silva et al., [23], have determined that existing components in *C. schoenanthus* essential oil, such as piperitone, p-cymene, and limonene, may have either direct or indirect anti-inflammatory effects. These findings are consistent with recent research that suggests *C. schoenanthus* essential oil has anti-inflammatory properties. A previous study by Leite et al., [21] revealed that *Cymbopogon winterianus* had an anti-inflammatory property. In regards to the current study's goal of determining the renal toxicity of a high dose of *C. schoenanthus* essential oil, increased inflammatory mediator levels, such as IL-1, in glomerular capillaries and proximal tubules, signal a complicated inflammatory infiltrate, according to Kotyzova et al., [24]. TNF-signaling also has two unique activities in the kidney, according to Mehaffey and Majid [25]. TNFR1 regulates blood pressure by decreasing hyperfiltration while increasing natriuresis. Through pro-inflammatory pathways, TNFR2 increases kidney tissue injury. TNF-α (tumor necrosis factor) is a protein that has a role in the development of tumors. TNF-α (tumor necrosis factor) is a pro-inflammatory cytokine that has been linked to salt-sensitive hypertension (SSH) and concomitant kidney damage.

The spleen, a major component of the reticuloendothelial system, appears to be a crucial actor in the 'cytokine storm' following infection and trauma, with the autonomic nervous system regulating the resulting systemic inflammation [26]. Inflammatory cytokine concentrations in the spleen are adversely linked with the spleen index [27]. Results listed in Table 5 and displayed in Fig. 7 identified congested red pulp with activated hematopoiesis and focal fibrosis in spleen sections regarded to mice with receiving 0.5 and 1% *C. schoenanthus* extract, the immunological involvement of the spleen and the cytotoxic action of *Cymbopogon shoenanthus* essential oil extract are examples of this. Al-Banna et al. [28] elevated pro-inflammatory cytokines TNF-α, IL-1, and IL-2 in the spleen and large intestine, followed by anti-inflammatory cytokines IL-4 and IL-10. According to Radwan et al., [29], splenomegaly caused by increased reticular fibers, red pulp area, and TNF-α contributed to the enlarged spleen volume. The marginal zone contains lymphocytes and macrophages that are functionally distinct from the red pulp's cord histiocytes. They appear vital in maintaining the anatomic structure of the marginal zone by attracting freshly differentiated B-lymphocytes, at least in animal models. Elmore [30] confirmed these findings, explaining that the splenic vein drains into the portal vein, portal hypertension can cause congestive splenomegaly, and the spleen's blood flow is highly specialized and corresponds to the spleen's various activities. The diameter of lymph nodules increased significantly in all spleen sections from the splenomegaly group, and this was linked to the immunological response that occurs in the spleen. According to Al-Malaak [31] and Luster et al., [32], the spleen is a relatively insensitive indication of immunotoxicity.

According to Das et al., [33], antioxidants are necessary for maintaining oxidation balance by successfully supporting the elimination of free radicals that are constantly created due to cellular oxidative stress. Free radicals inside cells are damaging to cellular and molecular functions, according to Sies et al., [34]. During regular metabolic activities in cells, reactive oxygen, and nitrogen species are created, causing inherent molecular damage to DNA, lipids, proteins, and other essential biomolecules. Furthermore, according to Lalthanpuii and Zarzokimi [35], the cumulative effect known

as oxidative stress is a crucial contributor to the development of numerous genetic and immunological issues. According to Pisoschi and Pop [36], antioxidants' protective activity extends beyond scavenging free radicals, including activation of antioxidation and detoxification enzymes, modulation of redox cell signaling, and gene expression. This approach maintains the body's oxidation and free radical elimination balance in a physiologically appropriate state.

The obtained results revealed that the MDA, GSH, SOD, and CAT activities of mice265 treated groups (0.5% and 1.0%) with CSEO as compared to control group manifested significant increase in serum MDA and GSH activity While, serum SOD and CAT level in mice treated group (received 0.5%) of CESO extract showed non-significant decrease. Otherwise, the mice remedied with 1.0% of CSEO extract showed non-significant improvement in SOD and CAT as compared with control group. The obtained results matched with previous studies which found that CS extract with high protective role as antioxidant agent.

From the histological observations, the overdoses from *Cymbopogon schoenanthus* essential oil adversely affected the examined organs. Nezhad et al. [37] indicated that the malondialdehyde (MDA) is a key indicator of oxidative stress-induced peroxidation. Patients with focal segmental glomerulosclerosis had significantly higher glomerular MDA immunostaining (FSGS). Glomerular MDA levels were highly correlated with the degree of glomerulosclerosis in patients with idiopathic FSGS. Vodošek Hojs et al. [38] revealed that in several studies, higher serum MDA levels were found in chronic kidney disease (CKD) patients compared to healthy control subjects. According to the findings, the negative effects on the kidney and spleen may be due to overdoses of *Cymbopogon schoenanthus* essential oil. But these negative effects may be temporary and disappear over time by stopping the bad use of the extract. In individuals with idiopathic FSGS, Nezhad et al. [37] found that glomerular MDA levels corresponded well with the degree of glomerulosclerosis.

5 Conclusion

Cymbopogon schoenanthus (*C. schoenanthus*) is a medicinal herb that has been traditionally used for the treatment of various ailments including kidney-related diseases. However, the use of *C. schoenanthus* as a medical herb for the kidney has been associated with some side effects. Studies have shown that high doses of *C. schoenanthus* can cause adverse effects such as gastrointestinal problems, liver and kidney toxicity, and cardiovascular problems. Additionally, the herb may interact with some medications and may not be safe for people with certain health conditions. While the use of *C. schoenanthus* as a medical herb for the kidney may offer some benefits, caution should be exercised in its use. It is important to consult a healthcare provider before using the herb, especially if you have underlying health conditions or are taking medications. So, the use of *C. schoenanthus* as a medical herb for the kidney should be approached with caution due to the potential side effects associated with its use.

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Declarations

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All of the tests were carried out in accordance with the rules of Jazan University's institutional animal ethics committee in Jazan, Saudi Arabia.

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