



Contents lists available at ScienceDirect

Asian Pacific Journal of Tropical Disease

journal homepage: www.elsevier.com/locate/apjtd



Original article doi: 10.1016/S2222-1808(15)60836-2

©2015 by the Asian Pacific Journal of Tropical Disease. All rights reserved.

Analgesic, antipyretic, nephritic and antioxidant effects of the aerial parts of *Bassia eriophora* (Family: Chenopodiaceae) plant on rats

Hasan Soliman Yusufoglu*

Department of Pharmacognosy, Faculty of Pharmacy, Prince Sattam Bin Abdulaziz University, Al-Kharj, Kingdom of Saudi Arabia

ARTICLE INFO

Article history:

Received 1 Aug 2014

Received in revised form 26 Aug 2014

Accepted 1 Sep 2014

Available online 26 May 2015

Keywords:

Bassia eriophora

Analgesic

Antipyretic

CCl₄ intoxication

Nephrotoxic

Antioxidant

ABSTRACT

Objective: To study analgesic, antipyretic, renal and antioxidant effects of the aerial parts of *Bassia eriophora* (Family: Chenopodiaceae) (*B. eriophora*), a wild plant in Saudi Arabia.

Methods: Alcoholic extract (90%) of the aerial parts of *B. eriophora* was tested for analgesic, antipyretic, nephritic and antioxidant activities, to show their therapeutic potential. For analgesic effect, hot plate and writhing methods were used while for antipyretic effect, rectal temperature method was used. The renal protective effects and antioxidant properties were determined through CCl₄-intoxicated animal method.

Results: Animals treated with dose of 250 and 500 mg/kg body weight, after 90 min showed significant analgesic effect (8.10 ± 0.18 and 8.10 ± 0.12) respectively, comparable to indomethacin (9.18 ± 0.22) in hot plate method, while in writhing method, the percentage reduction accounted for 55.14% and 68.38% at the dose of 250 and 500 mg/kg body weight respectively. The antipyretic effect using rectal temperature method after 90 min, at the dose of 500 mg/kg body weight was 35.66 ± 0.13 , comparatively more effective than indomethacin (35.10 ± 0.22). The significant reduction of CCl₄ on elevated creatinine, urea, uric acid, Ca, Na and K as well as increase on the depleted total protein after administration of the plant extract, indicated the safe use in kidney dysfunctions. The normalization of changed CCl₄ intoxication, malondialdehyde and nonprotein sulfhydryls levels designated antioxidant nature of this plant. The histopathological evaluation of the kidney also revealed that *B. eriophora* alcoholic extract may prevent the occurrence of kidney lesions.

Conclusions: *B. eriophora* may have analgesic, antipyretic and antioxidant activities, and may be safely used in renal toxicity conditions. Furthermore, pharmacological and clinical studies were required before therapeutic use.

1. Introduction

Some of analgesic and antipyretic drugs may cause renal failure due to decreased prostaglandin-mediated blood flow to the kidneys[1]. *Bassia eriophora* (Family: Chenopodiaceae) (*B. eriophora*) is a common sandy herbaceous plant known locally (in Saudi Arabia) as “ummulhas”, “gteena” and “alguteen”. Other related plants are commonly used in folk medicine to treat renal and rheumatic diseases[2]. The toxic effects on grazing animals revealed that few species of *Bassia* had toxic nature[3]. Current literature revealed that only a few species of *Bassia* had been investigated and were found to

contain basic acid glycosides, a type of triterpenoidal saponins[4]. Two acylated flavonoid glycosides as well as four known triterpenoidal saponins were isolated from the aerial parts of *Bassia muricata*[5]. Information on biological activity of *B. eriophora* is scarce. The extract of *B. eriophora* herb has not been characterized pharmacologically up to now. On the basis of available pharmacological active constituents and traditional therapeutics used, the present study is the first investigation of the alcoholic extract of *B. eriophora* on rats for analgesic and antipyretic properties. Furthermore, it presents the medicinal potentials of the kidney-protective activity of *B. eriophora* extract against CCl₄ induced kidney injury in rats.

2. Materials and methods

2.1. Preparation of extract

The aerial parts of *B. eriophora* plants were collected from a local

*Corresponding author: Hasan Soliman Yusufoglu, Department of Pharmacognosy, College of Pharmacy, Prince Sattam Bin Abdulaziz University, P.O. Box 173, Al-Kharj 11942, Kingdom of Saudi Arabia.
Tel: 00966-11-588-6012
Fax: 00966-11-588-6001
E-mail: hasanagazar@hotmail.com, h.yusufoglu@sau.edu.sa

place near Sattam Bin Abdulaziz University, Kingdom of Saudi Arabia in early March 2014. The collected plant was authenticated by taxonomist (Dr. M. Atiqur Rahman), of the College of Pharmacy, Medicinal, Aromatic and Poisonous Plants Research Center, King Saud University, Riyadh. A voucher specimen has been deposited in the herbarium of College of Pharmacy, Sattam Bin Abdulaziz University, Al-Kharj, Kingdom of Saudi Arabia. About 1 kg of the collected plant was percolated in 4 L alcohol (90%) at room temperature for 1 day. The extract was filtrated and evaporated using a rotary evaporator. The obtained extract was suspended in distilled water using tween 80 for various pharmacological studies.

2.2. Procurement and preparation of rats

Albino Wistar rats and albino Swiss mice of either sex were obtained from the Animal House, College of Pharmacy, Sattam Bin Abdulaziz University, Al-Kharj, Saudi Arabia. All animals were kept under standard laboratory conditions at room temperature of $(22 \pm 2) ^\circ\text{C}$, 55% humidity and were exposed to 12 h light/dark cycle fed on a standard chow diet and water. The protocol for the study was approved by the Ethical Committee of the College of Pharmacy, Sattam Bin Abdulaziz University, Al-Kharj, Kingdom of Saudi Arabia.

2.3. Analgesic activity (hot plate method)

The hot plate method described by Sani was adopted[6]. The four groups of animals ($n = 5$) were dropped gently on a hot plate maintained at $(55 \pm 0.5) ^\circ\text{C}$. The reaction time was taken as the interval extending from the instant the animal reached the hot plate until the moment the animal licked its forefeet or jumped off. The reaction time was measured 10 min before the oral administration of the drug (250 mg/kg and 500 mg/kg) and after 60, 90 and 120 min of treatments.

2.4. Analgesic activity (writhing test)

Writhing was induced in mice divided into four groups by intraperitoneal administration of 0.1 mL of 1% acetic acid. The number of writhing movements was counted for 20 min. The writhing test was performed after the administration of the vehicle or drugs.

2.5. Antipyretic study

Four groups of rats were injected subcutaneously with 15% yeast solution (10 mL/kg body weight) to induce hyperthermia[7]. The rectal temperature of each animal was recorded before 24 h after the yeast injection. Thereafter, the test groups were treated orally with 1 mL (250 and 500 mg/kg body weight) crude suspension of *B. eriophora*. The normal control group was given 1 mL (4 mg/kg body weight) normal saline while the positive control group was given 1 mL (4 mg/kg body weight) aqueous solution of indomethacin. The post treatment rectal temperature of each animal was recorded at 60, 90 and 120 min. Each result was calculated as the mean of three readings.

2.6. Nephrotoxicity study

After 7 days' acclimatization period[8], all selected animals ($n = 5$)

were arbitrarily divided into 5 groups, and tested as follows: Group I was received only normal saline control; Group II was received only CCl_4 ; Groups III and IV were received 250 and 500 mg/kg body weight crude suspension of *B. eriophora* orally for six weeks; Group V was received orally 10 mg/kg of silymarin for similar weeks. After 24 h, all animals received CCl_4 were anaesthetized, blood sample was collected by cardiac puncture and allowed to clot and the serum was separated. Using ether anesthesia, all the animals were sacrificed and kidneys were dissected out for various biochemical and histological studies. The kidneys of the animals, fixed in 10% formaldehyde, were processed, sectioned and stained with hematoxylin and eosin according to standard procedures.

2.7. Estimation of kidney function

The various serum samples collected after treatment of the animals were analyzed according to standard methods, for evaluating the effect of the *B. eriophora* extract on various biochemical parameters of rats such as creatinine, urea, uric acid as well as some chemical elements like Ca, Na and K. These analyses were done at Department of Pharmacy, King Saud University, Riyadh, Kingdom of Saudi Arabia using various diagnostic kits. Total protein (TP) level was estimated by using commercially available kits and it was calculated using the following equation:

$$\text{TP} = \frac{\text{ABS}_{\text{sample}}}{\text{ABS}_{\text{standard}}} \times \text{concentration of standard}$$

Where ABS = absorbance (660 nm).

2.8. Determination of malondialdehyde

The method reported by Utley *et al.* was followed[9]. In short, the removed kidney tissues were homogenized in 0.15 mol/L KCl to provide a 10% w/v homogenate. The absorbance was read at 532 nm and the content of malondialdehyde (nmol/g) was calculated.

2.9. Determination of nonprotein sulfhydryls (NP-SHs)

NP-SH was measured according to the previous method of Al-Harbi *et al.*[10]. The kidney tissues were homogenized in ice-cold ethylene diamine tetra acetic acid (0.02 mmol/L). 5,5'-dithio-bis(2-nitrobenzoic acid) was added and within 5 min absorbance was measured against a blank at 412 nm.

2.10. Statistical analysis

Values are given as arithmetic means \pm SE. Data was statistically analyzed by using One-way ANOVA followed by student's *t*-test.

3. Results

3.1. Analgesic activity

Analgesic activity of ethanolic extract of *B. eriophora* herbs was conducted by hot plate method (Table 1) and writhing method (Table 2). In the hot plate method, at 90 min, the mean reaction time for indomethacin of analgesia effect showed 9.18 ± 0.22 , while 250 and 500 mg/kg *B. eriophora* showed significant analgesic effect (8.10 ± 0.18 and 8.10 ± 0.12) respectively. The difference was statistically significant compared with normal saline control group. In the

writhing method, the indomethacin was showed 86.39% inhibitions of analgesia, while 250 and 500 mg/kg *B. eriophora* showed 55.14% and 68.38% inhibitions of analgesia respectively when compared with acetic acid control group.

Table 1

The analgesic effect of *B. eriophora* using hot plate method.

Treatment	Dose (mg/kg)	After treatment			
		Before treatment	0 min	60 min	90 min
Normal saline (control)	-	5.17 ± 0.14	5.36 ± 0.15	5.82 ± 0.13	5.59 ± 0.17
<i>B. eriophora</i>	250	5.61 ± 0.11	7.33 ± 0.16***	8.10 ± 0.18***	7.65 ± 0.17***
<i>B. eriophora</i>	500	5.76 ± 0.14	7.85 ± 0.12***	8.10 ± 0.12***	7.70 ± 0.14***
Indomethacin	4	5.31 ± 0.14	8.11 ± 0.17***	9.18 ± 0.22***	9.01 ± 0.23***

Values were expressed as mean ± SE; ***: $P < 0.001$. An analgesic effect of *Bassia* (250 and 500 mg/kg body weight) was evaluated using student's *t*-test.

Table 2

The analgesic effect of *B. eriophora* using writhing method.

Treatment	Dose	Number of writhing in 20 min	Inhibition (%)
Acetic acid (20%)	0.1 mL/kg	45.33 ± 3.25	-
<i>B. eriophora</i> + acetic acid	250 mg/kg	20.33 ± 1.62	55.14
<i>B. eriophora</i> + acetic acid	500 mg/kg	14.33 ± 1.25	68.38
Indomethacin + acetic acid	4 mg/kg	6.16 ± 0.87	86.39

Values were expressed as mean ± SE. An anti-inflammatory effect of *Bassia* (250 and 500 mg/kg body weight) was evaluated using student's *t*-test.

3.2. Antipyretic

The antipyretic study showed that *B. eriophora* was effective compared to normal saline control (Table 3). At 60, 90 and 120 min post treatment, the temperatures of indomethacin treated group (positive control) and the *B. eriophora* (250 and 500 mg/kg body weight) treated animals were statistically significant.

Table 3

The antipyretic effect of *B. eriophora* using rectal temperature method.

Treatment	Dose (mg/kg)	Normal rectal temperature	Rectal temperature after yeast administration 20 mL/kg of 20%	Rectal temperature after drug administration		
				60 min	90 min	120 min
Normal saline (control)	-	34.58 ± 0.12	39.35 ± 0.25	39.25 ± 0.24	39.20 ± 0.15	39.18 ± 0.20
<i>B. eriophora</i>	250	34.56 ± 0.18	39.10 ± 0.14	36.65 ± 0.25*	35.53 ± 0.25*	36.68 ± 0.21*
<i>B. eriophora</i>	500	34.66 ± 0.16	39.05 ± 0.17	37.26 ± 0.23**	35.66 ± 0.13*	35.83 ± 0.22***
Indomethacin	4	34.60 ± 0.22	38.95 ± 0.16	35.93 ± 0.17***	35.10 ± 0.22***	35.45 ± 0.25***

Values were expressed as mean ± SE. *: $P < 0.05$, **: $P < 0.01$, ***: $P < 0.001$. An antipyretic effect of *Bassia* (250 and 500 mg/kg, body weight) was evaluated using rectal temperature method.

Table 4

Effect of *Bassia* on kidney tissue creatinin, urea, uric acid, Ca, Na and K activity in CCl₄-intoxicated rats.

Treatment	Creatinin (mg/dL)	Urea (mg/dL)	Uric acid (mg/dL)	Ca (nmol/L)	Na (nmol/L)	K (nmol/L)	TP (g/L)
Normal (1 mL)	3.49 ± 0.10	31.70 ± 2.78	1.30 ± 0.84	5.07 ± 0.20	62.66 ± 3.46	4.05 ± 0.13	96.77 ± 4.03
CCl ₄ (1.25 mg/kg)	12.75 ± 0.64***a	113.26 ± 4.76***a	6.09 ± 0.27***a	18.46 ± 1.06***a	100.96 ± 1.87***a	12.46 ± 0.25***a	36.55 ± 1.55***a
<i>B. eriophora</i> + CCl ₄ (250 mg/kg, p.o.)	11.49 ± 0.62 ^b	57.96 ± 3.53 ^b	2.80 ± 0.13 ^b	10.64 ± 0.53 ^{ab}	91.30 ± 1.48 ^{***b}	6.11 ± 0.14 ^b	72.25 ± 2.66 ^{***b}
<i>B. eriophora</i> + CCl ₄ (500 mg/kg, p.o.)	10.19 ± 0.62 ^b	45.53 ± 1.98 ^b	2.75 ± 0.18 ^b	8.35 ± 0.43 ^b	89.75 ± 2.76 ^{***b}	5.38 ± 0.22 ^b	90.75 ± 3.48 ^{***b}
Silymarin (10 mg/kg)	7.85 ± 0.38 ^{***b}	52.03 ± 3.79 ^b	2.66 ± 0.25 ^b	13.07 ± 0.87 ^{***b}	69.56 ± 1.94 ^b	8.50 ± 0.38 ^{***b}	75.26 ± 2.85 ^{***b}

Values were expressed as mean ± SE. *: $P < 0.05$, **: $P < 0.01$, ***: $P < 0.001$. Kidney function of *Bassia* (250 and 500 mg/kg, body weight) was evaluated using CCl₄-intoxication rats method. ^a: Compared with normal group; ^b: Compared with CCl₄ group.

3.3. Kidney function

Administration of the herbs extract of *B. eriophora* (250 and 500 mg/kg body weight) prior to treatment with CCl₄ was found to protect kidney injuries of animals. Serum creatinine and serum urea levels were found to be significantly improved in rats treated with only CCl₄; whereas treatment with the herb extract of *B. eriophora* (250 and 500 mg/kg, body weight) significantly ($P < 0.05-0.001$) lowered their levels in the treated animals though dose independently (Table 4). The reductions in the levels of serum creatinine and urea were significantly ($P < 0.05-0.001$) prominent in the group treated with 500 mg/kg of the extract followed by that treated with 250 mg/kg of the extract. Silymarin (a reference drug) also caused significant ($P < 0.05-0.001$) reductions in the levels of serum creatinine and urea compared to the control. The levels of uric acid as well as some chemical elements like Na, K and Cl were less affected by the administration of the extract when compared with CCl₄. Total nephrotic tissue protein concentration in the *B. eriophora*, 250 and 500 mg/kg body weight, treated groups was higher than CCl₄ intoxicated group. The highest level recorded with 500 mg/kg dose was comparatively higher than silymarin control group (Table 4).

3.4. Estimation of antioxidant

3.4.1. Lipid peroxidation (LPO)

The effect of *B. eriophora* on the CCl₄-induced LPO was examined through observation of the levels of malondialdehyde in nephritic tissues. Nephritic malondialdehyde level was significantly ($P < 0.001$) elevated in the CCl₄-intoxicated control group [(6.73 ± 0.41) nmol/g tissue] than the normal animals [(1.32 ± 0.03) nmol/g tissue]. Silymarin (10 mg/kg, *i.p.*) treatment also prevented the CCl₄ elevation of malondialdehyde [(2.89 ± 0.17) nmol/g tissue]. Treatment of *B. eriophora* (250 and 500 mg/kg) with CCl₄ highly significantly ($P < 0.001$) prevented the elevation of malondialdehyde (Table 5).

Table 5

Effect of *B. eriophora* on kidney tissue TP, malondialdehyde and NP-SH activity in CCl₄-intoxicated rats.

Treatment	Malondialdehyde (nmol/g)	NP-SH (nmol/g)
Saline (normal) (2 mL/kg, <i>p.o.</i>)	1.32 ± 0.03	10.57 ± 0.72
CCl ₄ (1.25 mL/kg, <i>i.p.</i>)	6.73 ± 0.41 ^{***a}	4.55 ± 0.38 ^{***a}
<i>B. eriophora</i> + CCl ₄ (250 mg/kg, <i>p.o.</i>)	2.50 ± 0.02 ^{***b}	7.18 ± 0.54 ^{**b}
<i>B. eriophora</i> + CCl ₄ (500 mg/kg, <i>p.o.</i>)	1.71 ± 0.09 ^{***b}	6.15 ± 0.28 ^{**b}
Silymarin (10 mg/kg, <i>i.p.</i>)	2.89 ± 0.17 ^{***b}	9.27 ± 0.34 ^{***b}

Values were expressed as mean ± SE. ^{*}: $P < 0.05$, ^{**}: $P < 0.01$, ^{***}: $P < 0.001$. TP and antioxidant activity of *Bassia* (250 and 500 mg/kg, body weight) were evaluated using CCl₄-intoxicated rats method. ^a: Compared with normal group; ^b: Compared with CCl₄ group.

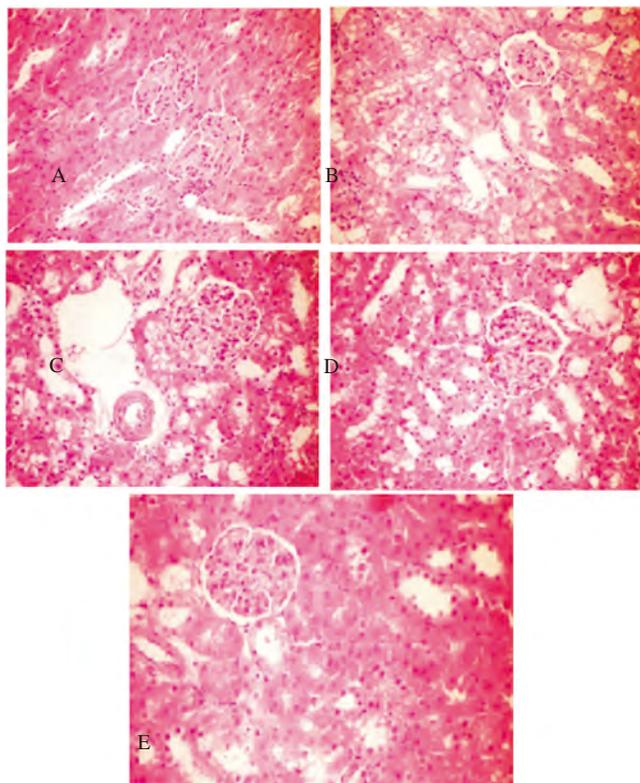


Figure 1. Histopathological section of renal tissues (hematoxylin and eosin, ×400).

A: Normal rat showing the normal renal histology; B: CCl₄-intoxicated rat showing vacuolization of cytoplasm of epithelial lining renal tubules; C: *B. eriophora* + CCl₄ (250 mg/kg body weight) showing vacuolization of epithelial lining of some renal tubules; D: *B. eriophora* + CCl₄ (500 mg/kg body weight) showing apparent normal renal parenchyma and E: Silymarin + CCl₄ (10 mg/kg) showing a clear normal renal parenchyma.

3.4.2. NP-SH assays

Rats intoxicated with CCl₄ showed a significant decrease [(4.55 ± 0.38) nmol/g] in nephritic NP-SH content as compared to the saline control rats [(10.57 ± 0.72) nmol/g]. Treatment with *B. eriophora* (either 250 or 500 mg/kg body weight) along with CCl₄, both of doses showed a significant increase ($P < 0.001$) in nephritic NP-SH (Table 5).

3.5. Histopathological studies

The microscopic study revealed that rats in the control group

treated with CCl₄ only showed various degrees of injuries such as vacuolization of cytoplasm of epithelial lining renal tubules while saline control showed the normal renal histology. Concurrent treatment with the ethanolic extract of *B. eriophora* (250-500 mg/kg) was found to reduce changes in kidney histology induced by CCl₄-intoxication (Figure 1).

4. Discussion

The analgesic effect of *B. eriophora* has not been previously reported and the mechanism which it occurs is not fully understood. The antipyretic effect of *B. eriophora* suggests again that the constituents of the extract may inhibit the synthesis of prostaglandins. It has also been reported that systemically administered CCl₄ in rats, increases the concentrations first in kidney other than in the liver[11].

The mechanism of CCl₄ renal toxicity is almost the same as that of liver, but kidney has high affinity for CCl₄ and contains cytochrome P450 predominantly in the cortex[12,13]. CCl₄ is extensively metabolized in the kidney generating more reactive metabolites. CCl₄-induced kidney injury is characterized by an increase in serum levels of creatinine, urea, uric acid, minerals, proteins as well as severe proximal renal tubular necrosis followed by renal failure. Increase in the level of serum creatinine is indicative of glomerular filtration rate reduction which is often associated with increases in serum urea, uric acid. Depletion in TP concentration can be estimated as a valuable index of severity of hepatic damage[14]. The decreased levels of TP in the serum of CCl₄-treated rats revealed the severity of hepatotoxicity. Thus, this suggests that *B. eriophora* can enhance the protein synthesis and balance the concentration of protein in the liver[13]. The administration of herbal extract of *B. eriophora* produced prominent decreases in serum levels of creatinine and urea induced by CCl₄ though the level of uric acid was not affected by the aerial parts of *B. eriophora* extract. Reactive oxygen species have been implicated in the pathogenesis of CCl₄-induced kidney injury[13]. This results in severe tissue damage and degeneration. The effect of reactive oxygen species in the body is usually suppressed by antioxidant enzyme systems. The suppression of CCl₄-induced nephrotoxicity by the extract may have resulted from the antioxidant and free radical scavenging potentials of the extract. Secondary metabolites in plants like flavonoids have been reported in related species[5]. The present study revealed that the chronic administration of CCl₄ caused marked impairment in kidney function with significant oxidative stress[15].

Serum creatinine, urea, and uric acid concentrations were higher in CCl₄-treated rats. The elevation of serum creatinine was due to changed kidney function caused by CCl₄. Urea is synthesized in the liver from ammonia, produced as a result of the deamination of amino acids and is the principal waste product protein catabolism, which is passed into blood stream and removed by kidney[16]. Administration of *B. eriophora* reduced the elevated levels of creatinine, urea and uric acid, which signifies that the *B. eriophora* possibly protects nephritic tissue against oxidative damages provoked by CCl₄ and indicates maintenance of renal function[17,18]. The observed hepato- and nephro-protective and antioxidant action of *B. eriophora* may be due to the occurrence of phenolic and flavonoidal contents. In the current study, the increase of malondialdehyde level in the kidney by CCl₄ proposes

the enhanced LPO which is an important pathogenic occurrence that damages biomembranes of cells[19]. LPO is thought to be an important oxidative stress which occurs when the balance between pro-oxidant and antioxidant has impaired[20]. Malondialdehyde is well known to be a reliable marker of oxidative stress or LPO[21].

Administration of rats with *B. eriophora* notably prevented CCl₄-induced malondialdehyde. Hence, the renal defensive activity of *B. eriophora* may be due to its antioxidative properties.

NP-SHs are well known to be involved in antioxidative damage. It protects cells against free radicals peroxides and various poisonous substances[22]. Thus, a depletion of glutathione within the living organisms can cause injury in tissues and malfunction[23]. In the current study, the kidney NP-SH level in CCl₄-treated group when compare to the control group was considerably diminished. These findings are in accordance with earlier reports where organs of rats when exposed with CCl₄, highly caused the depletion of sulfhydryl levels[24].

The depletion of NP-SH concentration in kidney by CCl₄ induction was resisted by pretreatment of rats with *B. eriophora* and the ameliorative effects of *B. eriophora* on kidney damage may be due to its free radical scavenging activity. The polyphenolic compounds in this extract may have been responsible for the kidney protective activity. These histopathological results indicated that *B. eriophora* preserved the structural integrity of the vacuolization of cytoplasm of epithelial lining renal tubules which was damaged by CCl₄-intoxication.

In conclusion, an analgesic induced by hot plate and writhing method and a hyperthermia induced by 15% yeast solution were significantly reduced by ethanolic extract of *B. eriophora*. The disturbance of kidney functions parameters such as creatinine, urea, uric acid, minerals and TP induced by CCl₄-intoxication was regained by *B. eriophora* extract. LPO and NP-SH assays indicated the antioxidant nature of the extracts that might be behind the nephro-protective activities. In last, photographic and histopathological kidney tissues confirmed the protective effect of *B. eriophora* extract against CCl₄ intoxication.

Conflict of interest statement

I declare that I have no conflict of interest.

References

- [1] Risser A, Donovan D, Heintzman J, Page T. NSAID prescribing precautions. *Am Fam Physician* 2009; **80**(12): 1371-8.
- [2] Al-Yahya MA, Al-Meshal IA, Mossa JS, Al-Badr AA, Tariq M. *Saudi plants: a phytochemical and biological approach*. Riyadh: King Saud University Press; 1990.
- [3] James LF, Williams MC, Bleak AT. Toxicity of *Bassia hyssopifolia* to sheep. *J Range Manag* 1976; **29**(4): 284-5.
- [4] Kamel MS, Mohamed KM, Hassanean HA, Ohtani K, Kasai R, Yamasaki K. Acylated flavonoid glycosides from *Bassia muricata*. *Phytochemistry* 2001; **57**(8): 1259-62.
- [5] Shaker KH, Al Jubiri SM, El-hady FKA, Al-Sehemi AG. New compounds from *Bassia muricata* and *Fagonia indica*. *Int J Pharm Sci Rev Res* 2013; **23**(1): 231-6.
- [6] Sani MHM, Zakaria ZA, Balan T, Teh LK, Salleh MZ. Antinociceptive activity of methanol extract of *Muntingia calabura* leaves and the mechanisms of action involved. *Evid Based Complementary Altern Med* 2012; doi: 10.1155/2012/890361.
- [7] Tag H, Namsa ND, Mandal M, Kalita P, Das AK, Mandal SC. Antipyretic and antibacterial activity of *Chloranthus erectus* (Buch.-Ham.) Verdcourt leaf extract: a popular folk medicine of Arunachal Pradesh. *Indian J Pharmacol* 2010; **42**(5): 273-6.
- [8] Al-Yahya M, Mothana R, Al-Said M, Al-Dosari M, Al-Musayeib N, Al-Sohaibani M, et al. Attenuation of CCl₄-induced oxidative stress and hepatonephrotoxicity by Saudi Sidr honey in rats. *Evid Based Complementary Altern Med* 2013; doi: 10.1155/2013/569037.
- [9] Utley HG, Bernheim F, Hochstein P. Effect of sulfhydryl reagents on peroxidation in microsomes. *Arch Biochem Biophys* 1967; **118**(1): 29-32.
- [10] Al-Harbi NO, Imam F, Al-Harbi MM, Iqbal M, Nadeem A, Sayed-Ahmed MM, et al. Olmesartan attenuates tacrolimus-induced biochemical and ultrastructural changes in rat kidney tissue. *Biomed Res Int* 2014; doi: 10.1155/2014/607246.
- [11] Sanzgiri UY, Srivatsan V, Muralidhara S, Dallas CE, Bruckner JV. Uptake, distribution, and elimination of carbon tetrachloride in rat tissues following inhalation and ingestion exposures. *Toxicol Appl Pharmacol* 1997; **143**: 120-9.
- [12] Yusufoglu HS, Alam A, Salkini AM, Alam P, Zaghoul AM. Anti-inflammatory and hepatoprotective study of *Astragalus plumosus* var. *akardagicus* and *Astragalus lamarcki* (family: Fabaceae) in Wistar albino rats. *Int J Biol Pharm Allied Sci* 2014; **3**(8): 1846-62.
- [13] Abraham P, Wilfred G, Cathrine. Oxidative damage to the lipids and proteins of the lungs, testis and kidney of rats during carbon tetrachloride intoxication. *Clin Chim Acta* 1999; **289**(1-2): 177-9.
- [14] Motawi TK, Hamed MA, Shabana MH, Hashem RM, Aboul Naser AF. *Zingiber officinale* acts as a nutraceutical agent against liver fibrosis. *Nutr Metab (Lond)* 2011; **8**: 40.
- [15] Al-Sowayan N, Mousa HM. Ameliorative effect of olive leaf extract on carbon tetrachloride-induced nephrotoxicity in rats. *Life Sci J* 2014; **11**(5): 238-42.
- [16] Orth SR, Ritz E. The nephrotic syndrome. *N Engl J Med* 1998; **338**(17): 1202-11.
- [17] Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. *Nephron* 1976; **16**(1): 31-41.
- [18] Davison AM, Cameron JS, Grunfeld JP, D. Kerr DNS, Ritz E, Winearls CG. *Oxford textbook of clinical nephrology*. Oxford: Oxford University Press; 1998, p. 36-9.
- [19] Nayagam AAJ, Manokaran S, Sudhakar N. Hepatoprotective efficacy of *Tricholepis radicans* DC. against CCl₄ induced liver toxicity in albino rats. *J Pharm Res* 2011; **4**(4): 1073-5.
- [20] Kumar RS, Asokkumar K, Murthy NV. Hepatoprotective effects and antioxidant role of *Scutia myrtina* on paracetamol induced hepatotoxicity in rats. *J Complement Integr Med* 2011; doi: 10.2202/1553-3840.1461.
- [21] Kitts DD, Yuan YV, Godin DV. Plasma and lipoprotein lipid composition and hepatic antioxidant status in spontaneously hypertensive (SHR) and normotensive (WKY) rats. *Can J Physiol Pharmacol* 1998; **76**(2): 202-9.
- [22] Lushchak VI. Glutathione homeostasis and functions: potential targets for medical interventions. *J Amino Acids* 2012; doi: 10.1155/2012/736837.
- [23] Ganie SA, Haq E, Hamid A, Qurishi Y, Mahmood Z, Zargar BA, et al. Carbon tetrachloride induced kidney and lung tissue damages and antioxidant activities of the aqueous rhizome extract of *Podophyllum hexandrum*. *BMC Complement Altern Med* 2011; **11**: 17.
- [24] Pinto C, Duque AL, Rodríguez-Galdón B, Cestero JJ, Macías P. Xanthohumol prevents carbon tetrachloride-induced acute liver injury in rats. *Food Chem Toxicol* 2012; **50**(10): 3405-12.