Nephroprotective, diuretic and antioxidant effects of some medicinal herbs in gentamicin-nephrotoxic rats

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Aim: To investigate the nephroprotective, diuretic and antioxidant effects of extracts of Petroselinum sativum, Eruca sativa and Curcuma longa herbs in gentamicin (GM)-nephrotoxic rats.

Material and Methods: Forty two adult male Sprague Dawley rats were randomly distributed into six equal groups. Group 1 was given sterile saline solution by intraperitoneal (i.p.) injection (negative control). Group 2 (nephrotoxic) was injected with GM (80 mg/kg, i.p.) for 8 days during the last week of the experiment. Groups 3, 4, 5 and 6 were orally pretreated with herbs extracts, alone and in combination, for 6 weeks along with GM during the last week. Blood and urine samples were collected for biochemical analyses. Kidney specimens were taken for estimating oxidant/antioxidant parameters and for histopathology.

Results: GM induced nephrotoxicity characterized by biochemical and histopathological alterations, increased lipid peroxidation and reduced activity of antioxidant enzymes in kidney tissues. Aqueous extracts of Petroselinum sativum, Eruca sativa and Curcuma longa herbs caused nephroprotective effect as it decreased in the elevated serum urea, creatinine and alkaline phosphatase (ALP) activity and normalized serum levels of Na+ and K+ electrolytes in GM-intoxicated rats. These extracts also increased the urine volume and urinary excretion of Na+ and K+, ameliorated renal tubular necrosis and increased activities of renal antioxidant enzymes in GM-intoxicated rats.

Conclusion: Aqueous extracts of Petroselinum sativum, Eruca sativa and Curcuma longa produce nephroprotective, diuretic and antioxidant effects in GM-nephrotoxic rats. These herbs may be beneficial for patients who suffer from kidney diseases and those on GM therapy.

INTRODUCTION
Nephrotoxicity induced by several synthetic drugs represents a serious problem for many populations in the world. Gentamicin (GM) is one of aminoglycoside antibiotics commonly used for the treatment of Gram negative bacterial infection in man. It is an effective drug against resistant bacterial strains to other antibiotics, but its nephrotoxic side effect has limited its therapeutic use [1]. Nowadays, the incidence of aminoglycosides-induced nephrotoxicity had increased and about 30% of patients treated with GM for more than 7 days showed signs of nephrotoxicity and neurotoxicity [2, 3]. Nephrotoxicity caused by GM seemed to be attributed to the oxidative stress caused by generation of reactive oxygen species [4, 5]. Aminoglycoside antibiotics were suggested to stimulate formation of reactive oxygen species (ROS) and cause renal oxidative stress [6]. On the other side, ROS scavengers and natural antioxidants can be used to alleviate nephrotoxicity induced by GM [7, 8]. Gentamicin was suggested to induce nephrotoxicity by inhibiting protein synthesis in renal cells. This mechanism specifically induced necrosis of cells in the proximal tubule, resulting in acute tubular necrosis which can lead to acute renal failure [9].

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role in the prevention and treatment of kidney diseases. In this concern, *Petroselinum sativum* (parsley) aqueous seed extract was reported to produce a diuretic effect in rats. The mechanism of action of parsley seems to be mediated through an inhibition of the Na+/K+ pump that would lead to a reduction in Na+ and K+ reabsorption leading thus to an osmotic water flow into the lumen, and diuresis [10]. Moreover, *Petroselinum sativum* prevented formation of calcium oxalate stones in rats with nephrolithiasis and reduced the number of calcium oxalate deposits [11]. *Eruca sativa* is widely used in folklore medicine as a remedy of renal ailments. *Eruca sativa* produced potent antioxidant and renal protective activities and also precluded oxidative damage inflicted to the kidney by mercuric chloride in rats [12]. Curcumin, the active principle of turmeric (*Curcuma longa*) ameliorated diabetic nephropathy in rats [13]. The antioxidative activity was found to be responsible for the nephroprotective action of curcumin. The ethanol extract of *Curcuma comosa* exhibited an effective protection against cisplatin-induced nephrotoxicity in mice that mediated through its antioxidant activity [14]. *Curcuma longa* (turmeric) extract was found to possess multiple therapeutic activities that block the cardiac, hepatic, and renal toxicities induced by doxorubicin and had antioxidant activity [15]. It was concluded that curcumin might be potentially useful in some kidney diseases by preventing renal inflammation [16].

The present study was carried out to investigate the nephroprotective, diuretic and antioxidant effects of *Petroselinum sativum*, *Eruca sativa* and *Curcuma longa* medicinal herbs, alone and in combination, in gentamicin-nephotoxic rats.

MATERIALS AND METHODS

Herbs

*Petroselinum sativum* (Parsley, Family *Apiaceae*) seeds; *Eruca sativa* (Rocket, Family *Brassicaceae*) seeds and *Curcuma longa* (Turmeric, Family *Zingiberaceae*) rhizomes were purchased from the Agricultural Seeds, Herbs and Medicinal Plants Company, Cairo, Egypt. The dry seeds and rhizomes of the herbs were finely grinded into fine powders and used for the preparation of aqueous extracts.

Gentamicin

Gentamicin (Garamycin® injection), an aminoglycoside antibiotic, was obtained from Memphis Company for Pharmaceutical and Chemical Industries, Cairo, Egypt. It is dispensed in the form of ampoules, each containing 40 mg/ml of gentamicin sulphate. The injected dose of gentamicin 80 mg/kg b.w.to rats was selected to induce acute nephrotoxicity [17].

Rats and feeding

Forty two adult male rats of Sprague Dawley strain weighing 150-155 g body weight and 8-10 weeks old were used in this study. The rats were purchased from the Laboratory Animal Colony, Helwan, Egypt. The animals were housed under hygienic conditions at a room temperature of 25 ± 2 °C with relative humidity of 50–55% and on 12 hr light/12 hr dark cycles. Rats were fed on commercial rat pellets which composed of 10% wheat bran, 44% soy bean powder, 20 % net protein, 5 % fats, 3.3%, fibers and fish meal, molasses, salts (sodium chloride, calcium carbonate, calcium phosphate) and methionine. These pellets are manufactured by Cairo Agriculture Development Company, Giza, Egypt.

Preparation of aqueous extracts of herbs

One hundred and fifty grams of fine powder of each herb were soaked in one liter of hot water (to obtain 15 % concentration) at 50°C for 2 hours and thereafter kept in a refrigerator with daily shaking for 5 days. The aqueous extract was obtained in by filtration with double layers of gauze to get rid of herb debris. For preparing the herb mixture, fifty grams of each herb powder were thoroughly mixed together, soaked in one liter of hot water at 50°C for 2 hours and processed as previously mentioned. The prepared aqueous extracts were kept in a refrigerator pending for further use.

Design of experiment

Forty two adult male Sprague Dawley rats were randomly divided into six equal groups, each of 7 animals. Group 1 was injected intraperitoneally (i.p.) with sterile saline (0.2ml/rat) and kept as normal control. Group 2 was injected i.p. with gentamicin in a dose 80 mg/kg for 8 consecutive days during the last week of the experiment to induce acute nephrotoxicity [17] and kept as nephotoxic control. Groups 3, 4, 5 and 6 were pretreated with one of the aqueous extracts of the three herbs each at 5% and their mixture at 15% concentration (1ml/rat), respectively, along with gentamicin during the last week. Twenty four hours after the last administration, animals were placed in separate metabolic cages for 24 hr and total urinary volume was measured. A drop of concentrated hydrochloric acid was added to urine before being stored at 4°C. Urine samples were analyzed for sodium and potassium levels. Blood samples were collected and used for serum separation. Serum samples were used for estimation of blood urea, uric acid, creatinine and alkaline phosphates as well as serum sodium and potassium levels. Kidney tissue specimens were collected from right kidneys and stored at -18°C for estimation of oxidant/antioxidant status. The left kidney specimens were preserved in 10% neutral
formalin for histopathology.

**Serum and urine analyses**

Concentrations of blood urea nitrogen [18]; uric acid [19] and creatinine [20] were estimated using specific diagnostic kits (Sigma Aldrich, St. Louis, USA). The activity of serum alkaline phosphates (ALP) enzyme was estimated [21] using standard reagent kits (Sigma Aldrich, St. Louis, USA). Serum and urine levels of sodium and potassium electrolytes were determined using flame photometer (Model FP 20 seas, Seag Radim Company, Italy) with specific diagnostic kit (BioMérieux, France) as described by Ali [22].

**Preparation of kidney homogenate**

One gram of the right kidney tissue was collected, washed in ice-cooled 0.9% NaCl and homogenized in ice-cooled 1.15% potassium chloride solution and 50 mMol potassium phosphate buffer solution (pH 7.4) to yield 10% homogenate (W/V). Homogenization was performed using ultrasonic homogenizer. The homogenate was then centrifuged at 4000 rpm for 5 minutes at 4°C. The supernatant was collected and kept for further use.

**Assessment of oxidant / antioxidant activity**

Reduced glutathione (GSH) content of kidney tissue was determined using chemical method [23]. The method is based on the reduction of 5, 5’-dithiobis (2-nitrobenzoic acid) with glutathione producing a yellow compound. The reduced chromogen was directly proportional to GSH concentration and its absorbance was measured at wave length 412 nm.

**Determination of lipid peroxidation (LPX)**

LPX in renal tissue was measured according to Ohkawa et al. [24]. The technique is based on the reaction of thiobarbituric acid with lipid peroxides malondialdehyde (MDA) in acidic medium at 95°C for 45 minutes to form thiobarbituric acid reactive substance (TBARS). The resulting pink color was extracted with n-butanol and its absorbance was determined spectrophotometrically at wave length 530nm.

**Determination of superoxide dismutase (SOD)**

The renal SOD activity was measured according to Nishikimi et al. [25]. This assay relies on the ability of SOD enzyme to inhibit the phenazine methosulphate-mediated reduction of nitroblue tetrazolium dye.

**Determination of glutathione peroxidase (GPx)**

Renal GPx activity was measured by the method of Paglia and Valentine [26]. This assay is an indirect measurement of the activity of GPx. The oxidized glutathione (GSSG), produced upon reduction of organic peroxide by GPx, was recycled to its reduced state by the enzyme glutathione reductase (GHR). The reaction was initiated by the addition of hydrogen peroxide, and the oxidation of NADPH to NADP+ is accompanied by a decrease in the absorbance at wave length 340 nm.

**Determination of catalase (CAT)**

Renal CAT activity was measured in tissue homogenate according to Aebi [27]. The assay is based on that catalase reacts with a known quantity of hydrogen peroxide. This reaction is stopped after exactly one minute with catalase inhibitor. In the presence of peroxidase, the remaining hydrogen peroxide reacts with 3, 5-Dichloro-2-hydroxybenzenesulfonic acid and 4-aminophenazone to form a chromophore with a colour intensity inversely proportional to the amount of catalase.

**Histological procedure**

Kidney specimens were taken and fixed in 10 % neutral formalin solution. The fixed specimens were trimmed, dehydrated in ascending grades of alcohol, cleared in xylene. They were embedded in paraffin boxes, sectioned at 4-6 microns thickness, stained with Hematoxylen and Eosin (H&E) and examined microscopically according to Carleton [28].

**Statistical analysis**

Data were expressed as mean ± standard error (SE). Differences between control and treated groups were tested for significance using one-way analysis of variance (ANOVA) followed by Duncan’s multiple range test [29]. Statistical analyses were performed using the SPSS (Statistical Package for the Social Sciences), software program.

**RESULTS**

Intraperitoneal injection of gentamicin (GM) in a dose of 80 mg/kg for 8 consecutive days to rats caused nephrotoxicity manifested by significant ($P < 0.05$) increases in serum levels of blood urea nitrogen, creatinine and activity of alkaline phosphatase (ALP) enzyme when compared with healthy control rats. Oral administration of aqueous extracts of *Petroselinum sativum*, *Eruca sativa* and *Curcuma longa* herbs, alone and in combination, along with GM induced significant ($P < 0.05$) decreases in the elevated levels of blood urea nitrogen, creatinine and activity of ALP when compared with GM-intoxicated rats as recoded in Table (1). Non significant changes were reported in serum levels of uric acid between the different experimental groups (healthy control, GM-intoxicated and herb-treated).
Table 1. Effect of aqueous extracts of *Petroselinum sativum* (PS), *Eruca sativa* (ES) and *Curcuma longa* (CL) herbs on serum urea and creatinine and alkaline phosphatase enzyme (ALP) in gentamicin-nephrotoxic rats.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Urea (mg/dL)</th>
<th>Creatinine (mg/dL)</th>
<th>ALP (U/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Healthy control</td>
<td>31.95±2.44d</td>
<td>0.58±0.02d</td>
<td>58.4±4.52d</td>
</tr>
<tr>
<td>Group 2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nephrotoxic control</td>
<td>70.46±3.54a</td>
<td>0.97±0.04a</td>
<td>77.6±4.21a</td>
</tr>
<tr>
<td>Group 3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PS 5 %</td>
<td>39.35±2.10b</td>
<td>0.68±0.02b</td>
<td>65.4±5.32b</td>
</tr>
<tr>
<td>Group 4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ES 5 %</td>
<td>40.42±2.24b</td>
<td>0.65±0.01b</td>
<td>64.8±4.22b</td>
</tr>
<tr>
<td>Group 5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CL 5 %</td>
<td>38.63±3.30b</td>
<td>0.67±0.03b</td>
<td>63.5±5.03b</td>
</tr>
<tr>
<td>Group 6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mixture 15 %</td>
<td>36.46±3.70c</td>
<td>0.56±0.04c</td>
<td>62.3±3.44c</td>
</tr>
</tbody>
</table>

Means ± SE with different superscripts in the same column are significant at $P < 0.05$ using one way ANOVA test.

**n=7 rats.**

Daily intraperitoneal injection of GM to rats for 8 days caused significant decreases in serum levels of sodium (Na+) and potassium (K+) electrolytes when compared with the healthy control group. Oral administration of aqueous extracts of *Petroselinum sativum*, *Eruca sativa* and *Curcuma longa* herbs and their mixture concomitantly with GM normalized the decreased levels of Na+ and K+ electrolytes in the serum when compared with GM-intoxicated rats as illustrated in Fig. (1).

**Fig. 1.** Effect aqueous extracts of *Petroselinum sativum*, (PS), *Eruca sativa* (ES) and *Curcuma longa* (CL) herbs on serum sodium Na+ and potassium levels in gentamicin-nephrotoxic rats.

Intraperitoneal injection of GM to rats for 8 days caused significant decreases in urine volume and concentrations of urinary Na+ and K+ electrolytes as compared to the healthy control group. Oral administration of aqueous extracts of *Petroselinum sativum*, *Eruca sativa*, *Curcuma longa* herbs and their mixture along with GM significantly ($P < 0.05$) increased urine volume and urinary levels of Na+ and K+ electrolytes as compared to GM-intoxicated rats as recorded in Table (2).

**Fig. 2.** Effect aqueous extracts of *Petroselinum sativum*, (PS), *Eruca sativa* (ES) and *Curcuma longa* (CL) herbs on kidney levels of reduced glutathione (GSH) and malondialdehyde (MDA) in gentamicin-nephrotoxic rats.

Rats injected daily with GM for 8 consecutive days had a significant ($P < 0.05$) decrease in the content of reduced glutathione (GSH) and an increase in the level of lipid peroxidation product, malondialdehyde (MDA), in kidney tissues when compared with the healthy control group. Oral administration of aqueous extracts of *Petroselinum sativum*, *Eruca sativa* and *Curcuma longa* herbs and their mixture concomitantly with GM caused a significant ($P < 0.05$) increase in GSH and a decrease in MDA contents in renal tissue when compared with GM-intoxicated rats as shown in Fig. (2).

Intraperitoneal injection of GM to rats for 8 consecutive days induced significant ($P < 0.05$) decreases in the activity of renal superoxide dismutase (SOD), glutathione peroxidase (GPx) and catalase (CAT) antioxidant enzymes when compared with the healthy control group. Oral administration of aqueous extracts of *Petroselinum sativum*, *Eruca sativa* and *Curcuma longa* herbs and their mixture concomitantly with GM significantly ($P < 0.05$) increased the activity of SOD, GPx and CAT enzymes when compared with GM-intoxicated rats (Table 3).
Table 2. Effect of aqueous extracts of Petroselinum sativum (PS), Eruca sativa (ES) and Curcuma longa (CL) herbs on urine volume and urinary sodium (Na+) and potassium (K+) levels in gentamicin-nephrotoxic rats.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Groups</th>
<th>Urine volume (ml)</th>
<th>Na⁺ (mEq/L)</th>
<th>K⁺ (mEq/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group 1 Healthy control</td>
<td>3.75±0.23 d</td>
<td>93.12±4.86 d</td>
<td>20.70±1.11 b</td>
</tr>
<tr>
<td></td>
<td>Group 2 Nephrotoxic control</td>
<td>3.2±0.25 d</td>
<td>90.55±2.27 c</td>
<td>18.12±0.07 e</td>
</tr>
<tr>
<td></td>
<td>Group 3 PS 5%</td>
<td>6.3±0.15 b</td>
<td>120.75±0.24 b</td>
<td>42.85±0.02 f</td>
</tr>
<tr>
<td></td>
<td>Group 4 ES 5%</td>
<td>7.3±0.15 b</td>
<td>155.79±0.14 b</td>
<td>41.76±0.03 a</td>
</tr>
<tr>
<td></td>
<td>Group 5 CL 5%</td>
<td>6.5±0.34 b</td>
<td>145.77±0.08 b</td>
<td>40.78±0.05 a</td>
</tr>
<tr>
<td></td>
<td>Group 6 Mixture 15%</td>
<td>7.5±0.24 a</td>
<td>167.95±0.04 a</td>
<td>40.88±0.03 a</td>
</tr>
</tbody>
</table>

Means ± SE with different superscripts in the same column are significant at \( P < 0.05 \) using one way ANOVA test.

n=7 rats.

Table 3. Effect of aqueous infusions of Petroselinum sativum (PS), Eruca sativa (ES) and Curcuma longa (CL) herbs on the activity of superoxide dismutase (SOD), glutathione peroxidase (GPx) and catalase (CAT) enzymes in kidney tissue of gentamicin-nephrotoxic rats.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Groups</th>
<th>SOD (U/mg protein)</th>
<th>GPx (nmol/min/mg protein)</th>
<th>CAT (nmol/min/mg protein)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group 1 Healthy control</td>
<td>51.8±0.18 a</td>
<td>0.50±0.02 a</td>
<td>0.186±0.001 a</td>
</tr>
<tr>
<td></td>
<td>Group 2 Nephrotoxic control</td>
<td>36.00±2.3 a</td>
<td>0.13±0.03 a</td>
<td>0.144±0.003 a</td>
</tr>
<tr>
<td></td>
<td>Group 3 PS 5%</td>
<td>39.00±2.62 a</td>
<td>0.25±0.04 a</td>
<td>0.123±0.004 a</td>
</tr>
<tr>
<td></td>
<td>Group 4 ES 5%</td>
<td>42.25±2.42 b</td>
<td>0.28±0.01 b</td>
<td>0.135±0.005 b</td>
</tr>
<tr>
<td></td>
<td>Group 5 CL 5%</td>
<td>44.64±3.75 b</td>
<td>0.39±0.03 b</td>
<td>0.169±0.002 b</td>
</tr>
<tr>
<td></td>
<td>Group 6 Mixture 15%</td>
<td>48.77±2.43c</td>
<td>0.44±0.02 b</td>
<td>0.177±0.002 b</td>
</tr>
</tbody>
</table>

Means ± SE with different superscripts in the same column are significant at \( P < 0.05 \) using one way ANOVA test.

n=7 rats.

Histological examination of kidneys of healthy rats showed normal histological structure of renal parenchyma (glomeruli and tubules) as illustrated in Fig. (3). Kidneys of rats intoxicated with GM (80 mg/kg, i.p.) for 8 successive days revealed marked necrosis of renal tubules associated with presence of protein casts in their lumens (Fig.4). Examination of kidneys of rats given orally the aqueous extract of Petroselinum sativum herb concomitantly with GM showed mild congestion of intertubular blood capillaries (Fig.5). In rats given the aqueous extract of Eruca sativa herb concomitantly with GM, the examination of kidney showed vacoulations of epithelial lining of renal tubules (Fig.6). In rats received the aqueous infusion of Curcuma longa herb along with GM, the microscopic examination of kidneys revealed little peritubular leukocytes infiltration (Fig.7). Concomitant administration of the mixture of Petroselinum sativum, Eruca sativa and Curcuma longa herbs along with GM showed almost normal histological architecture of renal parenchyma (Fig.8).

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The nephroprotective, diuretic and antioxidant activities of aqueous extracts of *Petroselinum sativum*, *Eruca sativa* and *Curcuma longa* herbs, alone and in combination, against gentamicin (GM) - induced nephrotoxicity in rats were investigated.

The results revealed that intraperitoneal injection of gentamicin (GM) to rats caused signs of nephrotoxicity manifested by significant increases in serum urea, creatinine and activity of ALP enzyme associated with decreases in serum levels of sodium and potassium electrolytes. Urine analysis showed significant decreases in urinary excretion of sodium and potassium in GM-intoxicated rats. In addition, lipid peroxidation in kidney tissues showed significant elevation of lipid peroxide malondialdehyde (MDA) and the antioxidant enzymes were markedly decreased in GM-intoxicated rats. Examination of kidney sections of GM-intoxicated rats revealed marked necrosis of renal tubules. These results were in agreement with findings of previous authors [1, 2, 3, 4, 5] who concluded that GM induces nephrotoxicity manifested by biochemical and histological changes in rats.

The mechanism of nephrotoxicity caused by GM was attributed to stimulation of generation of reactive oxygen species (ROS) causing tissue oxidative stress [4, 5, 6]. GM-nephrotoxicity associated with decreased serum levels of sodium and potassium suggested that the site of GM action is the distal convoluted tubules causing increased urinary excretion of sodium and potassium [3]. In addition, it was previously reported that high serum alkaline phosphatase (ALP) concentrations might be a marker of renal inflammation [30].

Oral administration of *Petroselinum sativum*, *Eruca sativa* and *Curcuma longa* herbs and their mixture caused nephroprotective and diuretic effects as they reversed the biochemical and histological alterations induced by GM in rats. These herbs also produced an
antioxidant activity as evident by decreasing lipid peroxidation byproduct (MDA), increasing content of reduced glutathione and restoring activities of antioxidant (SOD, GPx and CAT) enzymes in renal tissue.

The nephroprotective effect of *Petroselinum sativum* herb, reported in the present study, was similar to that reported by Afzal et al. [31] who found that a polyherbal formulation containing *Petroselinum sativum* (parsley) produced a nephroprotective effect in rats. This effect of *Petroselinum sativum* was attributed to its antioxidant activity as free radical scavenger or due to its high content of flavonoids [32]. The diuretic effect of *Petroselinum sativum* was reported by Kreydiyyeh and Usta [10] who found that parsley aqueous seeds extract produced a diuretic effect in rats. The previous authors concluded that the mechanism of action of parsley seems to be mediated through an inhibition of the Na+/K+ pump that would lead to a reduction in Na+ and K+ reabsorption thus leading to an osmotic water flow into the lumen, and diuresis.

Concerning *Eruca sativa* herb, it is widely used in folklore medicine and has a good reputation as a remedy of renal ailments. It was reported that *Eruca sativa* produced potent antioxidant and renal protective activities and precluded oxidative damage inflicted to the kidney by mercuric chloride in rats [12]. Recently, *Eruca sativa* L. extract was reported to produce an antioxidant effect due to its free radicals scavenging activity *in vivo* [33] and *in vitro* [34]. Moreover, *Eruca sativa* was reported to protect the liver against CCl4-induced hepatic injury through its potent antioxidant activity *in vivo* [35].

Regarding *Curcuma longa* herb, it was reported that curcumin derived from plant *Curcuma longa* ameliorated diabetic nephropathy in rats and the antioxidant mechanism being responsible for the nephroprotective action of curcumin [13]. Ademiluyi et al. [36] reported that dietary inclusion of ginger (*Zingiber officinale*) and turmeric (*Curcuma longa*) rhizomes attenuated gentamicin-induced nephrotoxicity in rats. The bioactive substance curcumin isolated from turmeric (*Curcuma longa*) rhizomes produced a renoprotective activity via its antioxidant effect [37]. The authors concluded that curcumin might be potentially useful in some kidney diseases by preventing renal inflammation. *Curcuma longa* (turmeric) extract was found to possess multiple therapeutic activities that block the cardiac, hepatic, and renal toxicities induced by doxorubicin [15] and by arsenic trioxide [38] and had as a free radical scavenger activity. In addition, the previous studies revealed that curcumin derived from *Curcuma longa* (turmeric) extract inhibited biofilm development of uropathogens [39]. Curcumin can protect the liver from the damage caused by N-nitrosodiethylamine in rats and has the potential to be used in a therapy of liver cancer [40]. It was suggested that curcumin might be potentially useful in kidney diseases by preventing renal inflammation [16].

The ameliorative effect of histopathological changes induced by GM in kidney of rats by the studied herbs was parallel with the reported biochemical alterations in the current study. The amelioration of renal tubular necrosis by the studied herbs in GM-intoxicated rats was similar to that reported by Afzal et al. [31] for *Petroselinum sativum*; by Sarwar et al. [12] for *Eruca sativa* and by Kheradpezhough et al. [41] for *Curcuma longa*.

In conclusion, *Petroselinum sativum*, *Eruca sativa* and *Curcuma longa* herb extracts produce nephroprotective, diuretic and antioxidant effects in gentamicin (GM) -nephrotoxic rats. Therefore, intake of aqueous extract of these herbs and their mixture may be potentially useful for patients who suffer from kidney diseases and those on GM therapy.

**CONFLICT OF INTERESTS**

None.

**REFERENCES**


http://www.jicep.com


