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Protective Effect of Parsley Leaves and Turmeric Roots Extracts Against Gentamicin Induced Nephrotoxicity in Male Rats

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Abstract: The nephroprotective, diuretic and antioxidant effects of parsley leaves extract (PLE) and turmeric roots extract (TRE) on gentamicin (GM) induced nephrotoxic rats were evaluated. Forty two adult male rats were randomly distributed into 6 groups of 7 animals each. Group 1 was negative (non treated) control and group 2 was daily injected with GM (80 mg/kg, i.p.) during the last 8 days of the experiment to induce nephrotoxicity. Groups 3, 4, 5 and 6 were orally pretreated with PLE in 100 and 200 mg/kg and with TRE in 200 and 400 mg/kg, respectively for 6 weeks and intoxicated with GM in the last 8 days. Blood and urine samples of the last 24 hr of the experiment were collected for biochemical analyses. Rats were sacrificed and both kidneys were taken for estimating lipid peroxidation, antioxidant enzymes activity and histopathology. The results showed that GM induced nephrotoxicity manifested by alterations in serum and urine biochemical parameters, increased tissue lipid peroxidation, decreased antioxidant activity and presence of renal tubular necrosis upon histopathology. Oral pretreatments with PLE and TRE caused a nephroprotective effect evident by significant decreases in serum levels of urea, creatinine and alkaline phosphatase enzyme in nephrotoxic rats. The extracts decreased serum sodium and potassium levels, tissue malondialdehyde (MDA) and increased activity of antioxidant enzymes. Both extracts also increased urine volume and urinary excretion of Na^+ and K^+ electrolytes, denoting a diuretic activity and mitigated renal tubular necrosis induced by GM. The nephroprotective mechanisms of both extracts could be attributed to inhibition of lipid peroxidation and enhancement of antioxidant enzymes activity. These results affirm the traditional use of these herbs in folk medicine for the prevention of kidney diseases. Therefore, parsley and turmeric herbs may be useful for patients who suffer from kidney diseases and who receive gentamicin therapy.

Key words: Parsley · Turmeric · Nephroprotective · Diuretic · Antioxidant · Biochemical analysis · Histopathology

INTRODUCTION

Acute renal failure refers to the sudden and usually reversible loss of renal function which develops over a period of days or weeks. Among causes of acute renal failure is acute tubular necrosis which occurs due to ischemia or nephrotoxic drugs such as cisplatin (anticancer) and gentamicin. Acute tubular necrosis accounts for 85% of the incidence among population. Gentamicin (GM) is an aminoglycoside antibiotic commonly used for the treatment of Gram negative bacterial infection and its treatment period should not be more than 7 days [1]. GM is more effective than other antibiotics against most resistant bacteria. The chemical stability of GM and its rapid bactericidal action has made it a first drug of choice in many clinical situations. Previous studies have been reported that 30% of the patients treated with GM for more than 7 days course showed signs of acute nephrotoxicity [2]. Interestingly, GM nephrotoxicity in animal experiments was positively correlated with its outcome in humans [3]. The specificity of GM to produce nephrotoxicity was linked to its accumulation and deposition in renal distal convoluted tubules and lysosomes [4]. GM nephrotoxicity seemed to be attributed to the oxidative stress caused by generation of reactive oxygen species [5]. On the other side, previous studies reported that the natural antioxidants from medicinal plants and herbs can prevent GM

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nephrotoxicity [6, 7]. Medicinal plants and herbs play an important role in the prevention and treatment of kidney diseases. Parsley (*Petroselinum sativum*, Family Apiaceae) is used as a culinary, garnishing and medicinal herb in the Mediterranean region of Southern Europe. Parsley extract was reported to produce a diuretic effect and good antioxidant activity [8]. Parsley leaves are rich in Apigenin and its glucosidal flavonoids that were found to possess anti-inflammatory especially for renal inflammation; antioxidant and anticancer activities [9, 10]. In addition, the aqueous extract of parsley reduced the number of calcium oxalate deposits and therefore parsley can be used for kidney and bladder stones [11]. Turmeric (*Curcuma longa*, Family Zingiberaceae) and its bioactive principle curcumin were found to ameliorate diabetic nephropathy in rats [12]. Turmeric root extract was reported to possess multiple therapeutic benefits as it abrogates the toxicity of the heart, liver and kidneys induced by doxorubicin (Adriamycin) and it has antioxidant activity [13, 14]. The later authors concluded that curcumin might be potentially useful for kidney diseases via preventing acute renal inflammation. The nephroprotective action of turmeric root extract was attributed to its good antioxidative activity in rats inflected with diabetic nephropathy [15]. Curcumin, the abundant polyphenolic compound of *curcuma longa* roots, was reported to exhibit renoprotective and antioxidant activities [16] as well as an anticancer effect [17].

The present study was carried out to assess the nephroprotective, diuretic and antioxidant effects of the ethanolic extracts of parsley leaves and turmeric roots against gentamicin-induced nephrotoxicity in rats and to clarify the potential mechanisms of action.

MATERIALS AND METHODS

Materials: Parsley (*Petroselinum sativum*, Family *Apiaceae*) leaves were procured from a local green grocery. Turmeric (*Curcuma longa* Family Zingiberacae) roots were purchased from Agricultural Seeds, Herbs and Medicinal Plants Company, Cairo, Egypt.The leaves of parsley were air dried, grinded into a fine powder and kept till alcohol extraction.

Gentamicin: Gentamicin (Garamycin® injection), is one of aminoglycoside antibiotics. It was obtained from Memphis Company for Pharmaceutical and Chemical Industries, Cairo, Egypt. It is dispensed in the form of ampoules; each containing 40mg/ml. Rats were intraperitoneally injected with gentamicin in a dose of 80 mg/kg to induce acute nephrotoxicity according to the method described by Bibu *et al.* [18].

Rats: Forty two mature male rats of Sprague Dawley strain weighing 140-150 g b.wt and 8-9 weeks old were used in this study. The rats were purchased from the Laboratory Animal Colony, Helwan, Egypt. Rats were housed under hygienic conditions at a room temperature of 22°C with relative humidity of 50% and on 12 hr light/12 hr dark cycles. Basal diet and water were provided *ad libitum.* In the last day of experiment, the rats were housed individually in metabolic cages for collection of 24 hr urine samples.

Preparation of Basal Diet: Basal diet was prepared according to Reeves *et al.* [19]. It consisted of 20 % protein, 10 % sucrose, 5 % corn oil, 2% choline chloride, 1% vitamin mixture, 3.5 % salt mixture and 5% fibers and the remainder is corn starch up to 100 %. The dietary supply of protein, fat, carbohydrates, vitamins and minerals in basal was in accordance with the recommended dietary allowances for rats (American Institute of Nutrition, AIN93).

Preparation of Alcoholic Extract: Two hundred grams of dried parsley leaves or turmeric roots powder were soaked in one liter of 90% ethyl alcohol and kept in a refrigerator with daily shaking for 5 days. This was followed by percolation for 5 times till complete herb exhaustion. The liquid ethanolic extracts were concentrated using vacuum rotatory evaporator at 50°C under reduced pressure. Starting with 200 g dry powder material of parsley and turmeric yielded 87.8 and 95.5 g gummy extract, respectively. Twenty grams of each gummy extract were dissolved in 98 ml distilled water and 2 ml of Tween 80 (suspending agent) to obtain 20% ethanolic extract (concentration of 200 mg/ml). The administered doses of parsley extract were 100 and 200 mg/kg b.wt and of turmeric extract were 200 and 400 mg/kg b.wt.

Experimental Design: Forty two adult male Sprague Dawley rats were randomized into 6 equal groups each of 7 animals. Group 1 was injected intraperitoneally (i.p.) with sterile normal saline (0.2 ml) and kept as a normal (negative) control. Group 2 was daily injected i.p. with GM in a dose of 80 mg/kg b.wt during the last 8 days of experiment to induce nephrotoxicity and kept as a nephrotoxic (positive) control. Groups 3, 4, 5 and 6 were orally pretreated with PLE in 100 and 200 mg/kg and TRE

in 200 and 400 mg/kg for 6 weeks, respectively and intoxicated with GM. In the last day of experiment, the rats were placed individually in metabolic cages for collection of 24 hr urine and the urine volume was measured using a graduated cylinder. Two drops of concentrated HCl acid were added to each urine sample before being stored at -20°C. Urine samples were analyzed for Na^+ and K^+ electrolyte levels. Blood samples were collected for serum separation which was used for estimation of levels of urea nitrogen, uric acid, creatinine, alkaline phosphate enzyme and Na^+ and K^+ electrolytes. Kidney tissue specimens were collected and stored at-70°C till used for estimation of renal lipid peroxide malondialdehyde (MDA) and reduced glutathione (GSH) contents and for assessment of renal antioxidant enzymes activity. Other kidney specimens were preserved in neutral 10% formalin till processed for histopathology.

Serum and Urine Analyses: Serum concentrations of urea nitrogen [20], uric acid [21], creatinine [22] and alkaline phosphates (ALP) enzyme [23] were chemically estimated using diagnostic kits (Sigma Aldrich, St. Louis, USA). Serum and urine levels of Na^+ and K^+ electrolytes were determined using flame photometer (Model FP 20 seac, Seag Radim Company, Italy) with chemical kits (BioMérieux, France) as described by Ali [24].

Preparation of Renal Homogenates: One gram of kidney tissue was collected, washed with ice-cooled 0.9% NaCl solution and homogenized with 100 ml of ice-cooled 1.15% solution of potassium chloride and 50 mM potassium phosphate buffer solutions (pH 7.4) to yield 10% homogenate (w/v). Homogenization was performed using ultrasonic homogenizer (Sonicator, model 4710, Cole-Parmer Instrument Company, USA). The homogenates were then centrifuged at 8000 rpm for 15 minutes at 4°C and the supernatants were collected for biochemical assays.

Determination of Renal Lipid Peroxidation (LPx): LPx in renal tissue was measured according to Ohkawa *et al.* [25]. The method 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. Reduced glutathione (GSH) content in kidney tissue was chemically determined as described by Sedlak and Lindsay [26].

Assay of Antioxidant Enzymes: Activities of antioxidant enzymes superoxide dismutase (SOD), glutathione peroxidase (GPx) and catalase (CAT) were chemically determined in renal tissue according to Spitz and Oberley [27], Paglia and Valentaine [28] and Sinha [29], respectively.

Histological Procedure: Kidney specimens were taken and preserved in 10% neutral formalin solution. The fixed specimens were trimmed, dehydrated in ascending grades of alcohol, cleared in xylene. The specimens were embedded in paraffin boxes, sectioned at 4-6 microns thickness and stained with Hematoxylen and Eosin (H&E) and then examined microscopically [30].

Statistical Analysis: Data were expressed as means ± standard deviations (SD). Statistical analysis was carried out using one-way analysis of variance (ANOVA) followed by Duncan's multiple range test according to Snedecor and Cochran [31] with SPSS (Statistical Package for the Social Sciences, version 15.0, Illinois, Chicago, USA) computerized program. Significances between controls and treated groups were tested at probability level of $P < 0.05$.

RESULTS

Intraperitoneal injection of gentamicin (GM) in a dose 80 mg/kg/day for 8 days to rats caused nephrotoxicity manifested by significant ($P < 0.05$) increases in serum levels of urea nitrogen (UN),creatinine (Cr) and alkaline phosphatase (ALP) enzyme when compared with the normal (negative) control group. Oral pretreatments with ethanolic extracts of parsley leaves (PLE) and turmeric roots (TRE) in GM-intoxicated rats for 6 weeks induced significant ($P < 0.05$) decreases in high serum levels of UN, Cr and ALP when compared with GM- intoxicated rats. No significant changes in serum uric acid were observed between normal control and intoxicated rats as depicted in Table 1.

Data in Table 2 showed that daily intraperitoneal injection of GM to rats for 8 days caused significant ($P<0.05$) decreases in serum levels of sodium (Na^+) and potassium (K^+) electrolytes when compared with the normal control group. Oral pretreatments with PLE and TRE to GM-intoxicated rats for 6 weeks reversed the low serum levels of Na^+ and K^+ electrolytes to nearly normal levels when compared with GM-intoxicated rats. Daily intraperitoneal injection of GM to rats for 8 days caused significant ($P<0.05$) decreases in the urine volume and

Table 1: Effect of ethanolic extracts of parsley leaves (PLE) and turmeric roots (TRE) on serum urea nitrogen, uric acid, creatinine and alkaline phosphatase enzyme (ALP) in gentamicin-nephrotoxic rats.

	Parameters			
Groups	Urea nitrogen (mg/dl)	Uric acid (mg/dl)	Creatinine (mg/dl)	ALP (U/L)
Group1: Normal control	31.95±2.44^{d}	1.48±0.12^{a}	0.58±0.02^{d}	158.4±4.52^{d}
Group 2: Nephrotoxic control	70.46±3.54^{a}	1.49±0.17^{a}	0.97±0.04^{a}	177.6±4.21^{a}
Group 3: PLE (100 mg/kg)	39.35±2.10^{b}	1.52±0.15^{a}	0.68±0.02^{b}	165.4±5.32^{b}
Group 4: PLE (200 mg/kg)	40.42±2.24^{b}	1.50±0.13^{a}	0.65±0.01^{b}	164.8±4.22^{b}
Group 5: TRE (200 mg/kg)	38.63±3.30^{b}	1.51±0.16^{a}	0.67±0.03^{b}	163.5±5.03^{b}
Group 6: TRE (400 mg/kg)	36.46±3.70^{c}	1.49±0.12^{a}	0.56±0.04^{c}	160.3±2.44^{c}

Means ± SD with different superscript letters in the same column are significant at $P < 0.05$ using one way ANOVA test and those with similar letters are non significant. n=7 rats.

Table 2: Effect of ethanolic extracts of parsley leaves (PLE) and turmeric roots (TRE) on serum sodium (Na^+) and potassium (K^+) electrolytes in gentamicin-nephrotoxic rats.

	Parameters	
Groups	Na^+ (MEq/L)	K^+ (Meq/L)
Group 1: Normal control	129.10±0.16^{b}	4.85±0.2 4^{b}
Group 2: Nephrotoxic control	110.55±0.27^{a}	2.12±0.27^{a}
Group 3: PLE (100 mg/kg)	124.75±0.24^{b}	4.84±0.12^{b}
Group 4: PLE (200 mg/kg)	125.79±0.14^{b}	.76±0.23^{b}
Group 5: TRE (200 mg/kg)	128.77±0.08^{b}	.78±0.15^{b}
Group 6: TRE (400 mg/kg)	127.95±0.04^{b}	.83±0.23^{b}

Means ± SD 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 ethanolic extracts of parsley leaves (PLE) and turmeric roots (TRE) on urine volume and urinary sodium (Na^+) and potassium (K^+) levels in gentamicin-nephrotoxic rats.

	Parameters		
Groups	Urine volume (mL)	Na^+ (MEq/L)	K^+ (Meq/L)
Group 1:Normal control	3.75± 0.23^{c}	96.12±4.86^{c}	20.70±1.11^{b}
Group 2:Nephrotoxic control	2.20± 0.25^{d}	90.55±2.27^{d}	18.12±0.07^{c}
Group 3:PLE (100 mg/kg)	6.30± 0.15^{b}	139.75±0.24^{b}	42.85±0.02^{a}
Group 4:PLE (200 mg/kg)	7.30± 0.15^{a}	155.79±0.14^{a}	41.76±0.03^{a}
Group 5:TRE (200 mg/kg)	6.50±0.34^{b}	145.77±0.18^{b}	40.78±0.05^{a}
Group 6: TRE (400 mg/kg)	8.50 ±0.24^{a}	160.95±0.04^{a}	40.88±0.03^{a}

Means ± SD with different superscripts in the same column are significant at $P < 0.05$ using one way ANOVA test. n=7 rats.

urinary levels of Na^+ and K^+ electrolytes when compared with the normal control group. Oral pretreatments with PLE and TRE in GM-intoxicated rats for 6 weeks significantly (P<0.05) increased the urine volume and urinary levels of Na^+ and K^+ electrolytes when compared with GM- intoxicated rats (Table 3).

Data in Table 4 showed that daily intraperitoneal injection of GM to rats for 8 days caused a significant (P<0.05) decrease in reduced glutathione (GSH) content and increase in malondialdehyde (MDA) in kidney tissues when compared with the normal control group. Oral pretreatment with PLE and TRE when orally given to GM-intoxicated rats for 6 weeks significantly (P<0.05) increased GSH and decreased MDA contents in renal tissues as compared with GM-intoxicated rats. It is clear from Table 5 that intraperitoneal injection of GM to rats for 8 days induced significant (P<0.05) decreases in activities of renal superoxide dismutase (SOD), glutathione peroxidase (GPx) and catalase (CAT) enzymes when compared with the normal control group. PLE and TRE when orally given to GM-intoxicated rats for 6 weeks significantly increased the activities of SOD, GPx and CAT enzymes as compared with GM-treated rats.

Histological examination of kidneys of normal rats showed normal histological structure of renal glomeruli and tubules (Fig. 1A). Kidneys of rats intoxicated with GM (80 mg/kg, i.p.) for 8 days revealed marked tubular necrosis (Fig. 1B). Examination of kidneys of nephrotoxic rats pre-treated with the small dose (100 mg/kg) of parsley leaves extract (PLE) showed mild necrosis in renal tubules with protein casts in their lumen (Fig.1C). In nephrotoxic rats given the large dose (200 mg/kg) of PLE, the examination showed only mild congestion of intertubular blood vessels (Fig.1D). Kidneys of GM- nephrotoxic rats received the small dose (200 mg/kg) of turmeric roots extract (TRE) showed large vaculations and peritubular leukocytes infiltration (Fig. 1E). Kidneys of nephrotoxic rats pretreated orally with the large dose (400 mg/kg) of TRE showed almost normal histological architecture of renal glomeruli and tubules (Fig. 1F).

Table 4: Effect of ethanolic extracts of parsley leaves (PLE) and turmeric roots (TRE) on kidney contents of reduced glutathione (GSH) and malondialdehyde (MDA) in gentamicin-nephrotoxic rats.

	Parameters	
Groups	GSH (nmol/min/mg protein)	MDA (nmol/min/mg protein)
Group 1: Normal control	34.57±1.89[a]	0.32±0.16[b]
Group 2: Nephrotoxic control	24.00±0.92[c]	0.73±0.23[a]
Group 3: PLE (100 mg/kg)	22.36±0.61[b]	0.21±0.20[c]
Group 4: PLE (200 mg/kg)	25.44±0.51[b]	0.24±0.10[b]
Group 5: TRE (200 mg/kg)	30.57±0.79[b]	0.28±0.19[b]
Group 6: TRE (400 mg/kg)	32.35±0.75[b]	0.29±0.20[b]

Means ± SD with different superscripts in the same column are significant at $P < 0.05$ using one way ANOVA test. n=7 rats.

Table 5: Effect of ethanolic extracts of parsley leaves (PLE) and turmeric roots (TRE) on the activity of superoxide dismutase (SOD), glutathione peroxidase (GPx) and catalase (CAT) antioxidant enzymes in kidney tissues of gentamicin-nephrotoxic rats.

	Parameters		
Groups	SOD (U/mg protein)	Gpx (nmol/min/mg protein)	CAT (nmol/min/mg protein)
Group 1: Normal control	51.8±0.18[a]	0.50±0.02[a]	0.186±0.001[a]
Group 2: Nephrotoxic control	36.00±2.3[c]	0.13±0.03[c]	0.144±0.003[c]
Group 3: PLE (100 mg/kg)	39.00±2.62[c]	0.25±0.04[b]	0.123±0.004[b]
Group 4: PLE (200 mg/kg)	42.25±2.42[b]	0.28±0.01[b]	0.135±0.005[b]
Group 5: TRE (200 mg/kg)	44.64±3.75[b]	0.39±0.03[b]	0.169±0.002[b]
Group 6:TRE (400 mg/kg)	48.77±2.43[c]	0.44±0.02[b]	0.177±0.001 [b]

Means ± SD with different superscripts in the same column are significant at $P < 0.05$ using one way ANOVA test. n=7 rats.

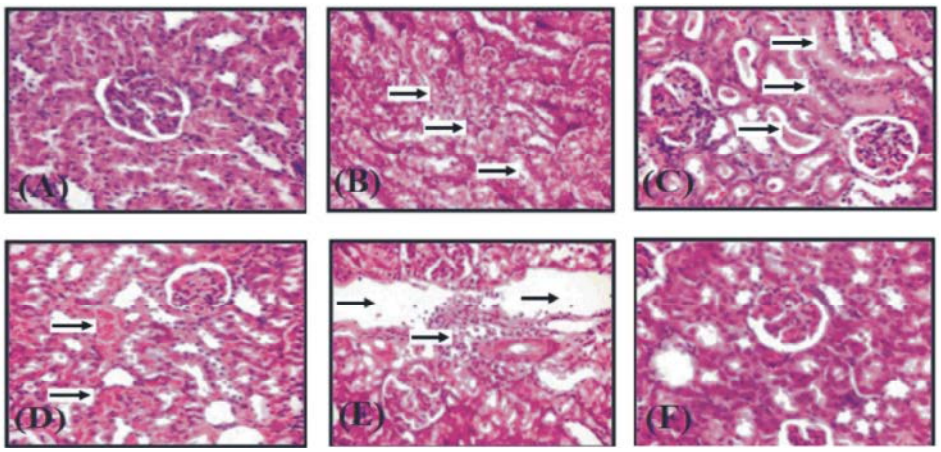

Fig. 1: Cross Section in a kidney

A): Negative control rat showing normal architecture of renal tubules and glomeruli (H & E stain, X 200)

B): Gentamicin-nephrotoxic rat showing marked necrosis of renal tubules (Arrows) (H & E stain, X200).

C): Nephrotoxic rat given orally the small dose of PLE showing mild necrosis of renal tubules (Arrow) with protein casts in their lumen (Arrow). (H & E stain, X 200)

D): Nephrotoxic rat given orally the large dose of PLE showing only mild congestion of intertubular blood capillaries (Arrows) (H & E stain, X 200)

E): Nephrotoxic rat given orally the small dose of TRE showing large vaculations (Arrows) and peritubular leukocytes infiltration (Arrow). (H & E stain, X 200)

F): Nephrotoxic rat and given orally the large dose of TRE showing almost normal histological structure of renal tubules and glomeruli. (H & E stain, X 200)

DISSCUSION

Nephrotoxicity represents a major health problem and accounts for high incidence among population all over the world. The nephroprotective, diuretic and antioxidant activities of parsley leaves and turmeric roots ethanolic extracts against gentamicin-induced nephrotoxicity in rats were investigated and the potential mechanisms were elucidated. Intraperitoneal injection of gentamicin (GM) to rats for 8 days in this study induced acute nephrotoxicity evident by significant increases in serum urea nitrogen, creatinine and ALP enzyme associated with decreases in serum levels of Na+ and K+. Urine analysis revealed decreases in urine volume and urinary excretion of Na+ and K+. There were also significant increases in renal lipid peroxide malondialhyde (MDA) content and decreases in antioxidant enzymes activity as well as marked tubular necrosis upon histopathological examination. These serum and tissue biochemical changes and histopathological alterations agreed with the previous reports [5, 32, 33, 34]. Interestingly, GM nephrotoxicity in rats was found to be positively correlated with its outcome in humans [3]. The specificity of GM to induce renal toxicity was attributed to its deposition and accumulation in the renal convoluted tubules and lysosomes leading to cytotoxicity [4].

The mechanism underlying GM nephrotoxicity may be attributed to increased generation of reactive oxygen species (ROS) leading to cytotoxicity due to oxidative stress [5, 35, 36]. GM nephrotoxicity was also associated with decreases in serum levels of Na+ and K+ electrolytes suggesting that the site of GM action is the distal convoluted tubules [33]. In addition, the high serum alkaline phosphatase concentrations induced by GM was used as specific marker of renal inflammation [37]. Oral pretreatments with parsley and turmeric extracts in GM-nephrotoxic rats caused nephroprotective, diuretic and antioxidant effects as they reversed serum and urine biochemical parameters and mitigated histopathological alterations in kidney induced by GM in rats. The nephroprotective and diuretic effects of parsley, reported herein, were similar to those recorded by Afzal *et al*. [38] who found that a polyherbal formulation containing parsley produced nephroprotective and diuretic effects in rats. The nephroprotective effect of parsley was attributed to the antioxidant activity due to its high content of flavonoids [39]. The diuretic effect of parsley was previously reported by Kreydiyyeh and Usta [8]. The authors concluded that the mechanism of diuretic 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, so causing dieresis.

Concerning turmeric herb, it was reported that the active principle of turmeric (curcumin) ameliorated diabetic nephropathy in rats and the antioxidant activity is being responsible for the nephroprotective action of curcumin [15]. The authors concluded that curcumin might be potentially useful in kidney diseases by preventing renal inflammation. Moreover, turmeric extract was found to possess multiple therapeutic activities that block the cardiac, hepatic and renal toxicities induced by doxorubicin [13]; arsenic trioxide [40] and acetaminophen [41]. Moreover, it was suggested that curcumin might be useful in kidney diseases via preventing renal inflammation induced by lipopolysaccharide [14]. In the current study, the histopathological changes (renal tubular necrosis) induced by GM in the kidney of rats and the ameliorative effects of parsley and turmeric herbs were parallel with the reported serum and urine biochemical alterations. The amelioration of renal tubular necrosis caused by the large doses of tested herbs was similar to that reported by Afzal *et al.* [38] for parsley and by Zhong *et al.* [14] for turmeric.

CONCLUSION

Gentamicin (GM) injection induces nephrotoxicity manifested by serum and urine biochemical changes and renal tubular necrosis in rats. Oral pretreatments with ethanolic extracts of parsley leaves and turmeric roots in GM-nephrotoxic rats produce nephroprotective, diuretic and antioxidant activities. These effects were confirmed via improvements of serum, urine and renal biochemical parameters as well as mitigation of acute renal tubular necrosis induced by GM. The nephroprotective mechanism of parsley and turmeric herbs may be due to reduction of lipid peroxidation and enhancement of antioxidant enzyme activity in kidney tissues. This study recommends that consumption of parsley leaves and turmeric roots in food may be beneficial for patients who suffer from kidney diseases and who receive GM therapy.

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