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Dose-Dependent Effect of Coriander (*Coriandrum Sativum L.*) and Fennel (*Foeniculum Vulgare M.*) on Lead Nephrotoxicity in Rats

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Abstract: *Nephrotoxicity is a complication due to the effect of some toxic chemicals on kidneys. Current study planned to screen the effect of coriander and fennel aqueous seeds extracts on lead-induced nephrotoxicity. Seventy-two adult male rats were equally divided to 6 groups: group (1) normal control, group (2) lead-toxicated rats were received 50 mg/kg b.wt of lead acetate by gastric tube daily, groups (3-6) were lead-toxicated and administered aqueous seeds extracts of coriander (250 and 500 mg/kg body weight/day) and fennel (100 and 150 mg/kg body weight/day), respectively. Lead-induced renal damage was evidenced by a significant elevation of serum and renal lead with reduction of serum delta amino levulinic acid dehydratase activity. Renal dysfunction was diagnosed by a significant elevation of kidney function tests accompanied with reduction in creatinine clearance. Results evidenced a significant increase of serum sodium and potassium concentrations and their depletion in urine. Renal oxidant-antioxidant balance was disturbed which evidenced by significant increase in renal malondialdehyde and nitric oxide and significant decrease in renal reduced glutathione, catalase, glutathione-S-transferase and superoxide dismutase activity. Treatment with coriander and fennel seeds extracts exerted a significant improvement of most of the biochemical parameters compared to lead group.*

Keywords: *lead; nephrotoxicity; coriander; fennel; rats.*

Abbreviations: *Lead (Pb), Glomerular Filtration Rate (GFR), Reactive oxygen species (ROS), Delta amino levulinic acid dehydratase (δALAD), Renal nitric oxide (NO), Malondialdehyde (MDA), Superoxide dismutase(SOD), Reduced glutathione (GSH), Glutathione S transferase (GST), Catalase (CAT) and Phytic acid (PA).*

1. INTRODUCTION

Nephrotoxicity is a major complication characterized by functional alterations including inhibition of protein synthesis, reduced glutathione depletion, lipid peroxidation and mitochondrial damage. Oxidative damage is thought to be one of the main mechanisms involved in nearly all chronic renal pathologies [1]**.** Exposure to chemical reagents like ethylene glycol, carbon tetra chloride, sodium oxalate and heavy metals like lead, mercury, arsenic and cadmium also induces nephrotoxicity [2]**.**

Lead (Pb) is a well-known multi-organ toxicant and it damage liver and kidney [3]. It is a divalent cation with a propensity to settle in the proximal tubule of the nephron, leading to nephrotoxicity. Lead accumulation in the proximal tubule leads to hyperuricaemia and gout, presumably by inhibiting uric acid secretion, and diminished glomerular filtration rate (GFR) [4].

Lead is known to cause oxidative damage in various tissues by bringing about imbalance in the generation and removal of reactive oxygen species [5]. It is known to cause free radical damage in tissues by two mechanisms: Increased generation of reactive oxygen species (ROS), including hydroperoxides, singlet oxygen and hydrogen peroxides, and by causing direct depletion of antioxidant reserves [6].

Many plants have been used for the treatment of kidney failure in traditional system of medicine throughout the world. Several herbs are prescribed for reducing renal damage and to avoid kidney related complications. These can be immense value in combating renal damage [7].

Coriander *(CoriandrumSativum L.)* belonging to family Umbelliferaeis widely distributed and mainly cultivated for seeds. It has been used as a flavoring agent in food products, perfumes and cosmetics [8]. It was shown that coriander extracts have phenolic compounds and flavonoids, suggesting that these compounds contribute to the antioxidative activity [9]. Coriander suppresses the deposition of lead by chelating the metal [10].

Coriander has been reported to exhibit several pharmacological effects such as antifertility**,** antiproliferative, anti-hyperlipidemic**,** digestive stimulant**,** hypotensive and antihyperglycemic [11]**.** *Coriandrum sativum* showed excretion of heavy metal in the urine of patients and also augmented the efficacy of antibiotics [3].

Fennel *(Foeniculum Vulgare M.)* is belonging to the family *Apiaceae* (*Umbelliferae*) with a characteristic aromatic odor. It is one of the most important medicinal plants grown within the Mediterranean region, in Europe and in Egypt [12]. Fennel seeds are generally eaten not only for the taste but also they are very healthy owing to the nutrition value attached to it. Fennel is also used for various health benefits that are derived from its anti-oxidants [13].

Fennel contains its own unique combination of phytonutrients-including the flavonoids rutin, quercitin, and various kaempferol glycosides-that give it strong antioxidant activity [14]. The major chemical components of fennel are flavonoids, polyphenols, carotenoids, minerals and vitamins [15].

Fennel used as carminative, digestive, lactogogue, diuretic and in treating respiratory and gastrointestinal disorders. Pharmacologically, fennel has been shown to possess anti-inflammatory, anti-diabetic, anti-bacterial, anti-fungal, anti-oxidant, analgesic, estrogenic, hepato-protective, anti-tumor activities. In addition, it is used as herbal medicine for kidney diseases [16].

So, this study aimed to investigate the dose-dependent ameliorative effect of coriander and fennel extracts on biochemical changes in serum and kidney tissue that occur in lead-induced nephrotoxicity in rats.

2. MATERIALS AND METHODS

2.1. Animals

Adult male albino rats (Sprague- Dawely) weighing about 180-200 g were obtained from El-Salam farm, Giza, Egypt. Rats were kept individually in wire cages; they were fed on standard commercial pellets diet [17] and water *ad libitum* in acclimatization period (7 days) and also throughout all the experimental period (45 days).

2.2. Plant Materials

Coriander and Fennel seeds were purchased from local market in Cairo and were ground into a fine powder. The aqueous extracts of coriander and fennel were prepared as previously described by ***Kansal et al.*** [11] and ***Sadrefozalayi and Farokhi*** [18] respectively. 100g of coriander were added to 500ml distilled water and 100g of fennel were added to 400ml distilled water. After 24 h maceration was done at room temperature (37 °C), the two mixtures were then heated for 30 min in the water bath at 65°C, and then they were filtered, concentrated by heating over the water bath (65 °C) and dried by rotary evaporator. The two extracts (semi-solid pastes) were stored at 4 °C and used to treat animals as needed at doses: 250 and 500 mg/kg body weight/ day [3] for coriander extract and at doses: 100 and 150 mg/kg body weight/ day for fennel extract [19].

2.3. Induction of Nephrotoxicity

Lead acetate Pb $(C_2H_3O_2)_2$ was purchased from Sigma for chemicals company Cairo. Egypt. Nephrotoxicity was induced by giving rats lead acetate dissolved in distilled water at dose 50 mg/kg body weight/ day by gastric tube [20].

2.4. Experimental Design

Rats were divided into 6 groups of 12 rats each as follows:

Group 1 (Normal control): rats were received distilled water by gastric tube daily.

Group 2 (Lead-toxicated): rats were received 50 mg/kg b.wt of lead acetate by gastric tube daily.

Group 3 (Lead-toxicated + Low dose of coriander): rats were received 50 mg/kg b.wt of lead acetate and 250 mg/kg b.wt of coriander extract by gastric tube daily.

Group 4 (Lead-toxicated + High dose of coriander): rats were received 50 mg/kg b.wt of lead acetate and 500 mg/kg b.wt of coriander extract by gastric tube daily.

Group 5 (Lead-toxicated + Low dose of fennel): rats were received 50 mg/kg b.wt of lead acetate and 100 mg/kg b.wt of fennel extract by gastric tube daily.

Group 6 (Lead-toxicated + High dose of fennel): rats were received 50 mg/kg b.wt of lead acetate and 150 mg/kg b.wt of fennel extract by gastric tube daily.

2.5. Handling of Urine, Blood and Kidneys

After the last administration, animals from each group were kept in wire-bottom stainless steel metabolic cages for collection of 24-hour urine samples. Urine specimens were filtered to remove sediment debris and particles and then urine volumes were measured and recorded. Urine specimens were stored at -20°C until analyzed for creatinine, total proteins, as well as sodium and potassium electrolytes.

At the end of the experimental period (45 days) and after overnight fasting, all rats were sacrificed and blood samples were collected from hepatic portal vein and portion of the blood was received into centrifuge tube and centrifuged at 1500 rpm for 15 min for obtaining serum while the other portion was received into heparinized tubes and centrifuged for obtaining plasma. Serum and plasma samples were stored at -20 °C for further assessment. Kidneys were separated immediately and washed by saline solution (0.9% NaCl) then blotted on filter paper and weighed and then stored at -20 °C for further assessment.

2.6. Biochemical Assays

Lead concentration in serum and kidneys tissue was determined by atomic absorption spectrophotometer as described by ***Subramanian***[21], serum delta amino levulinic acid dehydratase(δALAD) activity was assayed by ELISA using kits from Glory Science co., USA, serum and urine creatinine were determined by colorimetric method kits and used for the calculation of creatinine clearance, urea was estimated by using Urease-Berthelot method kits**,** while uric acid was determined by enzymatic colorimetric kits and urinary protein was determined using Folin-Lowry colorimetric method kits, also serum and urinary sodium concentrations were measured colorimetrically using kits**,** but serum and urinary potassium concentrations were determined by turbidimetric method kits**.** Renal nitric oxide (NO), malondialdehyde (MDA) and Superoxide dismutase (SOD) were determined followed the colorimetric method kits, while reduced glutathione(GSH) were measured chemically according to ***Beutler et al.*** [22]. Finally, plasma and renal glutathione S transferase (GST) were measured by U.V method kits while catalase (CAT) activity was determined by colorimetric kits.

3. STATISTICAL ANALYSIS

The data was analyzed using the Statistical Package for Social Science program (S.P.S.S. 9). One-way analysis of variance (ANOVA) was used. The difference among groups means were tested using the least significant differences (LSD) at ($p < 0.05$). Values were expressed as the Mean ± SEM [23].

4. RESULTS

In the present study, nephrotoxicity was successfully induced in rats by oral administration of lead acetate as indicated by a significant ($p< 0.05$) increase in serum and renal lead concentration by 12.7 and 8.8 folds, respectively and reduction in serum δALAD by 74.61 % comparing to normal control rats. Oral administration of coriander seeds extract at doses (250 & 500 mg/kg b.wt) and fennel seeds extract at doses (100 & 150 mg/kg b.wt)to lead- toxicated rats caused a significant decrement in the levels of lead in serum and kidney and elevation ($p< 0.05$) in δ ALAD activity compared to lead-toxicated group **(table 1).**

High dose of coriander and fennel seeds extracts significantly ($p< 0.05$) exhibited highly reduction in serum lead by 73.27% and 70.50%, respectively and renal lead by 63.05% and 65.06%, respectively, this dose dependent effect was not noticed for δ ALAD enzyme activity.

Table1. *Serum Delta Amino- Levulinic acid Dehydratase activity, serum and renal lead in the tested groups*

Groups / Parameters	Normal control	Lead-toxicated	Coriander- treated		Fennel- treated		L.S.D (p≤0.05)
			At dose 250 mg/kg b.wt	At dose 500 mg/ kg b.wt	At dose 100 mg / kg b.wt	At dose 150 mg / kg b.wt	
Serum Delta Amino- Levulinic acid Dehydratase (ng/ L)	54.32±1.16^{a}	13.79±0.62^{c}	37.70±0.62^{b}	38.14±1.21^{b}	39.63±0.76^{b}	39.36±0.66^{b}	2.5
Serum lead (µg/dl)	1.40±0.053^{d}	17.73±0.38^{a}	6.98±0.19^{b}	4.74±0.22^{c}	7.24±0.22^{b}	5.23±0.20^{c}	0.65
Renal lead (µg/g tissue)	5.72±0.098^{e}	50.20±1.17^{a}	27.85±1.08^{b}	18.55±0.46^{d}	24.98±1.07^{c}	17.54±0.89^{d}	2.5

Values are expressed as means ± S.E., n= 12

Means in a row without common letter are differ

The results represented in **table (2)** showed that lead-toxicated rats had a significant ($p< 0.05$) increase in kidney function tests (serum creatinine, urea, uric acid and urinary protein) by 101.54%, 2 folds, 84.31 % and 2.7 folds, respectively accompanied with reduction in creatinine clearance by 72.06%. Also a significant ($p< 0.05$) increase of serum sodium and potassium concentrations by 17.33% and 83.67%, respectively and their depletion in urine by 15.44% and 26.55 %, respectively was recorded.

Table2. *Some kidney function parameters as well as sodium and potassium in serum and urine in the tested groups*

Groups / Parameters		Normal control	Lead-toxicated	Coriander- treated		Fennel- treated		L.S.D (p≤0.05)
				At dose 250 mg/kg b.wt	At dose 500 mg/ kg b.wt	At dose 100 mg / kg b.wt	At dose 150 mg / kg b.wt	
Serum creatinine (mg/ dl)		0.65±0.01^{c}	1.31±0.07^{a}	0.69±0.02^{c}	0.72±0.03^{bc}	0.80±0.03^{b}	0.70±0.02^{c}	0.096
Creatinine clearance (ml/ min.)		0.68±5.29^{a}	0.19±1.50^{d}	0.37±2.42^{c}	0.47±3.23^{b}	0.47±3.78^{b}	0.47±3.91^{b}	0.1
Serum urea (mg/ dl)		14.27±0.54^{e}	30.65±1.10^{a}	19.65±0.25^{bc}	17.59±0.26^{d}	21.25±0.45^{b}	18.82±0.74^{cd}	1.77
Serum uric acid (mg/ dl)		14.28±0.66^{c}	26.32±0.82^{a}	18.82±0.94^{b}	15.02±0.24^{c}	18.38±0.85^{b}	15.62±0.75^{c}	2.1
Urinary protein (mg/ dl)		90±1.35^{f}	243.91±5.23^{a}	183.11±2.85^{b}	140.20±1.86^{d}	155.64±1.03^{c}	121.91±1.79^{e}	7.73
Sodium	Serum (mmol/ L)	132.86±0.33^{e}	155.89±0.40^{a}	145.79±0.58^{c}	140.83±0.81^{d}	150.0±0.39^{b}	144.51±0.45^{c}	1.46
	Urine (mmol/L)	137.53±0.89^{a}	116.29±035^{d}	121.01±079^{c}	126.79±0.97^{b}	125.67±0.53^{b}	125.48±0.79^{b}	2.12
Potassium	Serum (mmol/ L)	8.82±0.18^{d}	16.20±0.18^{a}	10.32±0.11^{c}	10.51±0.08^{c}	11.64±0.24^{b}	10.31±0.21^{c}	0.49
	Urine (mmol/L)	78.97±0.74^{a}	58.00±1.02^{e}	68.46±0.70^{d}	74.89±0.26^{b}	71.81±0.65^{c}	72.96±0.61^{bc}	1.98

Values are expressed as means ± S.E., n= 12

Means in a row without common letter are differ

Lead-toxicated rats administrated coriander or fennel seeds extract at the tested doses, significantly ($p< 0.05$) showed a marked renal protection evidenced by amelioration in the kidney function tests. A significant ($p< 0.05$) reduction in serum sodium and potassium levels and increase their excretion in urine are also noted comparing to lead-toxicated group. The highest doses of coriander and fennel seeds extracts significantly ($p< 0.05$) exhibited more effectiveness in restoration of most kidney function tests and amelioration of sodium and potassium levels in serum and urine.

From **table (3)** it is obvious that, lead administration to rats caused disturbance in renal oxidant-antioxidant balance evidenced by a significant ($p< 0.05$) reduction in the levels of renal reduced glutathione by 69.16% and antioxidant enzymes activity as plasma and renal CAT and GST by 48.79%, 58.46%, 73.28% and 71.87%, respectively also renal SOD was decreased by 78.85%, with elevation of renal NO and MDA as compared to normal control group. The statistical analysis exhibited an elevation of renal GSH as well as antioxidant enzymes activity and reduction in renal levels of NO and MDA when lead-toxicated rats orally given coriander and fennel seeds extracts at the tested doses comparing to lead group.

Table3. *Renal reduced Glutathione, plasma and renal antioxidant enzymes activity and renal nitric oxide and malondialdehyde in the tested groups*

Groups / **Parameters**		**Normal control**	**Lead-toxicated**	**Coriander- treated**		**Fennel- treated**		**L.S.D ($p\leq0.05$)**
				At dose 250 mg/kg b.wt	**At dose 500 mg/ kg b.wt**	**At dose 100 mg / kg b.wt**	**At dose 150 mg / kg b.wt**	
Renal Reduced Glutathione (mg/ g tissue)		75.16±0.86^{a}	23.18±0.97^{e}	48.26±1.41^{d}	49.98±1.90^{cd}	52.80±1.53^{c}	58.86±1.50^{b}	4.32
Catalase	Plasma (U/ L)	1762.44±30.3^{a}	902.48±2.6^{d}	1002.07±10.9^{c}	1170.5±34^{b}	981.53±17.0^{c}	1051.46±37.8^{c}	72.2
	Renal (U/ g tissue)	7.92±0.1^{a}	3.29±0.07^{d}	4.97±0.2^{c}	5.45±0.13^{b}	5.35±0.24^{bc}	5.45±0.2^{b}	0.47
Glutathione -S-Transferase	Plasma (U/ L)	677.72±9.1^{a}	181.08±2.2^{d}	313.70±5.27^{c}	504.4±11.22^{b}	479.69±10.8^{b}	505.44±12.04^{b}	26
	Renal (U/ g tissue)	3.20±0.12^{a}	0.90±0.02^{c}	2.08±0.04^{b}	2.24±0.05^{b}	2.14±0.05^{b}	2.20±0.05^{b}	0.176
Renal Superoxide dismutase (U/ g tissue)		729.34±11.04^{a}	154.29±3.4^{d}	483.7±18.78^{c}	508.61±16.9^{bc}	518.08±17.24^{bc}	524.38±12.90^{b}	40.56
Renal Nitric Oxide (µmol/ g tissue)		22.59±1.06^{e}	151.13±1.11^{a}	61.14±1.66^{b}	42.05±1.22^{d}	51.96±1.27^{c}	45.55±1.76^{d}	3.8
Renal Malondialdehyde (mmol/ g tissue)		3.85±0.12^{d}	8.30±0.16^{a}	5.84±0.11^{b}	5.53±0.09^{bc}	5.60±0.09^{b}	5.29±0.068^{c}	0.315

Values are expressed as means ± S.E., n= 12

Means in a row without common letter are differ

Dose-dependent effect was noticed in serum and renal lead, renal GSH and SOD by two doses of fennel and high dose of coriander seeds extract, in plasma CAT enzyme activity by high dose of coriander extract, and in renal catalase, NO and MDA by the high doses of coriander and fennel seeds extracts.

5. DISCUSSION

In the current study, lead administration induced nephrotoxicity significantly ($p< 0.05$) evidenced by elevation of serum and renal lead concentration with inhibition of serum δ ALAD activity. These results are in accordance with ***Manoj Kumar et al.*** [3] and ***Velaga et al.*** [24] δALAD is an indicator enzyme for lead toxicity and its activity is inhibited when lead binds to its active center. Lead toxicity increases the excretion of accumulated δ ALAD into the urine. The accumulated δ ALAD may autooxidize to - form reactive oxygen species and in this way induces lipid peroxidation [25]. The elevation of lead in kidney tissues is attributed to that the kidney may be a major target organ of lead toxicity, and that the epithelial cells of proximal convoluted tubules and Bowman's capsule seem to be more sensitive to lead induced nephrotoxicity. The proximal convoluted tubules are the primary sites of reabsorption and active transport leading to higher concentration of lead in the epithelial lining of these tubules [26].

Oral administration of coriander and fennel seeds extracts restored delta amino levulinic acid activity in lead-toxicated rats; this finding is in agreement with ***Kansal et al.*** [26] and ***Manoj Kumar et al.*** [3] who reported that natural herbs contain polyphenolic compounds acts as antioxidants which scavenge free radicals and thus regulate the level of δALAD enzyme activity**.** Also phenolic compounds potentiate the removal of lead by their metal chelating ability**.** Coriander may contain some chelating agent which has an affinity for the lead ion. Phytic acid (PA), a major phosphorus storage compound in most seeds and cereal grains, is known as a natural chelating agent. PA has strong ability to chelate multivalent metal ions result in the formation of very water-insoluble salts that are poorly absorbed from the gastrointestinal tract and consequently poor bioavailability [27]**.** Quercetin which present in coriander and fennel chelates lead by forming a coordination bond with the lead ions through its ortho-phenolic groups located on the quercetin B ring[28].As well as, regulating the ROS level in the kidney of rats, which might be ascribed to its ability to scavenge and prevent free radical generation[29] **.**

The present study declared a significantly elevation in all kidney function tests with reduction in creatinine clearance accompanied by increase in serum sodium and potassium concentration and decrease their concentration in urine in lead-treated rats. These results are confirmed with ***Suleman et al.***[30]***; Ramya and Prasanna*** [31] and ***Taha et al.***[32]**.** Lead accumulation in kidney cause damage in renal tubules, decreasing the number of the functional nephrons which weakens the reabsorption process and generate reactive oxygen species which damage the cells leads to apoptosis, these adverse effects on renal function resulted in elevation of nitrogen containing compounds as urea, creatinine and uric acid in the blood, proteinuria and reduction in creatinine clearance.

The increased level of blood urea and creatinine concentration in lead-toxicated rats suggests the inability of the kidney to excrete these products causing their increase in blood and decrease their excretion in urine [33]. The increments in uric acid concentrations may be due to degradation of purines or to an increase of uric acid levels by either overproduction or inability of excretion as uric acid is the end product of the catabolism of tissue nucleic acid, i.e. purine and pyrimidine bases metabolism. The enhancement in the total urinary protein excretion is due to decrease reabsorption of low molecular weight proteins by injured tubules [34].

Chronic exposure to low-levels of lead resulted in electrolyte retention and elevation of sodium and potassium; this is due to lead effects on renal tubular transport mechanisms [35]. Another mechanism of increase sodium and potassium level is the decrease in functioning nephrons that trigger multiple adaptive processes in the hyper functioning remaining nephrons including augmented rates of electrolyte reabsorption [36].

A significant improvement in all kidney function tests and regulation of electrolyte concentration (sodium and potassium) in serum and urine were clearly evidenced after administration of coriander and fennel seeds extracts at the tested doses. These results are cooperated with ***Aissaoui et al.*** [37] ***and Saeed et al.*** [38]**.** The ameliorating effect of coriander and fennel seeds extracts on the kidney function biomarkers may be due to their diuretic, antihypertensive and naturetic effects resulting in increased renal blood flow and GFR, promoting water and potassium excretion and restoration of the daily rate of renal sodium excretion [37]**,** [39].

Moreover, some active components which present in coriander and fennel seeds extracts, including flavonoids, polyphenols and carotenoids have an antioxidant, anti-inflammatory and free radicals

scavenging activity [40]**.** Quercetin has ability to decrease arginine consumption in urea synthesis by inhibiting hepatic arginase makes arginine more available for the synthesis of proteins. Such effect would enhance renal regenerating capabilities, abolish the augmented tubular reabsorption of electrolytes by hyper functioning nephrons and decrease vascular resistance, thus improving renal blood flow and glomerular filtration rate [36].

A significant decrease in renal GSH as well as all antioxidant enzymes activities beside the increase of the renal levels of NO and MDA was noticed in lead-toxicated-rats. These results are confirmed with ***Liu et al*** [41]; ***Reddyet al.*** [42]; ***Elmendorf*** [43] and ***Manoj Kumar et al.*** [3].

Heavy metal depletes glutathione and protein bound sulfhydryl groups resulting in enhanced production of reactive oxygen species such as superoxide ions, hydroxyl radicals and hydrogen peroxide. These oxygen species resulted in lipid peroxidation [44].The changes in enzymatic antioxidant activity (CAT, GST, SOD) and non-enzymatic antioxidant (GSH)may be due to lead generation of ROS or by reducing the antioxidant cell defense system, depleting glutathione, inhibiting sulfhydryl dependent enzymes, interfering with some essential metals as copper needed for antioxidant enzymes or by increasing cell susceptibility to oxidative attack by altering membrane integrity and fatty acid composition. Since antioxidant enzymes depend on various essential trace elements as selenium, copper and zinc for proper molecular structure and enzymatic activity are potential targets for lead toxicity [45].

There is a positive linear correlation between lead levels in blood (also in kidney or aorta) and the increase in kidney NO concentration that could be explained by a stimulating effect of lead on the activity of NO synthase that catalyze the formation of NO and citrulline from L-arginine, O_2, and nicotinamide adenine dinucleotide phosphate (NADPH) [46]**.** It is shown that lead in small doses can directly stimulate the endothelial nitric oxide synthase (eNOS) gene transcription or expression [47].

From the present study, it could be noticed a significant elevation in plasma and renal antioxidant enzymes activity and GSH with reduction in the renal levels of NO and MDA in lead-treated rats on administration of coriander and fennel seeds extracts at the tested doses, this was in accordance with ***Shaheen et al.*** [48]***; Rabeh and Aboraya*** [49] and ***El Baz et al.*** [50].

Quercetin present in coriander and fennel seeds extracts is recognized to have a strong scavenging activity of oxygen radicals and protection against lipid and protein oxidation by reversing oxidant–antioxidant imbalance and regulation of NO bioavailability in serum and kidney [51]. Flavonoids and phenolic compounds present in fennel aqueous extract possess various free radicals scavenging mechanism, e.g. by scavenging or quenching free radicals, by chelating metal ions, or by inhibiting enzymatic systems responsible for the generation of free radicals [52]**.** ***Lux and Naidoo*** [53] stated that the main principal constituents of fennel plants, considerable concentrations of essential trace element such as iron, selenium, manganese and zinc were identified. These are involved in multiple biological processes as constituent of antioxidant enzyme systems. Iron is a cofactor of catalase, which plays a role in antioxidant defense systems by catalyzing the decomposition of hydrogen peroxide [54]. The trace elements selenium (Se), copper (Cu) and zinc (Zn) are important cofactors of antioxidant enzymes such as superoxide dismutase (Cu-SOD, Zn-SOD), glutathione peroxidase (GPX) as well as protein with antioxidant properties, ceruloplasmin (CRL, copper-binding protein). So, coriander and fennel contain a mixture of bioactive compounds as well as essential trace elements could be of value to stimulate the body self defense mechanisms against oxidative stress by the maintenance of glutathione contents.

6. CONCLUSION

Herbs extracts exhibited a significant dose-dependent ameliorative effect against lead induced-nephrotoxicity in rats in some parameters such as depletion of serum and renal lead concentration, restoration in the δ ALAD enzyme activity, normalization of serum creatinine and uric acid with regulation of electrolytes levels in serum and urine, raise enzymatic and non-enzymatic antioxidants levels and decrease the oxidants level in plasma and kidney.

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