

# Research Paper: Renal Protective Effects of L-Carnitine on Lead-Induced Nephropathy in Wistar Rats



Marzie Hejazy<sup>1\*</sup>, Davood Najafi<sup>1</sup>

1. Department of Basic Sciences, Faculty of Veterinary Medicine, University of Tabriz, Tabriz, Iran.



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## ABSTRACT

**Background:** Lead is a heavy metal used in industries in developing countries. Lead exposure remains a widespread problem. Lead may induce molecular damage in the kidney as a consequence of Reactive Oxygen Species (ROS) formation, induction of caspase-3, and apoptosis.

**Methods:** Thirty male Wistar rats (Mean±SD weight: 300±20 g) were randomly divided into 3 equal groups: control (normal saline, oral), lead group (lead 100 mg/kg/d, oral) and lead+L-Carnitine (lead 100 mg/kg+L-Carnitine 200 mg/kg, intraperitoneal injection) for one week. At the end of the experiment, plasma creatine kinase activity, plasma creatinine and urea concentrations and plasma Superoxide Dismutase (SOD), Glutathione Peroxidase (GPx), catalase and nitric oxide levels were determined. Glutathione and malondialdehyde levels in renal tissue were also measured.

**Results:** Creatine kinase, creatinine and urea levels increased significantly, in the group treated with lead (P<0.05), compared to the control group. Administration of L-Carnitine in (Lead+carnitine treated group) significantly (P<0.05) decreased creatine kinase activity and plasma urea and creatinine contents. Enzymatic activity (SOD, GPx, and CAT) decreased significantly in the lead group, in comparison with the control group (P<0.05). Treatment with L-Carnitine significantly retrieved the depletion in enzyme activity (P<0.05). However, there were no significant differences in the GPx parameter between the Lead+carnitine group, in comparison with the control group.

**Conclusion:** L-Carnitine administration in rats with lead-induced nephropathy led to improved kidney protection, due to the reduction of Lipid Peroxidation (LPO). Furthermore, L-Carnitine prevents the adverse effects of Reactive Oxygen Species (ROS), which is an important biomolecules mechanism.

\* Corresponding Author:

Marzie Hejazy, PhD

Address: Department of Basic Sciences, Faculty of Veterinary Medicine, University of Tabriz, Tabriz, Iran.

Tel: +98 (41) 36378743

E-mail: mhejazy@ut.ac.ir

## 1. Introduction

**L**ead is a heavy metal used in industries in developing countries. Lead exposure remains a widespread problem [1]. Research has revealed that encounter with this heavy metal at any level is unsafe in children and many studies have demonstrated the harmful impact of lead exposure in the development of the body systems. Some studies suggest a relationship between renal problems and exposure to lead [2]. Exposure to lead occurs due to contamination of water and food resources and air pollution. Lead has a lot of toxic effects on various organs of the body, including the kidney [3-5].

Lead exposure can affect the development of the kidney in the fetal or the neonatal period, or result in renal impairment in adults [2, 6]. Early lead exposure may alter glomerular development that may cause renal disease, even after lead has already disappeared from the body. This may explain the etiology of some idiopathic renal diseases, like poorly developed renal system and eventually renal impairment [7, 8]. One study showed that the deposition of iron in proximal tubular cells of the kidney, together with histopathological lesions are associated with remained lead in the kidney, after lead administration in rats through drinking water. The role of erythrocytes in lead-induced nephrotoxicity in vitro was investigated in a co-culture system and in vivo in rats. The erythrophagocytosis of lead exposure in renal tubular cells contributes to lead-related renal damage [9].

L-Carnitine is an amino acid derivative, mainly obtained from food. It is also synthesized endogenously from the essential amino acids like methionine and lysine [10, 11]. Carnitine is an essential cofactor for translocation of active fatty acid. This transport is essential to allow  $\beta$ -mitochondrial oxidation of long-chain fatty acids and provide energy to cells [12]. L-Carnitine is an antioxidant that plays a preventive role in accumulation of lipid peroxidation end-products [13, 14].

L-Carnitine has successfully been applied in the treatment of different diseases. Beneficial roles of L-Carnitine has been demonstrated in several studies, such as cisplatin-induced injury of renal and small bowel, gentamicin nephrotoxicity, kidney ischemia-reperfusion, and chronic renal failure [15, 16]. L-Carnitine plays a preventive role in Reactive Oxygen Species (ROS) formation and decreases biomolecule damage. Furthermore, L-Carnitine has a sequestering role on ROS and a preventive role against renal toxicity of cisplatin, cyclosporine A, gentamicin, and doxorubicin [17-20]. The pres-

ent study investigated the protective role of L-Carnitine against lead-induced nephrotoxicity in rats.

## 2. Materials and Methods

### Animal treatment

Thirty male Wistar rats (Mean $\pm$ SD weight:300 $\pm$ 20 g) were housed in a standard controlled room, temperature (22 $^{\circ}$ C $\pm$ 2 $^{\circ}$ C), lighting (12:12 h light:dark cycle), humidity (40%-50%) and were fed with standard pallet diet. All animals had access to food and water ad libitum. The study was approved by University of Tabriz in accordance with the protocol of animal care and use, as well as the protocol provided by the Research Ethics Committee of the Medical Education in Iran (adapted April 17, 2006). Rats were randomly divided into 3 equal groups: 1. Control group: rats that received a single oral administration of normal saline for 7 days; 2. Lead group: rats that were treated with a single oral dose of lead 100 mg/kg/d for 7 days; and 3. Lead+L-Carnitine group: rats that were treated with a single oral dose of lead 100 mg/kg/d+L-Carnitine (200 mg/kg, intraperitoneal), for 7 days. All groups received the same volume of administration.

### Biochemical and Hematological assay

The rats were anesthetized with chloroform on day 8 and blood samples were taken by decapitation. Blood samples were immediately divided as per following: 1. EDTA-containing anticoagulant tube for hematology tests; and 2. A sample for the biochemical test. Blood serum was separated using centrifugation at 3000 rpm for 10 minutes and was stored at -20 $^{\circ}$ C until use. The kidney tissues were stored at -80 $^{\circ}$ C until use.

### Urea, creatinine, and creatine kinase activity assays

Plasma levels of creatinine and urea were evaluated with standard diagnostic kits (Pars Amazon, Iran). The activity of plasma Creatine Kinase (CK), an indicator of myopathy, was measured spectrophotometrically, using a standard diagnostic kit (Pishtaz Teb, Iran).

### Nitrate and nitrite assay

Nitrate and nitrite are the main oxidation products of Nitric Oxide (NO) which are used as an indicator of nitric oxide synthesis. The NO content of plasma was determined spectrophotometrically at 545 nm, based on the Griess reaction, using a mixture of naphthyl enylenediamine and sulfanilamide [21]. The samples were deproteinized. Nitrate was reduced to copper-coated cadmium

**Table 1.** Plasma biochemical test results in the control and treated rats

Experimental Groups	Urea (mg/dL)	Creatinine (mg/dL)	CK (U/L)	NO ( $\mu\text{mol/L}$ )
Control (n=10)	42.6 <sup>a</sup>	0.67 <sup>a</sup>	350.21 <sup>a</sup>	27.34 <sup>a</sup>
Lead (n=10)	302.53 <sup>b</sup>	4.23 <sup>b</sup>	839.21 <sup>b</sup>	15.84 <sup>b</sup>
Lead+Carnitine (n=10)	185.28 <sup>c</sup>	2.04 <sup>c</sup>	651.58 <sup>c</sup>	21.21 <sup>c</sup>
SEM	1.77	0.02	27.48	0.70

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Medical Toxicology & Forensic Medicine

Data are presented as the Mean $\pm$ SEM. CK: Creatine Kinase; NO: Nitric Oxide; a: Significant difference between controls, lead, Lead+Carnitine group,  $P<0.05$ ; b: Significant difference between controls and the lead group,  $P<0.05$ ; c: Significant difference between lead group and lead+Carnitine group,  $P<0.05$ .

nitrite in glycine buffer (pH 9.7). The sum of nitrite and nitrate contents (mmol/L) was measured using a standard sodium nitrate solution.

### Determination of glutathione and malondialdehyde levels

The samples of kidney tissue were homogenized in iced KCl for the measurement of glutathione and Malondialdehyde (MDA) levels. The homogenates were centrifuged at 3000 rpm for 15 minutes. MDA concentrations and lipid peroxidation indicator were measured spectrophotometrically at 532 nm and expressed as nmol MDA/mg in kidney tissue [22]. The Glutathione level (GSH) was determined spectrophotometrically at 412 nm, according to the Ellman's method and was expressed in mmol/g [23].

### Antioxidant enzyme measurement

The activity of Superoxide Dismutase (SOD) was determined with commercial kit for SOD activity mea-

surement (Randox Co.) SOD activity is expressed in U/mg proteins [24].

Catalase activity based on decomposition of  $\text{H}_2\text{O}_2$  was measured spectrophotometrically, at 230 nm. The results are expressed as a speed/mg constant of homogenized protein [25]. The activity of Glutathione Peroxidase (GPx) was assayed by Randox commercial kit at 340 nm [26]. The results are reported as U/mg proteins. The protein content of the plasma samples was determined [27].

### 3. Results

As shown in Table 1, concentrations of CK, creatinine and urea significantly increased ( $P<0.05$ ) in the lead group, compared to the control group. L-carnitine in (Lead+Car group) significantly ( $P<0.05$ ) decreased CK, urea and creatinine content in plasma. The plasma concentrations of NO significantly decreased in the lead group, compared to the controls. The nitric oxide levels were significantly elevated in the lead+carnitine group, compared to the lead group.

**Table 2.** Oxidative stress parameters in the control and treated rats

Experimental Groups	MDA (nmol/mg-Tissue)	GSH ( $\mu\text{mol/g}$ Tissue)	SOD (U/mg Protein)	CAT ( $\mu\text{g/mg}$ Protein)	GPx(U/mg Protein)
Control (n=10)	0.43 <sup>a</sup>	3.46 <sup>a</sup>	9.48 <sup>a</sup>	0.56 <sup>a</sup>	2.06 <sup>a</sup>
Lead (n=10)	0.79 <sup>b</sup>	0.93 <sup>b</sup>	7.25 <sup>b</sup>	0.28 <sup>b</sup>	1.14 <sup>b</sup>
Lead+Carnitine (n=10)	0.61 <sup>c</sup>	1.93 <sup>c</sup>	7.92 <sup>c</sup>	0.42 <sup>c</sup>	1.70 <sup>a</sup>
SEM	0.04	0.09	0.14	0.02	0.10

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Data are presented as the Mean $\pm$ SEM. MDA: Malondialdehyde; GSH: Glutathione; SOD: Superoxide Dismutase; CAT: Catalase; and GPx: Glutathione Peroxidase. a: Significant difference between controls, lead, Lead+Carnitine group,  $P<0.05$ ; b: Significant difference between controls and lead group,  $P<0.05$ ; c: Significant difference between the lead group and lead+Carnitine group,  $P<0.05$ .

According to [Table 2](#), the levels of MDA in the renal tissue significantly increased ( $P < 0.05$ ) in the lead group, compared to the controls. The lead+Carnitine group showed a significant decrease in MDA levels, compared to the lead group. The lead group showed a significantly decreased antioxidant enzymatic activity (SOD, GPx and CAT), compared to the control group. L-Carnitine significantly improved enzyme activity. However, there were no significant differences between the lead+Carnitine group and the controls with regard to the GPx parameter. The levels of GSH decreased in the lead group, compared to the controls. Administration of L-carnitine increased GSH levels significantly ( $P < 0.05$ ).

#### 4. Discussion

The results showed that treatment with L-Carnitine reduced CK activity, BUN levels, creatinine and alleviated MDA production, and the reduction of GSH. L-Carnitine has antioxidant effects and plays protective roles against oxidative stress in various tissues, including the kidney [[28](#), [29](#)]. Administration of L-Carnitine has been shown to inhibit the formation of MDA in serum and renal tissues, in response to renal impairment, due to ischemia-reperfusion [[30](#)].

Carnitine improves the antioxidant enzymes activities including SOD, GPx and CAT and increases GSH levels, and reduces the MDA concentration in rat renal tissues [[31](#)]. One study showed that L-Carnitine prevents the formation of MDA and improves GSH levels in the heart, kidney, aorta and cavernous bodies, and decreases plasma levels of creatinine and urea in rats afflicted with chronic renal failure [[32](#)]. We demonstrated that treatment with L-Carnitine, restored the activity of SOD, CAT and GSH and decreased the levels of MDA in the lead+Carnitine group.

Nitric oxide plays a crucial role in moderating tissue lesions and normal blood circulation in the healthy kidney, as well as various pathological renal diseases. In the present study, treatment with L-Carnitine significantly increased nitric oxide levels. Plasma or serum CK activity is a marker for muscle damage [[33](#), [34](#)]. The results showed a protective effect of L-Carnitine against muscle damage. Although L-Carnitine is known to protect renal tissue from chemotherapy agents, no studies investigated its effect on radiation-induced nephrotoxicity. Carnitine protects tissues through the elimination of oxygen radicals and other mechanisms [[35-37](#)].

This evidence may provide a preventive/therapeutic strategy for the lead-induced nephropathy. Previous stud-

ies reported antioxidant and protective effects of L-Carnitine against oxidative damage in various tissues, including the kidney [[32](#), [38](#), [39](#)]. Administration of L-Carnitine inhibited the MDA formation in the serum and renal tissue, in renal ischemia-reperfusion injury [[13](#), [40](#), [41](#)].

Although the exact mechanism of renal toxicity caused by lead is illustrated, there is evidence that lead can cause the formation of reactive oxygen metabolites and diminish the renal antioxidant enzyme activities [[5](#), [42](#)]. Studies showed that lead could induce DNA damage in renal tissue and that these effects are associated with free radicals formation, resulting in caspase-3-dependent apoptosis [[42](#), [43](#)].

#### 5. Conclusion

The present study indicate that ROS formation, lipid peroxidation, the exhaustion of the antioxidant state and decrease of NO levels may be involved in the pathophysiological mechanisms of lead-induced nephrotoxicity. Although our data do not define the precise mechanism of action of L-Carnitine in preventing lipid peroxidation, the reduction of ROS and decrease in antioxidant depletion and the improvement of NO levels may be the putative mechanisms in this model. Eventually, we hypothesized that L-Carnitine improves tissue health by decreasing oxidative parameters in lead-induced nephropathy.

#### Ethical Considerations

##### Compliance with ethical guidelines

The study was approved by University of Tabriz in accordance with the protocol of animal care and use, as well as the protocol provided by the Research Ethics Committee of the Medical Education in Iran (adapted April 17, 2006).

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##### Conflict of interest

The authors certify that they have no affiliation with or involvement in any organization or entity with any financial interest, or non-financial interest in the subject matter or materials dismissed in this manuscript.



## References

- [1] Liu CM, Sun YZ, Sun JM, Ma JQ, Cheng C. Protective role of quercetin against lead-induced inflammatory response in rat kidney through the ROS-mediated MAPKs and NF- $\kappa$ B pathway. *Biochimica et Biophysica Acta- General Subjects*. 2012; 1820(10):1693-703. [DOI:10.1016/j.bbagen.2012.06.011] [PMID]
- [2] Basgen JM, Sobin C. Early chronic low-level lead exposure produces glomerular hypertrophy in young C57BL/6 mice. *Toxicology Letters*. 2014; 225(1):48-56. [DOI:10.1016/j.toxiclet.2013.11.031] [PMID] [PMCID]
- [3] Mudipalli A. Lead hepatotoxicity & potential health effects. *Indian Journal of Medical Research*. 2007; 126(6):518-27. [PMID]
- [4] Pande M, Flora SJ. Lead induced oxidative damage and its response to combined administration of  $\alpha$ -lipoic acid and succimers in rats. *Toxicology*. 2002; 177(2):187-96. [DOI:10.1016/S0300-483X(02)00223-8]
- [5] Abdel-Moneim AE, Dkhil MA, Al-Quraishy S. The potential role of flaxseed oil on lead acetate-induced kidney injury in adult male albino rats. *African Journal of Biotechnology*. 2011; 10(8):1436-41.
- [6] Fadrowski JJ, Navas-Acien A, Tellez-Plaza M, Guallar E, Weaver VM, Furth SL. Blood lead level and kidney function in US adolescents: The third national health and nutrition examination survey. *Archives of Internal Medicine*. 2010; 170(1):75-82. [DOI:10.1001/archinternmed.2009.417] [PMID] [PMCID]
- [7] Buyuklu M, Kandemir FM, Ozkaraca M, Set T, Bakirci EM, Topal E. Protective effect of curcumin against contrast induced nephropathy in rat kidney: What is happening to oxidative stress, inflammation, autophagy and apoptosis. *European Review for Medical and Pharmacological Sciences*. 2014; 18(4):461-70. [PMID]
- [8] Keller G, Zimmer G, Mall G, Ritz E, Amann K. Nephron number in patients with primary hypertension. *New England Journal of Medicine*. 2003; 348(2):101-8. [DOI:10.1056/NEJMoa020549] [PMID]
- [9] Kwon SY, Bae ON, Noh JY, Kim K, Kang S, Shin YJ, et al. Erythrophagocytosis of lead-exposed erythrocytes by renal tubular cells: Possible role in lead-induced nephrotoxicity. *Environmental Health Perspectives*. 2015; 123(2):120-7. [DOI:10.1289/ehp.1408094] [PMID] [PMCID]
- [10] Boyacioglu M, Turgut H, Akgullu C, Eryilmaz U, Kum C, Onbasili OA. The effect of L-Carnitine on oxidative stress responses of experimental contrast-induced nephropathy in rats. *The Journal of Veterinary Medical Science*. 2014; 76(1):1-8. [DOI:10.1292/jvms.13-0202] [PMID] [PMCID]
- [11] Ozsoy S, Ozsoy B, Ozyildiz Z, Aytakin I. Protective effect of L-Carnitine on experimental lead toxicity in rats: A clinical, histopathological and immunohistochemical study. *Biotech Histochem*. 2011; 86(6):436-43. [DOI:10.3109/10520295.2010.529825] [PMID]
- [12] Xiang Y, Piao S, Zou H, Jin J, Fang M, Lei D, et al. L-Carnitine protects against cyclosporine-induced pancreatic and renal injury in rats. *Transplantation Proceedings*. 2013; 45(8):3127-34. [DOI:10.1016/j.transproceed.2013.08.041] [PMID]
- [13] Aydogdu N, Atmaca G, Yalcin O, Taskiran R, Tastekin E, Kaymak K. Protective effects of L-Carnitine on myoglobinuric acute renal failure in rats. *Clinical and Experimental Pharmacology and Physiology*. 2006; 33(1):119-24. [DOI:10.1111/j.1440-1681.2006.04336.x] [PMID]
- [14] Ghalwash M, Elmasry A, El-Adeeb N. Effect of L-Carnitine on the skeletal muscle contractility in simvastatin-induced myopathy in rats. *Journal of Basic and Clinical Physiology and Pharmacology*. 2018; 29(5):483-91. [DOI:10.1515/jbb-cpp-2017-0156] [PMID]
- [15] Heidari R, Jafari F, Khodaei F, Shirazi Yeganeh B, Niknahad H. Mechanism of Valproic acid-induced Fanconi syndrome involves mitochondrial dysfunction and oxidative stress in rat kidney. *Nephrology*. 2018; 23(4):351-61. [DOI:10.1111/nep.13012] [PMID]
- [16] Collins HL, Drazul Schrader D, Sulpizio AC, Koster PD, Williamson Y, Adelman SJ, et al. L-Carnitine intake and high trimethylamine N-oxide plasma levels correlate with low aortic lesions in ApoE<sup>-/-</sup> Transgenic mice expressing CETP. *Atherosclerosis*. 2016; 244:29-37. [DOI:10.1016/j.atherosclerosis.2015.10.108] [PMID]
- [17] Kopple JD, Ding H, Letoha A, Ivanyi B, Qing DPY, Dux L, et al. L-Carnitine ameliorates gentamicin-induced renal injury in rats. *Nephrology Dialysis Transplantation*. 2002; 17(12):2122-31. [DOI:10.1093/ndt/17.12.2122]
- [18] Boonsanit D, Kanchanapangka S, Buranakarl C. L-Carnitine ameliorates doxorubicin-induced nephrotic syndrome in rats. *Nephrology*. 2006; 11(4):313-20. [DOI:10.1111/j.1440-1797.2006.00592.x] [PMID]
- [19] Chang B, Nishikawa M, Sato E, Utsumi K, Inoue M. L-Carnitine inhibits Cisplatin-induced injury of the kidney and small intestine. *Archives of Biochemistry and Biophysics*. 2002; 405(1):55-64. [DOI:10.1016/S0003-9861(02)00342-9]
- [20] Origlia N, Migliori M, Panichi V, Filippi C, Bertelli A, Carpi A, et al. Protective effect of L-propionylcarnitine in chronic cyclosporine-a induced nephrotoxicity. *Biomedicine & Pharmacotherapy*. 2006; 60(2):77-81. [DOI:10.1016/j.biopha.2005.06.014] [PMID]
- [21] Cortas NK, Wakid NW. Determination of inorganic nitrate in serum and urine by a kinetic cadmium-reduction method. *Clinical Chemistry*. 1990; 36(8):1440-3. [PMID]
- [22] Ohkawa H, Ohishi N, Yagi K. Assay for lipid peroxides in animal tissues by thiobarbituric acid reaction. *Analytical Biochemistry*. 1979; 95(2):351-8. [DOI:10.1016/0003-2697(79)90738-3]
- [23] Ellaman G. Tissue sulfhydryl group. *Archives of Biochemistry and Biophysics*. 1959; 82(1):70-7. [DOI:10.1016/0003-9861(59)90090-6]
- [24] Sun Y, Oberley LW, Li Y. A simple method for clinical assay of superoxide dismutase. *Clinical Chemistry*. 1988; 34(3):497-500. [PMID]
- [25] Aebi H. [13] Catalase in vitro. *Methods in Enzymology*. 1984; 105:121-6. [DOI:10.1016/S0076-6879(84)05016-3]
- [26] Lawrence RA, Burk RF. Glutathione peroxidase activity in selenium-deficient rat liver. *Biochemical and Biophysical Research Communications*. 1976; 71(4):952-8. [DOI:10.1016/0006-291X(76)90747-6]
- [27] Lowry OH, Rosebrough NJ, Farr AL, Randall RJ. Protein measurement with the Folin phenol reagent. *Journal of Biological Chemistry*. 1951; 193(1):265-75. [PMID]

- [28] Liu X, Zhong F, Tang XL, Lian FL, Zhou Q, Guo SM, et al. Cordyceps sinensis protects against liver and heart injuries in a rat model of chronic kidney disease: A metabolomic analysis. *Acta Pharmacologica Sinica*. 2014; 35(5):697-706. [DOI:10.1038/aps.2013.186] [PMID] [PMCID]
- [29] Bonomini M, Di Liberato L, Del Rosso G, Stingone A, Marinangeli G, Consoli A, et al. Effect of an L-Carnitine-Containing Peritoneal Dialysate on Insulin sensitivity in patients treated with CAPD: A 4-Month, prospective, multicenter randomized trial. *American Journal of Kidney Diseases*. 2013; 62(5):929-38. [DOI:10.1053/j.ajkd.2013.04.007] [PMID]
- [30] Edres HA, Taha NM, Mandour AW, Lebda MA. Impact of L-Carnitine on Bisphenol A-induced kidney damage in rats. *Alexandria Journal for Veterinary Sciences*. 2018; 56(1):11-7. [DOI:10.5455/ajvs.283744]
- [31] Mafra D, Borges NA, de Franca Cardozo LFM, Anjos JS, Black AP, Moraes C, et al. Red meat intake in chronic kidney disease patients: Two sides of the coin. *Nutrition*. 2018; 46:26-32. [DOI:10.1016/j.nut.2017.08.015] [PMID]
- [32] Sener G, Paskaloglu K, Satiroglu H, Alican I, Kaçmaz A, Sakarcan A. L-Carnitine ameliorates oxidative damage due to chronic renal failure in rats. *Journal of Cardiovascular Pharmacology*. 2004; 43(5):698-705. [DOI:10.1097/00005344-200405000-00013] [PMID]
- [33] Marcovina SM, Sirtori C, Peracino A, Gheorghide M, Borum P, Remuzzi G, et al. Translating the basic knowledge of mitochondrial functions to metabolic therapy: Role of L-Carnitine. *Translational Research*. 2013; 161(2):73-84. [DOI:10.1016/j.trsl.2012.10.006] [PMID] [PMCID]
- [34] Armaly Z, Qader AA, Jabbour A, Hassan K, Ramadan R, Bowirrat A, et al. Effects of carnitine on oxidative stress response to intravenous iron administration to patients with CKD: Impact of haptoglobin phenotype. *BMC Nephrology*. 2015; 16:135. [DOI:10.1186/s12882-015-0119-0] [PMID] [PMCID]
- [35] Caloglu M, Yurut Caloglu V, Durmus Altun G, Oz Puyan F, Ustun F, Cosar Alas R, et al. Histopathological and scintigraphic comparisons of the protective effects of L-Carnitine and amifostine against radiation-induced late renal toxicity in rats. *Clinical and Experimental Pharmacology and Physiology*. 2009; 36(5-6):523-30. [DOI:10.1111/j.1440-1681.2008.05103.x] [PMID]
- [36] Nasri H, Abedi Gheshlaghi Z, Rafieian Kopaei M. Curcumin and kidney protection; current findings and new concepts. *Acta Persica Pathophysiologica*. 2018; 1:e01-6.
- [37] Samir SM, Abbas AM, Safwat SM, Elserougy HG. Effect of L-Carnitine on diabetes-induced changes of skeletal muscles in rats. *Journal of Basic and Clinical Physiology and Pharmacology*. 2018; 29(1):47-59. [DOI:10.1515/jbcpp-2016-0185] [PMID]
- [38] Rani PJA, Panneerselvam C. Effect of L-Carnitine on brain lipid peroxidation and antioxidant enzymes in old rats. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences*. 2002; 57(4):B134-B7. [DOI:10.1093/gerona/57.4.B134] [PMID]
- [39] Arslan E, Milcan A, Ünal S, Demirkan F, Polat A, Bağdatoglu Ö, et al. The effects of carnitine on distally-burned dorsal skin flap: An experimental study in rats. *Burns*. 2003; 29(3):221-7. [DOI:10.1016/S0305-4179(02)00305-4]
- [40] Ergün O, Ulman C, Kiliçalp AS, Ulman I. Carnitine as a preventive agent in experimental renal ischemia-reperfusion injury. *Urological Research*. 2001; 29(3):186-9. [DOI:10.1007/s002400100176] [PMID]
- [41] Lv S, Cheng J, Sun A, Li J, Wang W, Guan G, et al. Mesenchymal stem cells transplantation ameliorates glomerular injury in streptozotocin-induced diabetic nephropathy in rats via inhibiting oxidative stress. *Diabetes Research and Clinical Practice*. 2014; 104(1):143-54. [DOI:10.1016/j.diabres.2014.01.011] [PMID]
- [42] Liu CM, Ma JQ, Sun YZ. Puerarin protects rat kidney from lead-induced apoptosis by modulating the PI3K/Akt/eNOS pathway. *Toxicology and Applied Pharmacology*. 2012; 258(3):330-42. [DOI:10.1016/j.taap.2011.11.015] [PMID]
- [43] Liu CM, Ma JQ, Sun YZ. Quercetin protects the rat kidney against oxidative stress-mediated DNA damage and apoptosis induced by lead. *Environmental Toxicology and Pharmacology*. 2010; 30(3):264-71. [DOI:10.1016/j.etap.2010.07.002] [PMID]