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Effect of Taurine against Lead Induced Nephrotoxicity in Rats.

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ABSTRACT

The present study was designed to investigate the effect of taurine(Tau) against renal injury induced by lead in rats. Rats were randomly assigned to control, lead-treated (60 mg/kg/day) group, three different doses of taurine-treated (200 mg/kg/day, Tau200; 400 mg/kg/day, Tau400; 800 mg/kg/day, Tau800)groups. Lead was administered daily to rats through their drinking water, and taurine was administered by intragastric gavage. By the end of the 8th week, the blood lead concentration, kidney-viscera coefficient, activities of catalase(CAT), glutathione(GSH) and superoxide dismutase(SOD); level of malondialdehyde(MDA) in kidney tissues; serum levels of creatinine (CR)and urea nitrogen(BUN), the activity of ATPase in kidney tissues were determined following taurine treatment. Taurine was found to be effective in (1) decreasing the blood lead concentration, catalase, creatinine and urea nitrogen, which had been increased by lead exposure; (2) reducing malondialdehyde levels, an end-product of lipid peroxidation; (3) increasing glutathione levels that had been diminished by lead; and (4) improving ATPase activity of kidney tissues. These results indicated that taurine can partly prevent the kidney injury induced by lead.

Keywords: taurine; lead; nephrotoxicity; rats; AT Pase

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INTRODUCTION

Lead is an accumulative toxic element that has no known beneficial or desirable nutritional effect on animals (Teresa and Laura, 1997). The persistence of lead in the animals and humans and the associated health risk is a topic of current debate and concern (Juberg DR et al., 1997).Lead may exert toxic effects on several organ systems, liver, kidneys and brain have been considered as the target organs, but those on the kidney are the most insidious. Chronic exposure to this biotoxicant leads to its accumulation in these organs with maximum concentration per gram weight of tissue being recorded in kidneys.

The mechanisms of lead-induced toxicities have been explained in different ways. Beside its competition with essential metals like calcium and zinc, and its high affinity to thiol groups in proteins; the production of reactive oxygen species (Husain et al., 1997)as well as depressing endogenous antioxidants and enhancing lipid peroxidation have recently been reported as lead-induced effects (Othman and Missiry,1998; Missiry,2000). Many environmental toxicants with toxicity to the kidney have been identified in animal experiments. Lead is known to produce characteristic pathobiology changes in structure and function (Khalil et al.,1992) .Lead toxicity is notable for the presence of intranuclear inclusion bodies in kidney tubular epithelial cells. The intranuclear inclusions in acute and chronic lead poisoning have a characteristic ultrastructural morphology(Stiller and Friedrich, 1983)and a unique protein composition which may be responsible lead sequestration (Shelton and Egle,1982). Rats exposed to one or three injections of lead exhibited increased glutathione *S*-transferase (GST) activity in kidney(Planas and Elizalde, 1992).

Lead alone or in combination with cadmium produced a signicant inhibition of alkaline phosphatase activity in the kidneys and lead intoxication produced a strong inhibition of Na^{+}-K^{+}ATPase as well as Ca^{2+}-Mg^{2+} ATPase.

Taurine(Tau) is a β-amino acid and a kind of sulfur-bearing amino acid found in all tissues of most animal species and is the most abundant free amino acid in many tissues(Huxtable RJ,1992). Tau has been proposed to participate in the cellular mechanisms involved in the protection against oxidative damage, especially in the inhibition of lipid peroxidation (Bruna et al., 1995). The aim of the present study is to investigate of possible ameliorative effects of taurine on lead induced nephrotoxicity.

MATERIALS AND METHODS

Chemicals:

Taurine (99% purity) was obtained from Hebei New Century Chemical Co. Ltd. (Hengshui, China). Diagnostic kits for the activity or levels of SOD, GSH, CAT, MDA, Na^{+}-K^{+}ATPase, Ca^{2+}-Mg^{2+} ATPase, total protein, were all purchased from Nanjing Jiancheng Bioengineering Institute (Nanjing, China). The assay kits for creatinine (CR) and blood urea nitrogen (BUN) were purchased from Bio Sino Bio-technology and Science Inc (Beijing, China). All other chemicals were purchased from Sigma (St. Louis, MO).

Animals and experimental design:

All experiments were performed with male wistar rats weighing 100-125 g, purchased from Animal Experiment Center of Hubei Health Epidemic Prevention Station (Wuhan, China). The animals were housed in stainless steel cages in a temperature controlled room (22°C) with a 12 h light: dark cycle. They were fed with standard rat chow (Purina rat chow). The animals were randomized into five groups. Control group (n=8) served as the control and was given only standard rat chow and water for 8 weeks. Lead group(n=8) received 6mg/ml lead acetate in drinking water for 4 weeks and received distilled water for 4 weeks. Taurine-treated groups (n=7) received 6mg/ml lead acetate in drinking water for 4 weeks and then received 200mg/kg/day (Tau200), 400mg/kg/day (Tau400), 800mg/kg/day (Tau800) taurine in drinking water for 4 weeks respectively.

Sample collection:

On the 8th week, no food was supplied, as the experimental protocol scheduled only drinking water availability on the 12 h before sacrifice. Then rats were anesthetized with metofane, half of the blood samples were processed immediately for biochemical investigation and the rest blood samples was collected for wet

digestion for estimation of lead content. The collected kidneys were washed with 0.9% NaCl and immediately weighed, then kept at −80◦C for further analysis.

Analysis of metal:

Blood samples were wet digestion with perchloric and nitricacids, and the concentrations of lead in the digested samples were measured using an atomic absorption spectrophotometer (Spectra-240FSPE3110, purchase from corporation761 Main Ave, Norwalk, USA), at 217 nm wavelength and 6 ma current. The values were expressed "µg/g".

Enzymatic antioxidant activities and MDA levels:

The tissues were comminuted using liquid nitrogen. The activity of SOD, CAT, GSH, as well as MDA levels and protein content in the kidney tissues were measured by spectrophotometer (Unico UV2102, America) using commercial assay kits according to the manufacturer's directions, respectively. The total protein in the tissue homogenates was determined via the Coomassie Brilliant Blue method. The SOD activity was determined via the xanthine oxides method. GSH levels were determined using the method developed by Winters (1995). The CAT activity was spectrophotometrically measured and expressed as U/mg protein based on the rate of decrease of hydrogen peroxide. The concentrations of the lipid peroxidation product MDA in the kidney homogenates were determined via the thiobarbituric acid reactive substance assay base on the reaction of MDA with thiobarbituric acid to produce a complex that can be spectrophotometrically determined.

Detection of biochemistry parameters in serum and kidney:

Blood of CR, BUN, kidney ATPase activity were detected by spectrophotometer (Unico UV2102, America) using commercial assay kits according to the manufacturer's directions, respectively. Serum CR and BUN were analyzed using the Hitachi7100 automated biochemical analyzer. The kidney ATPase activity was spectrophotometrically measured and expressed as U/mgprot based on the ATPase decomposed the ATP and generate the amount of inorganic phosphorus.

Statistical analysis:

The results were reported as the mean±standard deviation. The quantitative differences between the groups were established by student's t-test. Statistical significance was accepted at $P<0.05$.

RESULTS

The kidney-viscera coefficient:

The kidney-viscera coefficient was defined as the ratio of the kidney weight to the total body weight of the rats. As shown in table 1, the kidney-viscera coefficient was significantly decreased by 6.79% ($P<0.01$) in the lead-treated group compared with the control group. The kidney-viscera coefficient in all the treatment groups remained lower than the control but higher than lead treated rats. And the kidney-viscera coefficient of treatment groups of Tau400 and Tau800 had significant difference when compared with lead-treated group ($P<0.05$).

Table 1: The kidney viscera coefficients in control and experiment groups at the end of 8 weeks.

Group	Kidney weight(g)	Body weight (g)	Ratio(mg/g)
Control	1.31±0.08	208.11±6.67	6.18±0.35
Lead	1.22±0.07	205.67±6.17	5.76±0.12$^{\#}$
Tau200	1.27±0.07	204.81±13.81	6.14±0.34
Tau400	1.27±0.08	205.12±10.67	6.31±0.63*
Tau800	1.29±0.05	209.69±13.81	6.23±0.43*

Significant when compared with the control group:$^{\#}P<0.05$.
Significant when compared with the lead treated group:*$P<0.05$.

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Lead concentration in blood:

Fig 1. The effects of taurine on blood lead concentration

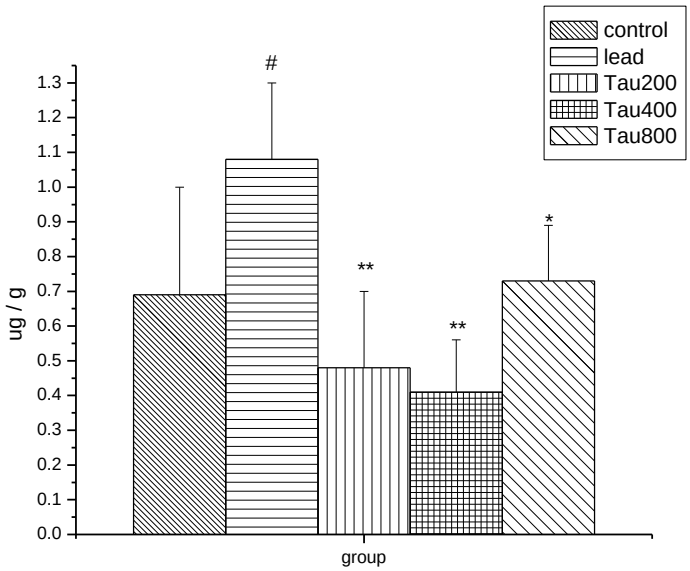

Fig 1: The effects of taurine on blood lead concentration. Data are expressed as the mean values obtained from three experiments. $^{\#}P$<0.05when compared with the control group. *P<0.05, **P<0.01 when compared with the lead treated group.

Figure 1 show the blood lead concentration of five groups at the end of the 8th week. Animals given lead for 4 weeks and allowed 4 weeks to cover had significantly higher blood lead levels than control rats(P<0.01).The blood lead levels in all the treatment groups remained higher than the control but showed insignificant difference from the control values. On the other hand, animals given lead for 4 weeks and allowed 4 weeks treatment with taurine had lower blood lead levels than lead treated rats(P<0.01 or *P*<0.05).

Kidney antioxidant enzymes and lipid peroxidation products

Table 2: The activity of antioxidant enzymes and MDA levels in the kidney of rats at the end of 8 weeks

Group	SOD (U/mgprot)	CAT (U/mgprot)	GSH (nmol/mg protein)	MDA (nmol/mg protein)
Control	53.7±3.5	22.1±3.1	45±2.7	25±1.6
Lead	41.2±2.6$^{\#\#}$	25.2±1.3	34±1.5$^{\#\#}$	43±2.7$^{\#\#}$
Tau200	48.5±1.5**	23.1±2.5	41±2.2*	32±1.5
Tau400	50.3±3.2**	24.3±1.8	42.4±2.4*	28±3.0*
Tau800	46.8±2.9*	23.2±2.3	40±1.8**	31.2±2.2*

Significant when compared with the control group:$^{\#}$P<0.05, $^{\#\#}$P<0.05.
Significant when compared with the lead treated group: *P<0.05, **P<0.01.

Table 2 represents the activities of antioxidant enzymes and the corresponding MDA levels. At the end of the treatment, SOD activity in lead-treated group was significantly decreased by 23.27% compared with the control group (P<0.01). However, when taurine was administered incombination with lead, SOD activity significantly increased by 17.7% in Tau200 group (P<0.01) and by 18.09% in Tau400 group (P<0.01) and by 6.95% in Tau800 group (P<0.05)compared with the lead-treated group. Lead exposure induced a significant increase in CAT activity of kidney tissues. Increased CAT activity in lead exposed cells was slightly decreased by further incubating the cells with taurine, although the results were not statistically.

Lead exposure significantly diminished GSH levels of kidney. GSH content of lead-exposed cells was notably increased in the taurine supplemented group. The MDA content in the lead-treated group was

significantly increased (P<0.01) compared with the control group. However, MDA content significantly decreased by further incubating the cells with taurine(P<0.05) compared with the lead group.

Clinical chemistry

BUN and CR concentrations were measured in the serum to monitor the toxic effect of lead and the protective effect of taurine. The BUN (Fig. 2) concentrations were significantly increased in the lead-treated group, compared with the control group (P<0.05). Increased CR (Fig. 3) in lead exposed rats was slightly decreased by further incubating with taurine, although the results were not statistically significant (P>0.05).

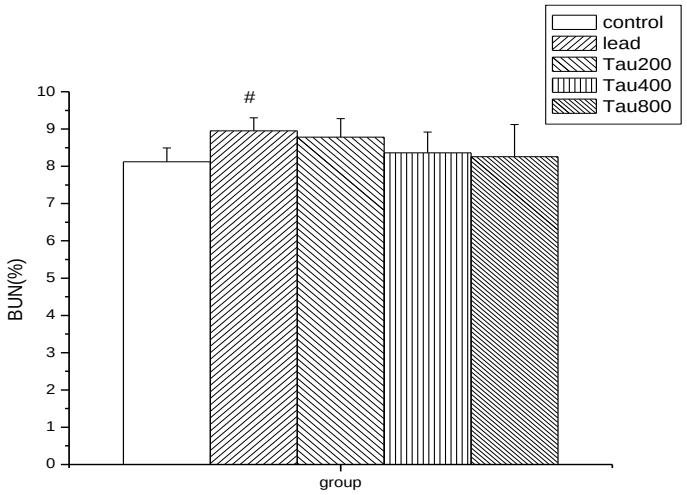

Fig 2: The effects of taurine on BUN. Data are expressed as the mean values obtained from three experiments. #P<0.05when compared with the control group.

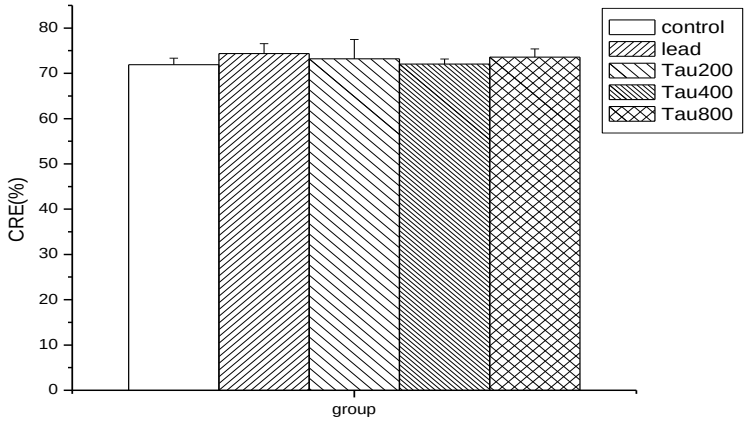

Fig 3: The effects of taurine on CR. Data are expressed as the mean values obtained from three experiments. ##P<0.05,##P<0.05when compared with the control group. *P<0.05, **P<0.01when compared with the lead treated group.

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ATPase activities of kidney in rats

Fig 4: The effects of taurine on activity of ATPase

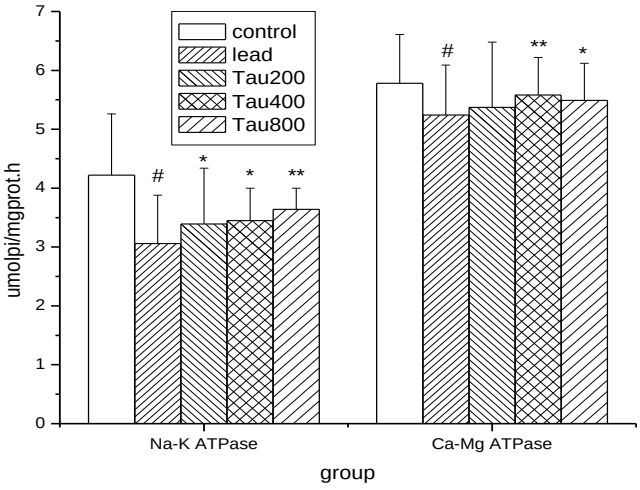

Fig 4: The effects of taurine on activity of ATPase. Data are expressed as the mean values obtained from three experiments. ##P<0.05, ##P<0.05 when compared with the control group. *P<0.05, **P<0.01 when compared with the lead treated group.

Fig 4 show the activity of ATPase: Na^+/K^+ATPase and Ca^{2+}/Mg^{2+}ATPase in the kidney. A significant decrease in Ca^{2+}-Mg^{2+}ATPase activity (*P*<0.05) and significant decrease in Na^+/K^+ATPase activity (*P*<0.05) in the kidney were recorded in lead treated rats as compared with the controls. Treatment with taurine during the last 4th week of the experiment significantly (*P*<0.01or *P*<0.05) increased the Na^+-K^+ATPase activities in the kidney, compared with lead group. Similarly, the Ca^{2+}-Mg^{2+}ATPase activities in rats given lead for 4 weeks and allowed 4 weeks treatment with taurine were significantly (*P*<0.01or*P*<0.05) higher than lead-treated group. No significant change could be noted in the Ca^{2+}-Mg^{2+}ATPase and Na^+-K^+ATPase activities in the group from the rats of different treatment groups.

DISCUSSION

Lead is one of the major pollutants in terms of global contamination and health impacts. Information about renal function modification and lead exposure has been reported (Batuman,1993; Benett,1985; Hong et al.,1980), including interstitial fibrosis, tubular atrophy, and decreased glomerular filtration, as well as its irreversible and asymptomatic evolution as a consequence of the exposure (Loghman,1997; Nolan and Shaikn,1992). In the present study, rats were subjected to exposure to lead for a period of 4 weeks followed by treatment with taurine in the 5th week. The results from this study indicated that lead-induced kidney impairment and the protective role of taurine in reducing the damage as evidenced by decreased BUN and CRE and increased Na^+/K^+ATPase and Ca^{2+}/Mg^{2+} ATPase activity in the kidney.

One of the main mechanisms of toxic action of lead is oxidative stress(Adonaylo and Oteiza,1999;Thurman et al.,1999; Husain et al.,2001; Patra et al.,2001;Tandon et al., 2002).

The kidney and the liver being organs playing a vital part in the metabolism of lead, are at especial risk of damage due to the oxidative action of these xenobiotics. SOD and CAT are the most important defense mechanisms against toxic effects of oxidative stress. (Kanbur et al., 2008; Karabacak et al., 2011; Liu et al., 2010; Mansour and Mossa, 2009). In the present study, free radical production as an outcome of oxidative stress induced by lead increased the activities of SOD and CAT in the rat kidney. The increased SOD and CAT may be the adaptive response of the body to ROS attack. The levels of MDA in lead-treated group were significantly increased compared with the control, this maybe the increases of SOD and CAT were not sufficient to protect the membrane lipids (Gargouri et al., 2011).

Serum BUN and CR are biochemical indicators of kidney damage. BUN and CR not only reflect the nitrogenous compounds metabolism in organism, but also the glomerular filtration function damage. In the present study, serum BUN and CR in lead treated rats had increased when compared with control group, the results confirmed other studies(Othman et al.,1998). Administration of taurine along with lead markedly hampered lead-induced toxic actions on kidney parameters. Serum BUN and CR in taurine treated rats had decreased when compared with lead treated rats. This may contribute to function as a direct antioxidant that scavenges or quenches oxygen free radicals, taurine can inhibit lipid peroxidation, and as an indirect antioxidant that prevents the increase in membrane permeability resulting from oxidant injury in many tissues (Chen,1993; Ganiyat et al., 2014). Moreover, taurine might lessen lead-induced oxidative injury either by forming chloramines, known to be more stable and less reactive molecules, with hypochlorous (HOCl) and HOCl-metalloproteins, or by binding free metal ions such as Fe2+ by its sulfonic acid group (Schuller-Levis et al., 1994).

ATPase is aglycoprotein that catalyzes the ATP hydrolysis, provides energyfor ion transportation, and has a great significance in maintaining renal tubular secretion and reabsorption. Other studies have indicated that the ATPase is susceptible to free radical-induced damage and can reverse the xenobiotics-induced reduction in ATPase activity (Lv et al., 2012). The Na+/ K+ pump catalyses the hydrolysis of ATP and couples it to the transport of Na+ and K+across the cell membrane thereby generating the transmembranous Na+/ K^+ gradient. Ca^{2+} ATPase catalyses the active transport of Ca^{2+} across the cell membrane to maintain low intracellular calcium content. Thus, the pumps are essential for the regulation of cell volume, uptake of nutrients, cell growth and differentiation and are critical for the normal functioning of excitable and non-excitable tissues(Thirugnanam and Carani,2003).Heavy metals, including cadmium and lead, are known to interfere with a broad spectrum of solute transport processes in the renal tubule (Ahn et al., 1999),and the inhibition of Na^+/ K^+ATPase by these toxins has been largely described in the literature (Carfagna et al., 1996).

In the present study, ATPase activity of lead treated rats had decreased when compared with controled rats while taurine can increase the ATPase activity. This could be attributed to the role of taurine in maintaining a normal IGF-I level (Dawson et al., 1999) and its antioxidant action against lipid peroxidation, thus conserving the internal antioxidants system. Stimulation of Na^+/K^+ATPase activity by taurine could produce a decrease in uptake of Ca^{2+} due to the decreased activity of Na^+/Ca^{2+}exchanger(Thirugnanam and Carani, 2003). Taurine has been reported to restore the depletion of erythrocyte membrane Na^+/K^+ATPase activity due to ozone exposure or cholesterol-enrichment concentrateons(Yamagami et al.,1995). Taurine stimulates the pumping rate of Ca^{2+}activated ATPase pump possibly by increasing the turnover rate of the pump secondary to a membrane modification. Further, taurine alters the properties of Ca^{2+} binding sites on membrane acidic phospholipids thereby modifying Ca^{2+}delivery to the channel. Taurine directly affects the hydrophilic site on the channel and modifies the kinetics of channel opening or closing. These polyvalent actions of taurine on Ca^{2+} movement protect the cells against Ca^{2+}overload (Huxtable, 1992).

Vitamin C has earlier been reported as apossible chelator of lead with similar potency as that of EDTA. However, no change was found in blood lead level in workers occupationally exposed to lead and supplemented with zinc and vitamin C.In the present study, treatment with taurine reduce lead burden in the Blood. This might be due to as a kind of sulfur- bearing amino acid, Tau might promote the expelling of the lead accumulated in the body. By the transsulfurase pathway, Tau can be transformed into glutathion(GSH) that containing Thiol group and participate in detoxification. Some studies indicated that intaking quantum satis Tau could increase bioavailability of GSH with the result of increasing lead excretion(Liu et al.,1997).
The data from this experiment indicate that taurine has the ability to protect the kidney from the damaging effects of exposure to lead and might stimulate the activity of the ATPase. In addition to this action and possibly others that remain to be defined, taurine has also been shown to reduce the toxicity and side effects of large numbers of drugs. Thus, the ideal treatment of lead poisoning seems to include taurine as antioxidantsin combination with lead chelators.

REFERENCES

[1] Adonaylo VN, Oteiza PI. Lead intoxication: antioxidant defense and oxidative damage in rat brain. Toxicology 1999;135: 77–85.
[2] Ahn DW, Kim, MY, Kim KR, Park YS. Cadmium binding and sodium-dependent transport in renal brush-border membrane vesicles, sodium-dependent transport in renal brush-border membrane vesicles.

Toxicol Appl Pharmacol 1999; 154:212–218.
[3] BatumanV. Lead nephropathy gout, and hypertension. Am.J. Med. Sci 1993; 305:241–247.
[4] Benett WM. Lead nephropathy. Kidney Int 1985; 28: 212–220.
[5] Bruna P, Gianfranco GP, Gavino A. Effects of taurine and hypotaurine on lipid peroxidation. Biochem and Biophy Res Comm 1995; 213:820-825.
[6] Carfagna MA, Ponsler GD, Muhoberac BB. Inhibition of ATPase activity in rat synaptic plasma membranes by simultaneous exposure to metals. Chem Biol Interact 1996;100: 53–65.
[7] Chen YX. Protective action of taurine on ischemiareperfusion liver injury in rats and its mechanisms. Chin Med J Engl 1993; 73: 276–279.
[8] Dawson JR, Liu S, Eppler B, Patterson T. Effects of dietary taurine supplementation or deprivation in aged male Fischer 344 rats. Mech. Ageing Dev 1999; 107:73–91.
[9] El-Missiry MA. Prophylactic effect of melatonin on lead induced inhibition of heme biosynthesis and deterioration of antioxidant system in male rats. J Biochem Mol Toxicol 2000;14: 57–62.
[10] Ganiyat A M, Aliu YO, Ambali S F, Ayo J O. Taurine alleviated biochemical alterations in male Wistar rats co-exposed to chlorpyrifos and lead. Journal of Toxicology and Environmental Health Sciences 2014;6:13-25.
[11] Gargouri B, Mansour RB, Abdallah FB, Elfekih A, Lassoued S, Khaled H. Protectiveeffect of quercetin against oxidative stress caused by dimethoate in human peripheral blood lymphocytes. Lipids Health Dis 2011; 10:149-153.
[12] Hong CD, Hanenson IB, Lerner S, Hammond PB, Pesce AJ, Pollak VE. Occupational exposure lead: effects on renal function. Kidney Int 1980; 18: 489–494
[13] Husain K, Scott BR, Reddy SK, Somani SM. Chronic ethanol and nicotine interaction on rat tissue antioxidant defense system. Alcohol 2001; 25:89–97.
[14] Huxtable RJ. Physiological actions of taurine. Physiol Rev 1992;72:101-163.
[15] Juberg DR, Klieman CF, Simona, CK. Position paper of the American Council on Science and Health.Lead and human health. Ecotoxicol Environ Safety 1997; 38:162–180.
[16] Kanbur M, Liman BC, Eraslan G, Altinordulu S. Effects of cypermethrin, propetam-phos, and combination involving cypermethrin and propetamphos on lipidperoxidation in mice. Environ Toxicol 2008;23:473–479.
[17] Karabacak M, Kanbur M, Eraslan G, Soyer Sarıca Z. The antioxidant effect of wheat germ oil on subchronic coumaphos exposure in mice. Ecotoxicol Environ Saf 2011;74:2119–2125.
[18] Khalil MF, Gonick HC, Cohen AH, Alinovi R, Bergamaschi E, Mutti A, Rosen VJ. Experimental model of lead nephropathy.1.Continuous high-dose lead administration. Kidney Int. 1992; 41:1192–1203.
[19] Liu CM, Zheng YL, Lu J, Zhang ZF, Fan SH, Wu DM, et al. Quercetin protects rat liveragainst lead-induced oxidative stress and apoptosis. Environ Toxicol Pharmacol 2010; 29:158–166.
[20] Liu M, Hus C, Chen L, Guo Y. Lead exposure causes generation of reactive oxygen species and functional impairment of rat sperm. Toxicology 1997;122:133–43.
[21] Loghman AM. Renal effects of environmental andoccupational lead exposure. Environ. Health Perspect 1997; 105:928–939.
[22] Lv C, Hong T, Yang Z, Zhang Y, Wang L, Dong M. Effect of Quercetin in the 1-methyl-4-phenyl-1, 2, 3, 6-tetrahydropyridine-Induced Mouse Model of Parkinson's Disease. Evid Based Complement Alternat Med 2012; 928:643-648.
[23] Mansour SA, Mossa A-TH. Lipid peroxidation and oxidative stress in rat erythrocytes induced by chlorpyrifos and the protective effect of zinc. Pestic Biochem Physiol2009; 93:34–39.
[24] Nolan CV, Shaikn ZA. Lead nephrotoxicity and associateddisorder: biochemical mechanisms. Toxicology 1992; 73:127–146.
[25] Othman AI, El-Missiry MA. Role of selenium against lead induced toxicity in male rats. J Biochem Mol Toxicol 1998; 12:345–349.
[26] Patra RC, Swarup D, Dwivedi SK. Antioxidant effects of tocopherol, ascorbic acid and l-methionine on lead induced oxidative stress to the liver, kidney and brain in rats. Toxicology 2001;162:81–88.
[27] Planas BF, Elizalde M. Activity of glutathione S-transferase in rat liver and kidneys after administration of lead or cadmium. Arch.Toxicol 1992; 66:365–367.
[28] Schuller-Levis G, Quinn MR, Wright C, Park E. Taurine protects against oxidant-induced lung injury: possible mechanisms of action. Adv Exp Med Biol 1994; 359:31–39.
[29] Shelton KR, Egle PM. The proteins of lead-induced intranuclear inclusion bodies .J Biol Chem1982;257:11802-11807.
[30] Stiller D, Friedrich HJ. Ultrastructural and ultrahistological investigations of lead-induced intranuclear

inclusion bodies in rat kidney.Exp Pathol 1983;24:144-155.

[31] Tandon SK, Singh S, Prasad S, Srivastava S, Siddiqui MK.. Reversal of lead-induced oxidative stress by chelating agent,antioxidant, or their combination in the rats. Environ. Res, Section A 2002; 90: 61–66.

[32] Teresa AG, Laura C. Biochemical changes in the kidneys after perinatal intoxication with lead and/or cadmium and their antagonistic effects when coadministered. Cotoxicology and Environmental Safety 2004;57:184-189.

[33] Thirugnanam AN, Carani VA. Inhibition of lipid peroxidation, protein glycation and elevation of membrane ion pump activity by taurine in RBC exposed to high glucose. Clinica Chimica Acta 2003; 336:129-135.

[34] Thurman RG, Bradford BU, Iimuro Y, Frankenberg MV, Knecht KT, Connor H.D, Adachi Y, Wall C, Arteel GE, Raieigh JA, Forman DT, Mason RP. Mechanism of alcohol-induced hepatotoxicity: studies in rats. Front. Biosci 1999; 4:42-46.

[35] Yamagami T, Naruse Y, Sokejima S, Kagamimori S .Effects of taurine on depletion of erythrocyte membrane Na-KATPase activity due to ozone exposure or cholesterol enrichment. J Nutr Sci Vitaminol 1995; 41:627– 34.