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EFFECT OF VITAMIN E PRETREA TMENT ON CHRONIC ECOTOXICTY OF Co, Pb AND Hg NITRATES INDUCED NEPHROTOXICITY IN RATS

S. Hanafy [1], and M. E Soltan [2].

[1] Department of Zoology and [2] Chemistry, Faculty of Science, Aswan, South Valley University

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Abstract

It is known that heavy metals widely contaminated fresh water ecosystem, exerts toxic effects in body organs. The occurrence of heavy metals contaminants in excess of natural loads, has became a problem of increasing concern. The present work was conducted to study the effect of vitamin-E on renal toxicity induced by the heavy metals Co, Pb and Hg in albino rats. In this experiment, the heavy metals Co, Pb and Hg as nitrates were administered either alone or as a mixture and animals were pretreated with vitamin E for 7 days followed by concomitant administration with Co, Pb and Hg alone or as a mixture. At the end of the experiment and after 4 weeks, blood samples and kidney tissues were taken for biochemical and histological study. Results showed that these heavy metals induced many histopathological alterations in the kidney together with elevation in the serum level of creatinine and urea. The rank order of metal cytotoxicities were Hg > Co > Pb. Vitamin E significantly improved the toxic lesions induced by the three metals as reflected by improvement in histological as well as biochemical data. The protective effect of the vitamin-E is not to be attributed to its known antioxidant effect but to lower the metal concentration in renal tissues.

Introduction

Heavy metals may be derived from the weathering of rocks or, increasingly, they may be introduced into the atmosphere and hydrosphere by human activities (Drever, 1997). Metals are released into aquatic system from many sources, often at sublethal concentration. Living organisms require trace amounts of some heavy metals, including Co, Cu, Fe, Mn, Mo, V, Sr and Zn. Excessive levels of essential metals, however, can be detrimental to the organism. Non-essential heavy metals of particular concern to surface water systems are Cd, Cr, Hg, Pb, As and Sn (Kennish, 1992). Organisms in contaminated fresh water ecosystems are exposed to a variety of toxicants for their entire lifetime. Bolognesi et al., (1999) reported that heavy metals are stable and persistent environmental contaminants.

Lead is a widespread environment contaminant found in air, canned food, drinking water and paints, creating an environmental public health problem. Because of size and charge similarities, Pb can substitute for Ca and included in bone. Children are especially susceptible to Pb because developing skeletal systems require high calcium levels, Pb that is stored in bone is not harmful, but if high levels of calcium are ingested later, Pb in the bone may be replaced by ca and mobilized. Once free in the system, Pb may cause nephrotoxicity, neurotoxicity and hypertension (Kennish, 1992).

Farrag et al., (1998) and Amine et al., (1998) studied the histological and biochemical changes in the liver and kidney and ultrastructural of rat kidney induced by lead.Their results showed that chronic lead intoxications has a profound effect on the structure and function of the liver and kidney. Also, they found highly accumulated lead in the intratubular fluid than in any other fluids due to exposure of the renal cortex to very high toxins . Rashwan et al., (2000), studied the effects of lead acetate on the cerebellum and hippocampus of neonates in albino rats. They found that many components in the hippocampus and cerebellum was affected as vascular neuronal and glial components leading to disturbed endogenous homeostasis. Also, Zaiser and Miletic (2000) reported that chronic exposure to 500 ppm of lead resulted in gender dependent effects. In male rats, the magnitude and duration of long – term potentiation (LTP) were

identical to those in controls, while in females LTP was significantly attenuated. Adonoylo and Oteiza (1999) reported that oxidative damage associated with the presence of lead in the brain has been proposed as one possible mechanism involved in Pb toxicity.

Concerning cobalt, Barceloux (1999) reported that cobalt is an essential element necessary for the formation of vitamin B12 (hydroxo cobalamin); however, excessive administration of this trace element produces goiter and reduced thyroid activity. An interstitial pulmonary fibrosis has been associated with industrial exposure to hard metal dust (tungsten and cobalt), but not to cobalt alone. Exposure to cobalt alone produces an allergic contact dermatitis and occupational asthma.

Recent epidermiological studies have raised the concern about mercury as an environmental hazard. The major physical forms of mercury, to which human are exposed, are mercury vapour, Hgo, methyl mercury compounds; mainly from amalgum, in industries using Hg and also found in seafood and fresh water fish. Acute mercury poisoning might be met with either in accidental occupational crisis or suicidal attempts. Mercuric chloride poisoning leads to functional and structural alterations in many organs such, as kidney, liver, lung, CNS and testis (Radi and Farghaly, 2000).

Mercury posses a great risk to humans, especially in the form of methyl mercury. When Hg enters water it is often transformed by microorganisms into the toxic methyl mercury form. Symptoms of acute poisoning are pharyngitis, gastroenteritis, vomiting, nephritis, hepatitis and circulatory collapse. Chronic poisoning is usually a result of industrial exposure or a diet consisting of contaminated fish. Chronic poisoning may cause liver damage, neural damage, and teratogenesis (Usep, 1987). Toxicity often results from bioaccumulation in fatty tissues and penetration of membrane barriers. Thus ionic Hg (II) is toxic to the mammalian kidney and corrosive at sites of mucosal absorption, whereas CH3Hg+ crosses the placenta and blood – brain barrier, acting as a teratogen (Campbell et al., 1992). Lee et al,(1983) reported that urinary metallothionein levels were elevated in response to Cd, Hg, Cu and Zn but not Pb; Hg had the most profound effect at equimolar doses. Also, Liu et al., (1992) suggested that increased urinary excretion of zinc and copper related to the

manifestation of renal toxicity and or the synthesis of metallothionen in kidney induced by mercury.

Institoris et al., (2001 a,b) demonstrated the effects of the insecticide permethrin alone or in combination with arsenic III or Hg II and the combined exposure with propoxur and the heavy metals on certain toxicological, haematological and immune function, leading to the conclusion that combined exposures by the investigated substances modify the toxic effects of the single compounds and these findings rise the probability that the interactions observed can also be present in human situations altering the health hazard of this four chemicals.

The kinetics role of vitamin E was followed in serum, liver and kidney, Appenroth et al, (1997) reported that the administration of vitamin E, 12 hour Prior to cisplatin, diminished the toxic effect of cisplatin in young and adult rat kidney. Also, Abdel- Naim et al., (1999) indicated that due to their antioxidant activity, vitamin E and prubcol have potential protective effects against gentamicin nephrotoxicity. Vitamin E administered together with adriamycin could reverse some of degenerative changes caused by adriamycin in guinea pig kidney (Gorgun et al., 1999). Simultaneous administration of vitamin E (5mg / Kg. intramusculary for 7 days) reduced cadmium intoxication in blood, liver and kidney of rats (Tandon et al., 1992). Therefore, the present work was conducted to study the effect of the heavy metals (Co, Pb and Hg) on the rats to evaluate the ecological consequences of these long – term contamination and the effect of vitamin E pretreatment on chronic ecotoxicity of mixture of these metals on the nephrotoxicity from histological and biochemical point of view.

Materials and Methods

Animals and Treatment :

Adult male albino rats, Ratts norvegicus weighing 100 to 120 gm were used in the present investigation. They were maintained under standard laboratory condition of temperature and were fed on standard rodent chow with water provided ad libitum . After one week of acclimatization to the laboratory environment, the animals were divided into the following groups:

group I (5 rats) served as control and were given dist.water; **group II** (15 rats) were subcutanously injected with 0.5 mg / 100 g body weight of the heavy metals Co, Pb and Hg as nitrates respectively day by day for four weeks; **group III** were exposed to equitoxic mixtures of the last three metals in concentration (0.25 mg / 100 g body weight); **group IV** were exposed to pretreatment with vitamin E (alpha tocopherol 250 1U / 100g) by oral gavage for four weeks; **group V** was pretreated with vitamin E for 7 days followed by concomitant administration with Co, Pb and Hg solutions like **group II**; **group VI** was vitamin E pretreatment for 7 days followed by concomitant administration with mixture of the last three metals as group III. 10 animals in group II and group III were maintained without exposure for another 2 weeks for the recovery .

Preparation of heavy metal solutions:

The stock heavy metal solutions (2000mg 1-1) were prepared from each metal (2mg/ ml) are given in Table 1. The mixture solution (0.5 mg / ml of each metal) was prepared by mixing equal volumes from each stock metal solution and bidistilled water. All the chemical used were of Analor grade (98 – 99.99% E. Merck) .

Table (1) : Composition of fed metal solutions.

Metal	Fed metal salution	Source	Mol. Wt	Assay (%)	Wt=2000mgl-1 (g)
Co	$Co(NO_3)_2.6\,H_2O$	Merck	291.03	99.99	9.8766
Hg	$Hg\,(NO_3)_2.H_2O$	Merck	342.61	98	3.4160
Pb	$Pb\,(NO_3)_2$	Merck	3310.2	99.99	3.2162

At the end of the experiment (after 4 weeks treatment), blood samples were obtained and centrifuged at 4, 000 X g for 15 minutes. Serum was used for urea and creatinine assays. Urea was estimated by the enzymatic method according to Henary, (1974). It is hydrolysed in the presence of water and urease to produce ammonia and carbon

dioxide. The ammonium ions react with hypochlorite and salicylate to give a green colour which determined photometrically at wave length 600 nm. Creatinine was evaluated by the method of Henary, (1974). After deproteination of serum, creatinine reacts with picrate in presence of 1.5 N sodium hydroxide to form an amberyellow colour that is measured photometrically at wave length 530 nm.

For histological study , rats were decapitated and their kidneys were removed immediately and fixed in 10 % formalin. The fixed samples were dehydrated in ascending grade of ethanol, cleared in chloroform and embedded in paraffin wax. Then sections of 5 microns thickness were cut, mounted and stained with haematoxylin and eosin.

Results

Histological findings:

Kidneys showed variable degrees of degenerative changes after treatment with the used heavy metals. The main characteristic findings after long term Co $(NO_3)_2$ solution administration were shrunken and degenerated renal tubule cells. The nuclei showed disturbance in position, shape, size and staining affinity in comparison to control group (Fig. I). Most Malpighian corpuscles revealed narrowing of the capsular space with irregular parietal layer of Bowman's capsule, wide intertubular space between damage tubules were also seen (Fig.2). The histopathological changes with Hg $(NO_3)_2$ solution administration including desquamation, necrosis, atrophy of renal tubules and loss of glomeruli. Renal tubule cells appeared with poorly stained cytoplasm and degenerated nuclei (Fig. 3). Chronic lead intoxication has a profound effect on the structure of the rat kidney. The main characteristic findings in the present work were the observed intranuclear inclusions in the epithelial cells lining renal tubule .It could be assumed that the highly accumulated lead in the intratubular fluid than in any other body fluids, has pointed the exposure of the renal

cortex to high toxins. Most glomeruli revealed shrinkage and widening of capsular space (Fig. 4). On the other hand chronic exposure to the mixture of the last three metals showed marked destruction and distortion of the proximal and distal convoluted tubuls. The lining epithelium of the tubules was detached from the basement membrane, some Malpighian corpuscle demonstrate wide capsular space and some pyknotic nuclei were also seen. This change was more or less similar to the histological changes observed in the previous group . Congested dilated capillaries were also seen with homogenous acidophilic hyaline casts (Fig. 5).

Long term administration with high dose of vitamin E showing no variable changes in renal tubule cells in comparison to control group. However some Malpighian corpuscle demonstrated wide capsular space (Fig. 6) . Vitamin E pretreatment has a protective and antitoxic effects in rats as reflected by improvement in histological changes. Throughout the pretreatment with vitamin E for 7 days followed by chronic administration with Pb $(NO_3)_2$ solution for 4 weeks, both nucleus and cytoplasm of renal epithelal cells were intensely stained,but some renal tubules showed wide tubular lamina and some glomeruli showed degenerative changes (Fig.7). Pretreatment with vitamin E followed by chronic administration with Co $(NO_3)_2$ solution showed a minimal tissue damage, the glomeruli showed wide glomerular space and renal tubule cells were swolled with large rounded nuclei. The tubular arrangement and cytoplasmic basophilia were more or less similar to the control group (Fig.8) . Pretreatment with vitamin E followed by administration with Hg $(NO_3)_2$ solution showed more cytoplasmic basophilia and atrophied glomeruli but with minimal tissue damage compared to group II (Fig. 9). Pretreatment with vitamin E followed by administration with a mixture of equimolar doses of the three metals, resulted in diminution of damage mediated by the treatment with these metals and the observed change were degeneration of some renal tubules and congestion of blood vessels (Fig. 10). Also, it was found that the rank order of metal cytotoxicities were Hg > Co>Pb. On the other hand in the recovery groups, the previously observed changes were still present with regression of their intensity. The most histopathological alterations were desquamation, necrosis, atrophy and loss of renal tubule cells polarity with degenerated nuclei (Fig. 11). Also, treatment

with a mixture of the three metals and after 15 days post withdrawal ,the renal tissue showed congested dilated blood vessel with homogeneous acidophilic hyaline casts, marked destruction and distortion of the renal tubules with detachment from their basement membrane and some pyknotic nuclei (Fig. 12).

Biochemical data:

Both urea and creatinine in the sera of treated rats were found to exhibit a marked elevation after treatment with different types of metals

1- Serum creatinine :

Data in table (II) indicated a marked elevation in serum creatinine of rats after long – term exposure to Co, Pb, Hg, as nitrate solutions, and mixture of them.. These elevation were found to be significant ($P< 0.05$) and the rank order of cytotoxicity were Hg > Co > Pb. Long term vitamin E pretreatment alone not alter serum creatinine, whereas vitamin E - supplemented animals for 7 days followed by chronic exposure of Co and Pb induced significant decrease in serum creatinine. Treatment with vitamin E and Hg or mixture of the three metals induced insignificant decrease in serum creatinine . No significant changes in serum creatinine were recorded between the recovery groups and those treated with the heavy metals or their mixture (tableII).

2-Blood Urea:

Chronic treatment of rats with the $Co(NO_3)_2$, $Pb(NO_3)_2$,$Hg(NO_3)_2$ solutions and a mixture of equimolor doses of these metals for 4 weeks was found to exhibit a significant ($P< 0.05$) elevation (Table II). The increase reached its highest value after treatment with Hg $(NO_3)_2$ solution, while the lowest value was after the treatment with Pb $(NO_3)_2$ solution . Vitamin E pretreatment has a protective and antitoxic effects. Blood urea was significantly declined after treatment with vit. E plus Co $(No_3)_2$, and Pb $(NO_3)_2$ and the mixture of them while treatment with vit.E plus $Hg(NO_3)_2$ induced insignificant decrease. There was insignificant difference in blood urea level between the recovery group and metal-treated groups (table II).

Discussion

Co, Pb and Hg have been recognized as the most toxic industrial and environmental pollutants of which there is a continuing hazard to biological organisms especially animals and human exposure. The present investigation includes a study of the histopathological alterations induced in the kidney of rat as a result of these metals application. The main characteristic findings after long term Co $(NO_3)_2$ solution administration were shrunken and degenerated renal tubule cells, disturbance in position, size, shape and staining affinity of the nuclei and wide intertubular space between damage tubules. Treatment with Hg $(NO_3)_2$ solution induce a severe acute toxicity to rat kidney including desquamation, necrosis, atrophy and loss of renal tubule cells and glomeruli. Poorly stained cytoplasm and degenerated nuclei were also seen. Chronic lead intoxication has a profound effect on the structure of the rat kidney. The main characteristic finding were the presence of intranuclear inclusions in the epithelial cell lining and degeneration of glomeruli. Moreover, chronic exposure to the mixture of these metals showed marked destruction and distortion of the proximal tubules, and congestion of blood capillaries with homogenous acidophilic hyaline casts were also seen. This is supported by the work of Amine et al., (1998) and Farrag et al, (1998) who concluded that, chronic lead intoxication has a profound effect on the structure and consequently on the function of the liver and kidney of male albino rats. The most histological changes in the kidney were marked destruction and distortion of the proximal and distal convoluted tubular lining epithelium. The nuclei showed marked variation in size, shape and density and contained nuclear holes and intranuclear inclusions in the epithelial cell lining renal proximal tubules. It could be assumed that the highly accumulated lead in the intratubular fluid, than any other body fluids has potentiated the exposure of renal cortex to very high toxins. They also found marked fibrosis and increase in interstitial tissue fibroblasts between degenerated tubules. Congested dilated capillaries were also seen with homogenous acidophilic hyaline casts in medullary interstitial tissue and most Malpighian corpuscle revealed narrowing of the capsular space with irregular parietal layer of Bowman's capsule. Similarly, Shehata et al., (2000) studied the toxic effects of compined exposure to cadmium and Nickel on white albino

rats. Their results revealed a significant increase in blood Cd and Ni levels. Urea, uric acid and creatinine levels were significantly increased. The most histopathological changes were recorded in lungs, heart and kidneys. They also reported that approximately 50% of the body burden of Cd can be found in the kidney Cd produces proximal tubular dysfunction and injury characterized by increase in urinary excretion. This injury may progress to chronic interstitial nephritis (Goldstein and Schnellmann, 1996).

In this study, it has been observed that long term administration with high dose of vitamine E showing no variable changes in renal tubule cells in comparison to control group. It was found that vitamin E pretreatment has a protective and antitoxic effects in rats as reflected by improvement in histological changes . Also, this study has been shown that, heavy metals produced significant increase ($P<0.05$) in serum creatinine and blood urea nitrogen. The changes in these parmeters were improved by pretreatment with vitamin E .

The effect of dietary vitamin E on renal tissue damage and lipid peroxidation was investigated by Hamazaki et al., (1988) following treatment with ferric nitrilotriacetate (Fe- NTA). Almost 100% renal proximal tubular necrosis was observed in vitamin E deficient rats following Fe- NTA. In the vitamin E supplemented rats, no injury was observed in the proximal convoluted (cortical) tubules. Also, Igbal et al., (1998). Showed the modulatory effect of vitamin E on Fe – NTA induced renal oxidative stress, toxicity and hyper proliferative response in rats. Fe –NTA- treatment induced lipid peroxidation and hydrogen peroxide generation which are accompanied by a decrease in the activities of renal antioxidant enzymes and depletion in the level of renal glutathion and a sharp increase in blood urea nitrogen and serum creatinine. Treatment of animals with vitamin E daily for one week prior to the administration of Fe- NTA resulted in the diminution of Fe-NTA mediated damage. In addition, the depleted level of glutathione and inhibited activities of antioxidant enzymes recovered to significant level $P < 0.05$. Similary, the enhanced blood urea nitrogen and Serum creatinine level showed a reduction of about 50% at a higher dose of vitamin E. They suggesting that vitamin E is an effective chemopreventive agent in kidney and may Suppress Fe- NTA induced renal toxicity. Tandon et al., (1992) investigated the influence of vitamin E on cadmium (Cd) intoxication in rats. The exposure to Cd

(1mg/kg intraperitoneally for 7 days) decreased the activity of hepatic and renal glutamic oxalacetic and glutamic pyruvic transaminases and alkaline phosphatase accompanied by increase in the level of urinary protein. Simultaneous administration of vitamin E reduced these Cd induced biochemical alterations. The accumulation of Cd in blood, liver and kidney also decreased significantly upon co-exposure to vitamin E. Also, Shaikh et al., (1999) investigated the role of oxidative stress in chronic Cd toxicity and its prevention by co-treatment with antioxidants. Renal toxicity, indicated by elevation in urinary lactate dehydrogenase activity protein. Chronic Cd administration resulted in gradual rise in hepatic as well as renal cortex glutathione levels. Coadministration of antioxidant of vit. E with Cd, controlled Cd induced lipid peroxidation and protected the animals against hepatic as well as renal toxicity. Abdel- Naim et al ., (1999) reported that gentamicin induced nephrotoxicity was evidenced by marked elevation in serum urea and creatinine levels. Vitamin E pretreatment significantly lowered the elevated serum urea and creatinine levels. Also, Gorgun et al., (1999) found that vitamin E administered together with adriamycin could reverse of the degenerative changes coused by adriamycin. According to the present results, compined exposure with a mixture of vitamin E and heavy metals examined can modify the detection limit of the single compound and / or may alter their toxic effects. The rank order of metal cytotoxicities were Hg > Co > Pb. In other studies ,Hodson, 1988 and Maracine and Segner, 1998 found that metal metabolism has significant effects on metal accumulation, distribution in the tissues and toxic effect particularly under conditions of chronic and low – dose exposure. The cytotoxicities of six metal salts to the continuous rainbow trout cell line RT G – Z were determined by means of the neutral red (NR) uptake inhibition assay. The rank order of metal cytotoxicities were Hg > Cd > Zn > Cu > Pb > Ni (Maracine and Segner, 1998).

From these results, it is speculated that the disturbance in the metabolism of Co, Pb and Hg as nitrates in the kidney may be a much more sensitive index with morphological damage and impaired renal function to heavy metals exposure. The histological findings were accompanied by high elevation of the renal function data. Also, vitamin E significantly improved the toxic lesions induced by these metals injection. It was concluded that vitamin E pretreatment has a protective

and antitoxic effects in rats reflected as improvement in the histopathological as well as the renal biochemical data.

References

Abdel – Naim, A. B.; Abdel – Wahab, M. H. and Attia, F. F. (1999): Protective effects of vitamin E and probucol against gentamicin – induced nephrotoxicity in rats . Pharmacol Res, 40 (2): 183 – 7.

Adonaylo, V. N. and Oteiza, P. I (1999): Lead intoxication: antioxidant defenses and oxidative damage in rat brain. Toxicology, 15; 135 (2-3): 77-85.

Amine, A. M.; Abdel Molla, A. A. and Yehia, M. A. (1998): Histopathological, histochemical and ultrastructiral studies on rat kidney under the effect of lead. The 22nd scientific conference of Egyptian society of histology and cytology; Page: 28.

Appenroth, D.; Frob, S.; Kersten,L.; Splinter, F. and Winnefeld, K. (1997): Protective effects of vitamin E and C on cisplatin nephrotoxicity in developing rats. Arch Toxicol;71(11): 677 – 83.

Barceloux, D. G. (1999): Cobalt. J. Toxical Clin Toxicol,37 (2):201–6 .

Bolongnesi, C.; Landini, E.; Roggieri, P.; Fabbri, R. and Viarengo, A. (1999): Genotoxicity biomarkers in the assessment of heavy metal effects in mussels: experimental studies. Environ .Mol. Mutagen; 33 (4): 287 – 92 .

Campbell, D.; Gonzales, M. and Sullivan, J. (1992): Mercury. In hazardous materials Toxicology: Clinical principles of environmental health, J. B. Sullivan and G. R. Krieger (eds), Williams and Wilkins, Baltimore, 824 – 833.

Drever, I. I. (1997): the Geochemistry of Natural Waters. Prentice Hall; NI.

Farrag, K. A.; Abu- Rabia, N. M. and abdel- Raheem, H. M. (1998) Histological and biochemical changes in the kidney and liver of male albino rats induced by chronic lead intoxication. The 22nd Scientific conference of Egyptian Society of histology and cytology; PP:63.

Goldstein, R. S. and Schnellmann, R. G. (1996): Toxic responses of the kidney In : Ca sarett and Doulles Toxicology. The basic science of poisons, klaassen, C. D.; Amdur, M. O. and Doull, J. (eds). 5th ed,Mc Graw.Hill,New York,PP:417 – 442.

Gorgun, M.; Erdogan, D.; Abban, G.; Turkozkan, N. and El beg, S. (1999): Effect of vitamin E on adriamycin – induced nephrotoxicity at the ultrastructural level in guinea Pigs. Nephron; 82 (2) : 155 – 63.

Hamazaki, S.; Okada, S.; Ebina, Y. and Midorikaua, O. (1988): Effect of dietary vitamin E on ferric nitrilotriacetate induced nephrotoxicity in rats. Toxical Appl. Pharmacol., 15 : 92 (3): 500 -6.

Henary,R.G.(1974): Clinical chemistry,principals and techniques,2nd ed.Harbour and Raw,London.

Hodson, P. V. (1988): The effect of metal metabolism on uptake, disposition and toxicity in fish. Aquat. Toxical. 11:3 -8.

Institoris, I.; Olga, S. ; Undeger , U.; Basaran, N. and Desi, I. (2001a): Immunotoxicological investigation of subacute compined exposure by permethrin and the heavy metals arsenic III and mercury (II) in rats. International Immuntoxicology; 1 : 925-933.

Institoris, L.; Olga, S.; Undeger, U.; Basaram,N;and et al., (2001 b) : Detection of the effect of repeated dose combined propoxur and heavy metals exposure by measurement of certain toxicological, haematological and immunofunction parameters in rats. Toxicology, 163: 185 – 193.

Igbal, M.; Rezazadah, H.; Ansar,S. and Athar, M. (1998): Alpha – Tocopherol (Vit. E) ameliorates ferric nitrilotriacetate (Fe-NTA) – dependent renal proliferative response and toxicity: diminution of oxidative stress – Hum Exp. Toxicol., 17 (3): 163 – 71 .

Kennish, M. J. (1992): Ecology of Esturies: Anthropogenic effects. CRC Press. Inc., Boca Roton, F. L.

Lee, Y. H.; Shaikh, Z. A. and Tohyama, G. (1983): Urinary metallothionein and tissue metal levels of rats injected with cadmium, mercury, lead, copper or zinc- Toxicology; 27 (3-4): 337 – 45.

Liu, X.; Nordberg, G. F. and Jin, T. (1992). Increased urinary excretion of zinc and copper by mercuric chloride injection in rats Biometals; 5 (1): 17 – 22.

Maracine, M. and Segner, H. (1998): cytotoxicity of metals in isolated fish cells comparative Biochemistry and physiology, Part A. 120 : 83 – 88.

Radi, S. H. and Farghaly, E. F. (2000): Toxic effect of mercuric chloride on testis of rat and the detoxifying rale of verapamil. The Egyptian Soci of Histo & cytol. 23rd Scientific conference. PP. 64.

Rashwan, S. S.; Fauzy, S. A.; Aboul Fotouh, G. I. and Elgendy, M. S. (2000): The effect of lead on the cerebellum and Hippocampus of Neonates in albino rats (histological, immunohistochemical and ultrastructural study). The Egypt. Soc. Histo. And Cytal. 23rd Scientific conference. PP. 71.

Shaikh, Z. A. Vu, T. T. and Zaman, K. (1999). Oxidative stress as a mechanism of chronic cadmium – induced hepatotoxicity and renal toxicity and protection by antioxidants. Toxicol Appl pharmacol; 154 (3): 256 – 63.

Shehata, A.; Sharkawy, A. and Mubarak, M. (2000): Toxic effects of combined exposure to cadmium and Nickel on white albino rats. Assiut Vet. Med. J. 44 (87): 279 – 294.

Tandon, S. K.; Sing h, S. and Dhawan, M. (1992): Preventing effect of vitamin E in cadmium intoxication. Biomed Environ . Sci, 5(1): 39-45.

Usep A, U. S. (1987): Environmental protection Agency. Quality criteria for water. EPA Publication 440/5 – 86 -001. U. S. Gov. Prin office, Washington, D. C.

Zaiser, A. E. and Miletic, V. (2000): Differential effect of inorganic lead on hippocampal long – term potentiation in young rats in vivo – Brain Resh.; 367 : 201 – 204.

Table II: Changes in urea and creatinine in the sera of experimental rats..

Parameters / Groups		Creatinine Mean ± SD	Urea Mean ± SD
Control (GI)		0.75 ± 0.03	5.05 ± 1.25
Heavy Metals alone	Co (GII)	0.99 ± 0.08[a]	15.68 ± 1.25[a]
	Pb (GII)	0.93 ± 0.09[a]	8.94 ± 1.91[a]
	Hg (GII)	1.08 ± 0. 9[a]	18.86 ± 0.01[a]
	Mixture(GIII)	0.95 ± 0. 1[a]	9.91 ± 2.05[a]
Vitamin E alone (GIV)		0.75 + 0.09	5.06 ± 1.29
Vit. E + heavy metal	Co (GV)	0.79 ± 0.04[b]	6.01 ± 1.15[b]
	Pb (GV)	0.80 ± 0.4[b]	5.90 ± 1.05[b]
	Hg (GV)	0.96 ± 0.08	14.25 ± 2.85
	Mixture(GVI)	0.85 ± 0.06	5.80 ± 1.35[b]
Recovery	Co (GII)	0.95± 0.91	15.03 ± 0.98
	Pb (GII)	0.91± 0.55	7.76 ± 0.80
	Hg (GII)	1.06 ± 0.18	16.02 + 1.25
	Mixture(GIII)	0.93 ± 0.01	9.09 ± 0.05

-Both urea and creatinine expressed as mg / 100 ml

-(a):Significant increase in comparison with control.

-(b):Significant decrease in comparison with metal-treated groups.

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with wide tubular lamina. Notice degenerated glomeruli. H &E (X 400).

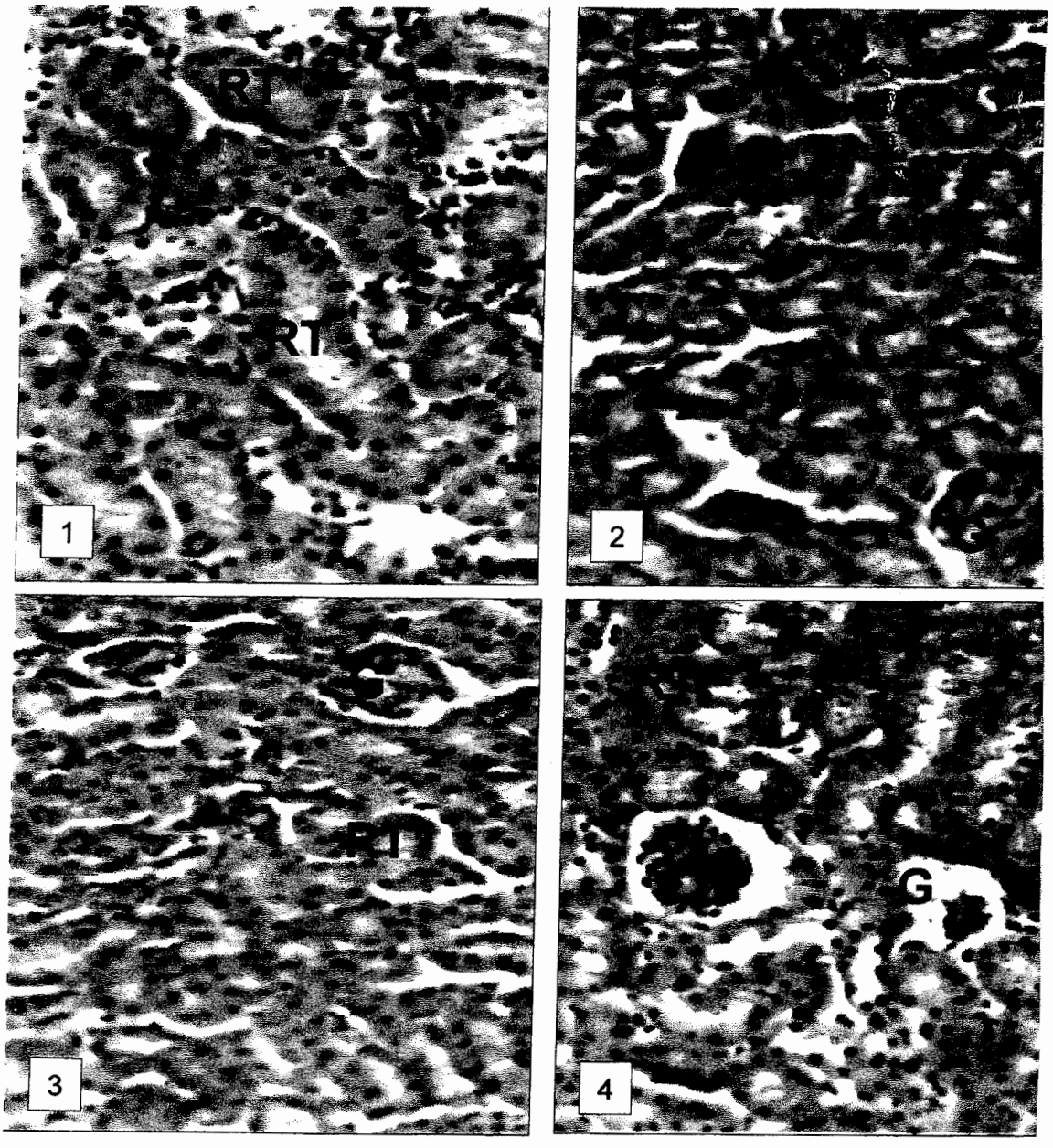
Fig. (8): Kidney section in rat exposed to Vit. E pretreatment followed by chronic administration with Co $(NO_3)_2$ solution showing the tubular arrangement and cytoplasmic basphilia more or less similar to the control group except the swelling of renal tubules & wide glomerular space.H& E (X 400).

Fig. (9): Kidney section in rat exposed to Vit. E pretreatment followed by chronic administration with Hg $(NO_3)_2$ solution showing minimal tissue damage in both the renal tubules (RT) and the glomeruli (G) compared to the group II. H& E (X 400).

Fig. (10): Kidney section in rat exposed to Vit. E pretreatment followed by chronic administration with a mixture of the three metals weeks showing congested blood vessel (BV) and some pyknotic nuclei were seen (arrow). H & E (X 400).

Fig. (11): Kidney section in rat after 15 days post withdrawal of Hg $(NO_3)_2$ administration, showing desquamation, necrosis, atrophy and loss of renal tubule cells (RT). H & E (X 400).

Fig. (12): Kidney section in rat after 15 days post withdrawal of a mixture of the three metals showing congested blood vessel (BV), marked destruction of both the renal tubules & the glomeruli (G). Some pyknotic nuclei were seen (arrow). H & E (X 400).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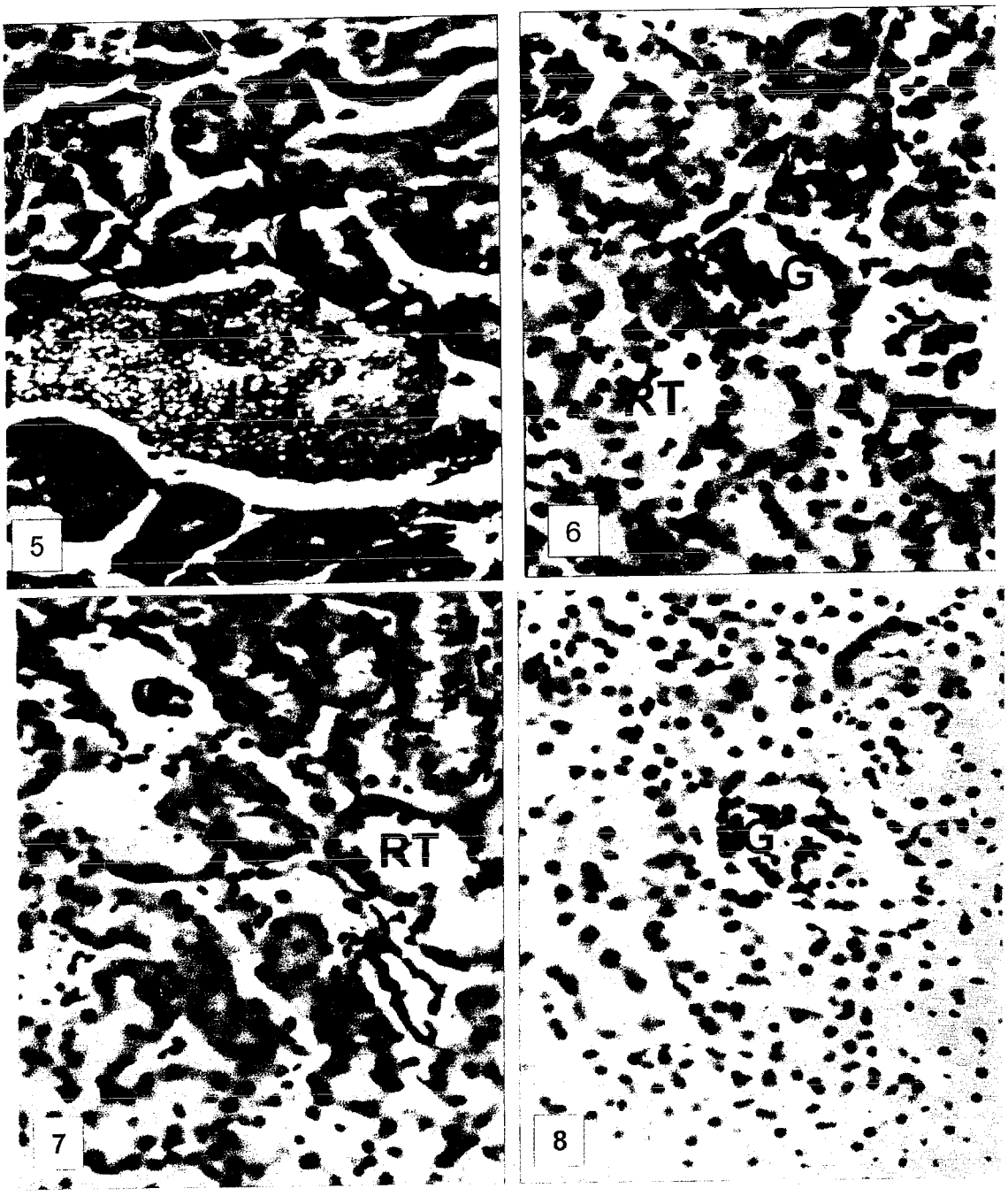
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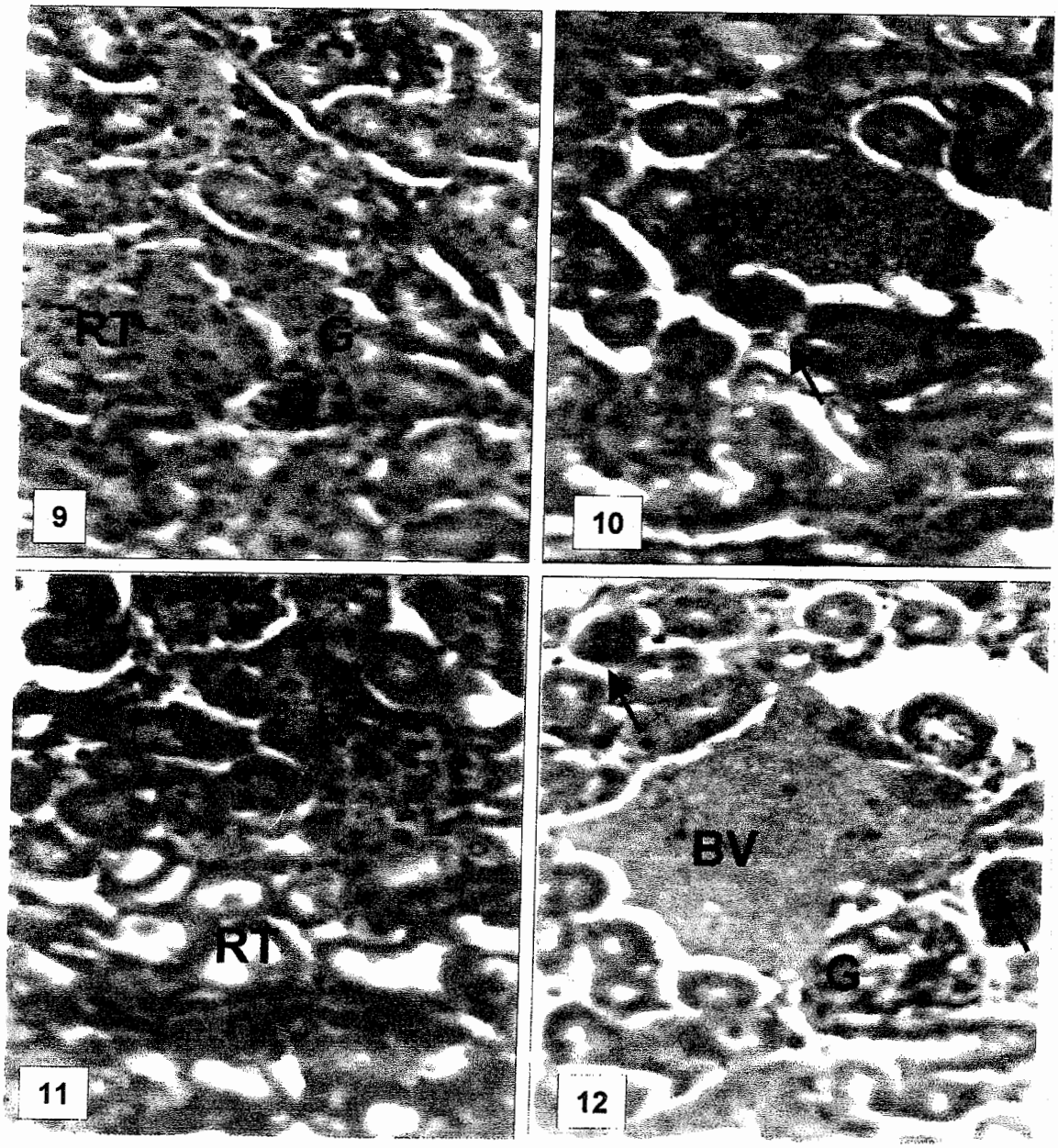
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تأثير فيتامين E الواقى عند التعرض للتسمم البيئى المزمن من نترات الكوبالت والرصاص والزئبق والذى يتسبب فى حدوث التسمم الكلوى عند الفئران.

سعاد حنفى محمود - محمد المنتصر سلطان

ملخص البحث :

- من المعروف أن انتشار المعادن الثقيلة تؤدى إلى تلوث المياه العذبة فى النظام البيئى حيث يظهر تأثيرها السام على أعضاء الجسم.
- لذلك تمت هذه الدراسة لبيـ لتأثير السام لمركبات الكوبالت والرصاص والزئبق على كلى الفئران و تأثير فيتامين E فى حماية الكلية ضد التأثير المحدث من تلوث الماء بتلك المعادن.
- اشتملت الدراسة على مجموعة فئران ضابطة وعلى ٦ مجموعات من الفئران المعالجة وقد تم استخدام محاليل من نترات الكوبالت والرصاص والزئبق كل مركب على انفراد وهذه هى المجموعة الثانية أما المجموعة الثالثة تم معالجتها بخليط من المركبات الثلاثة السابقة. المجموعة الرابعة تم معالجتها بفيتامين E فقط وقد استخدمت كمجموعة ضابطة والمجموعة الخامسة تم معالجتها أولاً بفيتامين E لمدة ٧ أيام ثم تعرضها للمعالجة بتركيز ٠,٥ مليجرام من المحاليل السابقة كل مركب على انفراد مثلما حدث فى المجموعة الثانية أما المجموعة السادسة تم معالجتها أولاً بفيتامين E لمدة ٧ أيام ثم تعرضها للمعالجة بتركيز ٠,٢٥ ملى جرام من خليط من الثلاث مركبات السابقة مثلما حدث فى المجموعة الثالثة.
- فى نهاية التجربة وبعد مرور أربعة أسابيع تم أخذ عينات الدم والكلى من كل المجموعات الضابطة والمعالجة للدراسة البيوكيميائية والهستولوجية.
- أظهرت النتائج حدوث تسمم كلوى نتيجة ارتفاع معنوى فى مستوى اليوريا والكرياتنين يصاحبها تغيرات هستولوجية مرضية أما المجموعات المعالجة بفيتامين E قبيل تعرضها للمركبات المستخدمة (Hg, Pb, Co) فقد حدث تحسن معنوى فى مستوى كل من اليوريا والكرياتنين كما حدث تحسن ملحوظ فى التغيرات الهستولوجية وهذا معناه أن لفيتامين E تأثير واقى. وجد أن ترتيب المواد المستخدمة حسب درجة سميتها هى الزئبق>الكوبالت>الرصاص.

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