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ORIGINAL ARTICLE

PROTECTIVE EFFECT OF TAURINE AND GLUTATHIONE AGAINST MERCURY INDUCED TOXICITY IN THE LIVER TISSUE OF RATS

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ABSTRACT

The present study is aimed to investigate the protective effect of taurine and glutathione in liver tissue of mercuric chloride intoxicated rats. The sub-lethal dose of mercuric chloride (2mg/kg body wt. of the animal) was administrated in rats orally for 30 days. In the present study, the histophathological changes were observed in liver tissue of rats. During the mercuric chloride treatment, the intoxicated liver tissue shows the irregular hepatocytes and vacuolaes were observbed. During the taurine and glutathione treatment, the restoration of histoarchitecture of liver tissue was noticed. The present study suggest that the taurine protects the the liver tissue than glutathione.

Key words: Mercury, Taurine, Glutathione, Histology, Liver

1. INTRODUCTION

Human activities are mainly responsible for promoting the pollution in the environment by the way of introducing unwanted toxic compounds. There is an accumulating contamination of water sources and food chain with these compounds. Four principle categories of pollutants, which jeopardize the environments, are radionucleotides, petroleum hydrocarbons, pesticides and heavymetals. Among these, heavy metals are the most dangerous ones because of their stability in the biological system (Lu, 1996). Hence, industrial pollution of the environment with metal compounds is becoming a significant problem (Foulkes, 1990).

Mercury is highly lipid soluble and enters the blood from the both lungs and mucosa. It traverses cell membrane (including the blood brain barrier and placental barrier) rapidly, partitions between plasma and red blood cells and becomes widely distributed (Engqvist *et al.*, 1998). According to the agency for toxic substances and disease Registry (ATSDR) of the US department of Health and Human Services, mercury is most frequently found in the environment (ATSDR, 2001). Annual worldwide emission of mercury into the atmosphere has been estimated at 2,200 metric tones (Stopford and Goldwater, 1975). One third of these emissions are estimated to originate from natural sources (volcanic eruptions and decay of mercury containing sediments) and two third from man made sources. Twenty five percent of total worldwide emissions come from fossil fuels combustion. In the United States, 26 per cent (64.7 tons / years) of atmospheric mercury emissions come from medical waste incineration such as cremation (ATSDR, 1999). Mercury is released naturally from the earth's crust by mining, fossil-fuel combustion and other industrial activities. In the non-occupationally exposed population, however, dental amalgam is typically the major source of mercury (WHO, 1989).

Taurine (2-amino ethane sulfonic acid) is the major intracellular free β-amino acid, which is normally present in most mammalian tissues (Chesney, 1985). It is not utilized in protein synthesis, but rather is found free or in simple peptides. It plays various important physiological roles including osmoregulation, bile acid conjugation modulation of the proliferation; viability and prevention of oxidant induced injury in may tissues (Chesney, 1985; Huxtable, 1992;

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Redmond *et al*., 1996; Sankar Samipillai and Jagadeesan, 2004). The beneficial effects of taurine as an antioxidant in biological systems have been attributed to its ability to stabilize biomembranes (Wright *et al*., 1986; Sankar samipillai and Jagadeesan, 2005). Scavenge reactive oxygen species (Wright *et al*., 1985) reduced the production of lipid per oxidation end products (Huxtable, 1992).

GSH is a low molecular weight sulfhydryl-containing compound in mammalian cells (Janaky *et al*., 1999). GSH is an essential tripeptide made up of the amino acid such as glutamate, cysteine, and glycine (Huxtable, 1986). The glutathione (GSH) is a cellular thiol, which is present in all mammalian tissues (Cooper, 1997). It rovides a reducing milieu for the maintenance of protein thiols and antioxidant, reduction of ribonucleotides and protection against oxidative and free radicals-mediated damage and other types of toxic injury (Deleve and Kaplowitz, 1990; Meister, 1991).

The redox status of mitochondrial GSH particularly plays a vital role in cell injury since mitochondrial GSH exerts a major role in the homeostatis of $Ca2^{+}$ (Beatrice *et al*., 1984) and thiols (Kosower and Kosower, 1983) to regulate the permeability of the inner membrane. This is the most abundant endogenous non-protein thiol (Kleiman and Richie, 2000), which carries out various physiological functions such as detoxification of free radical and peroxides, regulation of cell growth and protein function and maintenance of immune function (Kleiman and Richie, 2000). From this point of view, the present study has been designed to observe the changes of histoarchitecture of liver tissues of rats when treated with sub-lethal dose of $HgCl_2$ and simultaneously withdrawal effect of $HgCl_2$ with the help of taurine and glutathione respectively.

2.MATERIALS AND METHODS

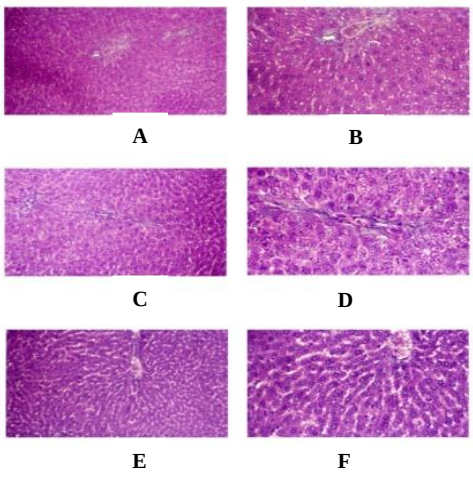
The Wister strain rats (45 days old) of the Wister strain weighing ranging from 200±5g were used in this experiments.They were divided at random into four groups (each of six rats). All the animals were fed on a standard rat feed and water ad Libitum. Experimental protocol was approved by the Institutional Animals Ethics Committee (IAEC) of RMMCH, Annamalai University. Wistar albino rats were divided into four groups each consisting of six animals: Group-I saline (0.9% NaCl)-treated control group ; Group-II Mercuric chloride (2 mg/kg orally.,for 15 days single dose)-treated group (Hg); Group-III Mercuric chloride (2 mg/kg orally single dose) + Taurine(5.0 mg/kg daily orally. for 15 days) treated group (Hg + Glutathione),Group-IV Mercuric chloride (2 mg/kg orally single dose) + Glutathione (5.0 mg/kg daily orally. for 15 days) treated group (Hg + Glutathione), Group V Taurine (50 mg/kg daily for 15 days)-treated control group and Group VI Glutathione (50 mg/kg daily for 15 days)-treated control group. The animals were sacrificed under light ether anesthesia and kidney tissues were dissected. The dissected kidney tissue used for the following estimation.

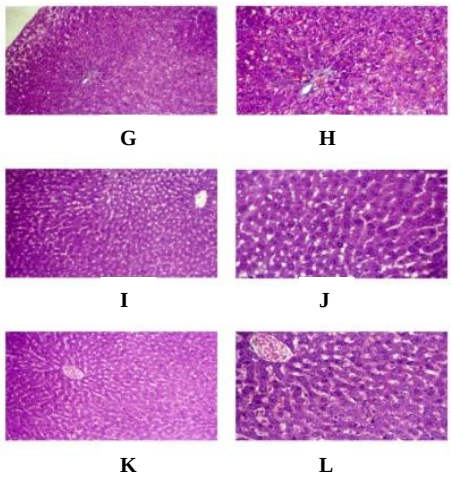
After the cervical dislocation, the experimental animals were sacrificed and selected liver was quickly isolated in cold room and fixed in buffered formaldehyde solution for 3 hrs. The tissue was washed in running tap water and processed following the standard technique (Gurr, 1959) for microtomy. The tissues were dehydrated in ascending grades of alcoholic series. The dehydrated tissue was cleaned in xylol as embedded in paraffin wax (58°C – 60°C). Serial sections were cut at 6-8 μm thickness and there were deparaffinized in xylol and after passing through descending grades of alcoholic series. The specimen sections were counter stained with aqueous haemotoxylin-Eosin stains. The stained sections were mounted on DPX for microscopical studies.

3.RESULTS

Fig.1A and B shows the untreated control of the paraffin sectioned and eosin stained section of the liver tissue of rats. This figure shows the histoarchitecture of liver at low magnification. It is composed of parenchyma cells (hepatocytes) which are cylindrical in shape with a venous channels. The hepatocytes are uniformly arranged throughout the section. Hepatocytes are roundish, polygonal, containing clear spherical nucleus. They are located among sinusoids forming cord like structures known as hepatic cell cords. Under the higher magnification in Fig.1 B the kupffer cells are recognized by the shape of their nuclei Fig. B shows that the hepatic cell cords are composed of one of two rows of hepatocytes. In between the rows, a tiny channel is formed which drains peripherally in a lobule to bile ducts. The bile ducts are made up of simple cuboidal or columnar epithelial cells. The blood supply of the liver lobule is via the sinusoids, which form a sponge work between the plates of hepatic cells. Central veins are centrally located in the lobules. It forms the smallest radicals of the hepatic vein. Portal canals are surrounded by small amount of fibroconnective tissue. The bile duct, portal vein and hepatic vein are collectively called portal triad.

Fig. 1 Liver tissue of control and treated rats





At sublethal dose of mercuric chloride intoxicated rat, liver tissue shows complete damage of its histoarchitecture, because mercury toxicity has induced discrete pathological changes. The hepatocytes possess irregular size and shape. The distribution of the hepatocytes is not uniform in all regions (Fig.1 C and D). Under the higher magnification the degeneration of cytoplasm was evident in most of the hepatocytes. In some area the clumping of hepatocytes is evident. In addition atrophic formation of vacuoles, rupture in blood vessels, necrosis and disappearance of hepatocytic cell wall and disposition of hepatic cords are also seen in all regions. Complete damage of bile ducts is also noticed. Due to $HgCl_2$ treatment, the size of the portal vein has also increased, and damaged columnar epithelium is evident.

Taurine treatment on 30 days $HgCl_2$ intoxicated rat liver tissue shows a complete regeneration from the toxic effect of mercury. The number and size and shape of the hepatocytes are restored. The arrangement of hepatic cells are regular. Reappearance of bile duct is also evident for decreasing the mercury toxicity by taurine. Restoration of portal and central vein is also noticed. Restoration of hepatic cell cords and regenerated columnar or cuboidal epithelium lining in the bile duct is also evident for its regeneration promoted by taurine (Fig.1 E and F). GSH treatment on $HgCl_2$ intoxicated rat liver tissue shows the incomplete regeneration. The size and shape of the hepatocytes are restored but the uniform arrangement is not seen. The reappearance of bile duct is also noticed but the columnar or cuboidal epithelium is partially damaged. Vacuoles are also seen in some areas. Hepatic cell cords are not evident. But damaged blood vessels are regenerated. In some hepatocytes desquamated cell wall is also noticed (Fig.1 G and H).

Taurine alone treated groups rat liver shows the complete normal histoarchitecture as in untreated control animal. The regular size and shape of the hepatocytes are seen. The uniformed arrangement of hepatocytes and its cords are evident (Fig. I and J).Glutathione alone treated groups rat liver shows the incomplete histoarchitecture. The central vein is completely filled by blood mass. The size and shape and arrangement of hepatocytes are normal but in some areas densely granulated hepatocytes are seen. Maintanence of hepatic cards are also noticed Fig.1 K and L).

4.DISCUSSION

The high toxicity produced by the mercury and its compounds are due to high solubility in lipids, high penetrating action in cells, inhibitory action on enzyme and high absorbance in cell. Mercury is rapidly absorbed into the body and accumulates in many tissues leading to several tissue damage and cell deaths. It primarily affects neurological tissues (Crinnion, 2000). Elemental mercury is absorbed easily and can cross the blood-brain barrier (Tollefson and Cordle, 1986; Lebel *et al*., 1996). Mercury and its metabolites have the toxic effect of degrading the biological protein, inhibiting enzyme synthesis and interrupting membrane transport and uptake and release of

The inorganic mercury poisoning leads to functional and structural alterations in liver and other tissues (Radi and Farghaly, 2000). The chronic poisoning of mercury and its compounds may cause liver and neural damages (USEPA, 1987).

The histopathological studies are remarkable and promising fields to understand the extent to which changes in the structural organization occur in the organ due to toxicity in the environment. Due to their toxicity, tissues lead to alterations in functional system. The histopathological changes are irreversible while altered function system is considered as a reversible effect. The extent of damage varies with organ, nature of toxicity, medium and test duration (Rana *et al*., 1982; Vijaya Madhavan and Iwai, 1979). Induced cell death plays a fundamental role in toxicant induced damage. Necrosis is caused by acute metabolic disruption with ATP depletion ion deregulation, mitochondrial and cell swelling and activation of degradation enzyme. These processes are associated with the rupture of the plasma membrane, karyolysis and cell content release generally leading to an inflammation (Prokuryakov *et al*., 2003). It is a major form of cell death, characterized by a series of distinct morphological and biochemistry alterations (Cohen, 1997).

In the present study histopathological changes have been investigated in liver tissue of rats, *Rattus norvegicus*, treated with sub-lethal dose of mercuric chloride for 30 days. Histopathology is used to study the impact of toxic materials as it provides the real picture of the toxic effects of xenobiotics in vital functions of a living organism. Mercury also causes hepatotoxicity and but it is deposited in the brain, liver and kidney (Gunderson, 1986). Liver is the main site for all metabolic activities and also for all detoxification reactions. It is strongly bound to sulfur, which is in sulfhydryl enzymes by replacing the hydrogen atom to form covalent bond as mercaptides (Klassen *et al*., 1996). It is also capable of biotransformation of forein chemicals (Mehandale, 1985). Heavy metal poisoning induced physiological and biochemical changes in the liver can be regarded as an index for the identification of pollutant stress (Rao *et al*., 1995; Shambunath Bose *et al*., 1994).

Heavy metals are known to induce cell injury, especially; liver and it may be great contribution to hepatotoxicity (Nolan and Shaikh 1992; Zalups, 1993). Hepatotoxicity is the outcome of

a complex sequence of interactions between the toxicant and target macromolecules, between damage and intracellular repair systems and intracellular signaling among different cell types within the liver (He *et al*., 2005). These factors affect the cellular defense, repair system and regulates a wide variety of cellular functions within the liver (Rose *et al*., 1997). The present study shows the reduced size of hepatocytes, irregular shape of the hepatocytes, blood vessels are damaged and vacuoles are formed in the liver tissue treated with sub lethal dose of mercuric chloride in rats. Liver injury is associated with activation of hepatic stellate cells. In chronic injury, stellate cells activation and the consequent secretion of matrix by the activated stellate cells result in liver fibrosis and ultimately cirrhosis (Iredale *et al*., 1998). In addition, in the present study, necrosis of hepatocytes, swelling, rupture of cell membrane, vacoulation of cytoplasm and karyolysis are observed in the liver of rats when treated with sub-lethal dose of mercuric chloride. Sharma *et al*., (2002) reported that similar type of pathological changes were observed in the liver tissue of mice when treated with mercuric chloride. Kayama et *al.* (1995) also reported that the kuffer cells are induced to produce cytokines after heavy metal treatment. These cytokines are responsible for certain manifestation of liver damage caused by heavy metal. Pagliara *et al*. (2003) showed that heavy metal induced liver hepatocytes followed by apoptosis mediated by oxidative stress in kuffer cells. In the present study, reduced and irregular shape and size of kuffer cells are also observed in the liver tissue of rats when treated with sub-lethal dose of mercuric chloride. Kuffer cells are usually referred to as fixed hepatic microphages which have diverse functions including phagocytosis, endocytosis, immunomodulation and synthesis and secretion of numerous biological active mediations (Laskin *et al*., 2001). These cells have been linked in the pathogenesis of liver injury induced by various hepatotoxins (Yamano *et al*., 2000). It is believed that the regulating role of kuffer cells in chemically induced liver damage is mediated through their production of superoxides and cytokines (Yamano *et al*., 2000). Laskin *et al*., (2001) reported that kuffer cells produce and release superoxide anions, hydrogen peroxide, nitric oxide and hydrolytic enzymes. Similar results were reported by Harsted and Klassen (2002). They reported depletion in kuffer cells which lead to liver damage in cadmium treated rats.

Heavy metal could be xenobiotic, which interferes with inter cellular signaling between kuffer cells and hepatocytes (Calcumuggi *et al*., 1992). In the present study, kuffer cells are effectively depleted by mercuric chloride. This findings caroborates the role of kuffer cells in mercury induced liver damage. (Amine *et al*., 1998; Farrag *et al*., 1998). Mercury chloride has been treated to investigate *in vivo* the role of kuffer cells in a variety of hepatotoxic processes and kuffer cells have been shown to protect animals from chemical induced liver damage (Yamano *et al*., 2000).

During the recovery period (Mercuric chloride followed by taurine and mercuric chloride followed by glutathione), the size of the hepatocytes has increased shape of the hepatocyte is normally arranged, damaged blood vessels are regenerated. This result indicates that the supplementation of taurine and glutathione ameliorates the hepatic necroinflammatory lesions induced by mercury. This may be due to membrane stabilization function of taurine and glutathione. Similary, Huxtable (1992); Chesney, (1985) reported that taurine improved liver function test related to hepatocellular necrosis and/or increases the membrane permeability.

In the present study, the hepatocytes and their nucleus increased in their size and the nucleoli appeared to be more prominent. Similar results were observed by Shalan *et al*, (2005) in rat liver when treated with lead. They suggested that the supplementation of vitamin C ameliorated the hepatic necro inflammatory lesions in metal induced liver damage. The taurine and glutathione treated rats showed the marked histoarchitecture in its improvement. The present study showed that the supplementation of taurine and glutathione could protect the liver tissue from the adverse effects of hepatoxicity. Similar result was made by Margarat *et al*. (2001). They reported histoachitectural regeneration in liver tissue of mice when treated with penicillamine in mercury intoxicated mice. The histopathological recovery associated with reduction in ROS production (vide in chapter 11) after taurine treatment was also observed (Balkan *et al*., 2001). Waters *et al*., (2001) showed that taurine was found to improve liver function test and hepatocyte necrosis. They reported that taurine which shows a considerable antiapototic activity in various kind of tissue, could have different effect on mechanisms involved in regression of liver fibrosis which is associated with hepatic stellate cells apoptosis. The present study concludes that the taurine protects the liver damage than glutathione.

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6.REFERENCES

Agency for toxic substances and Disease Registry (ATSDR). 1999. Toxicological profile for mercury. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service. www.atsdr.cdc.gov/toxprofiles/tp46.html

Agency for Toxic substances and Disease, Registry (ATSDR). 2001. CERCLA Priority List of Hazardous substances. Atlanta, GA. US Department of Health and Human services, Public Health Service. www.atsdr.cdc.gov/clist.html

Amine, A.M., Abdel., Molla, A.A. and Yehia, M.A. 1998. Histopathological histochemical and ultrastructural studies on rat kidney under the effect of lead : In proceedings of the 22nd scientific conference of Egyptian society of histology and cytology p. 28.

Balkan, J., Dogru-Abbasoglu, S., Kanbaghi, O., Cevikbes, U., Aykac-Tokder, G. and Uysal, M. 2001. Taurine has a protective effect against thioacetamide-induced liver

cirrhosis by decreasing oxidative stress. *Hum. Exp. Toxicol*. 20: 251-254.

Beatrice, M.D., Stiers, D.L. and Pletter, D.R. 1984. The role of glutathione in the retention of Ca^{2+} by liver mitochondria. *J. Biol. Chem.* 259: 1279-1287.

Calcamuggi, G., Lanzio, M., Dughera, L., Babini, G. and Emanuelli, G. 1992. Endotoxin tolerance and polymyxin B modify liver damage and cholestasis induced by a single dose of α-napthylsiothiocyanate in the rat. *Arch. Toxicol*. 66: 126-130.

Chesney, R.W. 1985. Taurine: Its biological role and clinical implications. *Adv. Pediatr*. 32: 1-42.

Cohen, G.M. 1997. Caspases : the executioners of apoptosis, *Biochem. J.* 326: 1-16.

Cooper, A.J.L. 1997. Glutathione in the brain disorders of glutathione metabolism In : Rosenberg, R.N., Prusiner, S.B., Dimauro, S., barchi, R.L., Kunk., L.M. (Eds). The molecular and genetic basis of neurological disease. Butterworth Heinemann, Bostaon pp. 1195-1230.

Crinnion, N.D. 2000. Environmental medicine, part three long-term effects of chronic low-dose mercury exposure. *Alt. Med. Rev*. 5. 209-223.

Deleve, I.D. and Kaplowitz, N. 1990. Importance and regulation of hepatic glutathione. *Semin. Liv. Dis.* 10: 251-266.

Engqvist, A., Colmsjo, A. and Skare, I. 1998. Specification of mercury excreted in feces from individuals with amalgam fillings. *Arch Environ health*. 53: 205-213.

Farrag, K.A., Abu-Rabia, N.M., Abdel-Raheem, H.M. 1998. Histological and biochemical changes in the kidney and liver of male albino rats induced by chronic lead intoxication. In : Proceedings of the 22nd scientific conference of Egyptian society of histology and cytology pp.63.

Foulkes, E.C. 1990. Biological effects of heavy metal. In: Metal carcinogen, vol II. CRC Press, Florida, USA.

Fracasso, M.E., Perbellini, L., Solda, S., Talamini, G.and Franceschetti, P. 2002. Lead induced DNA strand breaks in Lymphocytes of exposed workers: role of reactive oxygen species and protein kinase C. *Mut. Res* 515: 159-169.

Gunderson, E.L. 1986. FDA total diet study, April 1982-April 1986. Dietary intake of pesticides, selected elements and other chemicals. Distributed by : Association of official analytical chemists. Arlington. VA.

Gunderson, E.L. 1986. FDA total diet study, April 1982-April 1986. Dietary intake of pesticides, selected elements and other chemicals. Distributed by : Association of official analytical chemists. Arlington. VA.

Harstat, E.B. and Klassen, C.D. 2002. Gadolinium chloride pretreatment prevents cadmium chloride induced liver damage in both wild-type and MT-Null mice. *Toxicol. Appl. Pharmacol.* 180 : 178-185.

He, Q., Kim, J. and Sharma, R.P. 2005. Fumonism B, hepatotoxicity in mice is attenuated by depletion of kuppffer cells by gadolinium chloride. *Toxicology*. 207 : 137-147.

Huxtable, R. 1986. Biochemistry of sulfur. New york. Plenum press. 64-316.

Huxtable, R.J. 1992. physiological action of taurine. *Physiol. Rev*. 72: 101-163.

Iredale,J.P., Benyon,R.C.,Pickering,J., Mccullen, M., Northrop,M. and Pawley,S.1998. mechanism of spontaneous resolution of rat liver fibrosis. Hepatic stellate cell apoptosis and reduced hepatic expression of metallothionase inhibitors. *J.Clin.Invest*. 102:538-549.

Janaky, R., Ogita, K., Pasqualotto, B.A., Bains, J.S., Oja, S.S., Yoneda, Y. and Shaw, C.A. 1999. Glutathione and signal transduction in the mammalian CNS. *J. Neurochem*. 73: 889-902.

Kayama, F., Yoshifa, T., Elwell, M.R. and Lesster, M.I. 1995. Role of tumor necrosis factor in cadmium induced hepato toxicity. *Toxicol. Appl. Pharmacol.* 131: 224-234.

Klassen, C.D., Amdurand, M.O., and Doull, J. 1996. Casarett and Doull's Toxicology the basic science of poisons, 3rd Edn Macmillan Pub. Comp. New york.

Kleinman, W.A and Richie, J.P. Jr. 2000. Status of glutathione and other thiols and disulfides in human plasma. *Biochem. Pharmacol* 60: 19-29.

Kosower, N.S. and Kosower, E.M. 1978. The glutathione status of cells. *Intl. Review. Cytol*. 54: 109.

Laskin, D.L., Wenberge, B. and Laskin J.D. 2001. Functional hertrogenetity in liver and lung macrophage. *J. leuukoc Bio.* 70:163-170.

Lebel, J., Mergeler, D. and Lucotte, M. 1996. Evidence of early nervous system dynsfucntion in amazonion populations exposed to low-levels of methyl mercury. *Neurotoxicol*. 17 : 157-167.

Levinson,A.A. 1974. Introduction to exploration Geochemistry, Applied publishing limited. Clary.

Lu, F.C. 1996. Basic toxicology, fundamentals target organs and risk assessment. 3rd ed. Taylor and Fracis Pub. London.

Margarat,A., Jagadeesan, G. and Sethupathy,S. 2001. Compoarative effect of penicillamine and taurine on mercury poisoned mice,*Mus musculus.Poll. Res.* 20: 1-4.

McCabe, Jr. M.J., Whitekus, M.J. hyun, J., Eckles, K.G., McCloum, G.and Rosenspire, A.J. 2003. Inorganic mercury attenuates CD95-mediated apoptosis by interfering with formation of the death inducing signaling compex. *Toxicol. Appl. Pharmacol*. 190: 146-156.

Mehendale, H.M. 1985. Hepatic toxicity In : Modern toxicology (Eds) Gupta, P.K. and Salunkhe, D.K. Vol. I. Metropolitan book Co Pvt. Ltd. New delhi, 225-276.

Meister, A. 1991. Glutathione deficiency produced by inhibition of its synthesis and its reversal. Application in research and therapy *Pharmacol. Ther*. 51: 155-194.

Nolan, C.V. and Shaikh, Z.A. 1992. Lead nephrotoxicity and associated disorders : Biochemical mechanisms. *Toxicol.* 73: 127-146.

Pagliara, P., Chionna, A., Carla, E.C., Caforiao, S. and Dini, L. 2003. Lead nitrate and godolinum chloride administration modify hepatocyte cell surface. *Cell. Tiss. Res.* 312 : 41-48.

Peixoto, N.C., Roza, T., Flores, E.M.M. and Pereira, M.E. 2003. Effect of zinc and cadmium on HgCl2-S-ALA-D inhibition and Hg levels in tissue of suckling rats.

Proskuryakov, S.Y., Konoplyannikov, A.G., and Gobai, V.L. 2003. Necorsis a specific form of programmed cell death. *Exp. Cell. Res.* 283 : 1-16.

Radi, S.H. and Farghaly, E.F. 2000. Toxic effect of mercuric chloride on testis of rat and the detotoxifying rate of verapmil. The Egyptian society of histology and cytology. 23rd scientific conference p.64.

Rana, S.V.S., Jayakumar, A. and Agarwal, R.P. 1982. Functional versus morphological changes in the liver after heavy metal poisoning in rats. Proceeding of all India symposium on physiological response of animal to pollution.

Rao, M.V., Chinoy, N.J., Suthar, M.B. and Rajvanshi, M.I. 2001. Role of ascorbic acid on mercuric chloride induced genotoxicity in human blood cultures. *Toxicology in vitro* 15: 649-654.

Rao, M.V., Gayathri, R.P. and Deepa, K. 1995. Effect of glutathione on mercuric chloride toxicity in liver and kidney of mice. *Ind. J. Environ. Toxicol.* 5 : 59-62.

Redmond, H.P., Wang, J.H. and Bouchier Hayas, D. 1996. Taurine attenuates nitric oxide and reactive oxygen intermediate dependent hepatocytes injury. *Arch. Surg.* 131: 1280-1287.

Rose, M.L., Germolec, D.R., Schoonhoven, R.and Thurman, R.G. 1997. kuffer cells are casually responsible for the mitogenic effect of peroxisome proliferators. *Carcinogenesis.* 18: 1453-1456.

Sankar Samipillai, S and Jagadeesan, G. 2004. Role of taruine on protein metabolism of selected tissues in mercury intoxicated mice. *Mus musculus* (Linn). *Ind. J. Environ. Toxicol*. 14: 29-33.

Sankar Samipillai, S. and Jagadeesan, G. 2005. Influence of taurine on phosphatases activity in selected tissues of mercuric chloride intoxicated mice. *J. Exp. Zool*. 8: 295-300.

Shalan, M.G., Mostafa, M.S., hassouna, M.M., Hassab, E. Nabi, S.E. and E1-Refaie, A. 2005. Amelioration of lead toxicity on rat liver with vitamin C and silymarin supplements. *Toxicology*. 206: 1-15.

Shambhunath Bose, Banibratta Mukhopathy, Shibani and Sheller Bhattacharya, 1994. Correlation of metal distributionreduced glutathione and metallothionein levels in liver and kidney of rat. *Ind. J. Expl. Biol.* 32 : 679-681.

Sharma, V.P., Dixit, B.S., Banarji, R. and Seth, P.K. 2002. Organochlorine insecticide residues and fluoride concentration in ground water of Unnao. *Ind. Poll. Res.* 21: 349-353.

Stopford, W., and Goldwater, L.J. 1975. Methly mercury in the environment: a review of current understanding. *Environ. Health. Perspect.* 12: 115-118.

Tollefson, L. and Cordle, F. 1986. Methyl mercury in fish : a review of residue level, fish consumption and regulatory action in the united states. *Environ. Health. Perspect.* 68 : 203-208.

USEPA. 1987. Quality criteria for water EPA. Publication 440/5-86-001 U.S. Gov. Prin. Office. Washington. DC.

Vijaya Madhavan, K.T. and Iwai, I. 1979. Histochemical observations on permeation of heavy metal into taste buds of gold fish. *Bull. Jap. Soc. Fish.* 4 : 631.

Waters, E., Wang, J.H., Redmond, H.P., Wu, Q.D., Kay, E. and Bouchier-Hayes, D. 2001. Role of taurine in preventing acetaminophen-induced hepatic injury in the rat. *Am. J. Physiol. Gastrointest Liver Physiol.* 280 : 1274-1279.

WHO, 1989. "Mercury – Environmental aspects". Environmental health Criteria 86, publication of WHO, Geneva ISBN. 92-4-154586.

Wright, C.E., Tallan, H.H., Lin, T.T., Syurman, J.A. and Gaull, G.E. 1986. Taurine biolgical update. *Ann. Rev. Bichem* 55: 427-453.

Yamono, T, Decicco L., A. and Bikans L.E. 20001.Attenuation of cadmium –induced liver injury in ganescent male fisher 344 rats role of kupffer cells and inflammatory cytokines. *Toxiol Appl. Pharmacol.* 162:P68-75.

Zalups, R.K. 1993. Early aspects of the international distribution of mercury after the intravenous administration of mercuric chloride *Toxicology.* 79: 215-218.