AMELIORATION OF MERCURIC CHLORIDE INDUCED NEPHROTOXICITY AND OXIDATIVE STRESS BY GARLIC EXTRACT

N. ABIRAMI, R. JAGADEESWARI
PG and Research Department of Biochemistry,
Dr. N.G.P. Arts and Science College, Kovai Medical Centre for Research and Education Trust, Coimbatore -641 035, Tamilnadu, India.

ABSTRACT

Effect of Garlic against mercuric chloride induced toxicity in albino rats was studied. Oral administration of mercuric chloride (100mg/kg/p.o) for 30 days resulted in significant increase in LPO Basal level and LPO FeSO4 induced and significant decrease in GSH (Glutathione) and Vit C as compared to the normal and control group. Simultaneous administration of Garlic along with Mercuric chloride, produced a pronounced neproprotective effect against mercuric chloride induced toxicity in rats by restoring the normal levels of biochemical parameters.

INTRODUCTION

Kidney is the major excretory organ that is exposed to various toxic insults leading to nephrotoxicity. Inorganic mercury present in the environment is a well established toxicant to human health . It is well known that inorganic mercury causes severe kidney damage after acute and chronic exposure. A good deal of evidence suggests the beneficial effect of regular dietary intake of garlic on mild hypertension, hyperlipidemia and malignant diseases.1-3 Garlic also possesses anti-microbial and immuno stimulatory properties, enhanced fibrinolytic activity and exerts favourable effect on platelet aggregation and adhesion.4-5 Our present study, aims to determine the nephroprotective role of garlic (Allium sativum.L) against mercury induced toxicity.

MATERIALS AND METHODS

(I) Plant Material Used

Garlic (Allium sativum.L) was obtained from the local market. The cloves were separated, scales were removed, washed with water and shade dried. The dried cloves were then ground into a fine powder. The powder was washed with distilled water-filtered through cheese cloth and the filtrate was administered orally to rats.
(II) **Experimental induction of nephrotoxicity**

Mercuric chloride was chosen to induce nephrotoxicity in rats. Mercuric chloride at the dose of 2mg/kg bw/ip is nephrotoxic in rats. Hence this dosage was chosen for intraperitoneal administration.

(III) **Experimental Setup**

Rats were divided into five groups comprising of six animals each:

- **Group I**: Served as control
- **Group II**: Received garlic (100mg/kg/po) for 30 days.
- **Group III**: Administered mercuric chloride (2mg/kg/bw/ip) thrice
- **Group IV**: Rats were induced toxicity with mercuric chloride (2mg/kg/bw/ip) and then treated with garlic (100mg/kg/po) for 30 days. (curative).
- **Group V**: Rats were pretreated with garlic (100mg/kg/po) for a period of 30 days and then toxicity was induced with mercuric chloride (2mg/kg bw/ip) (prophylactic).

**Collection of Rat tissue**

At the end of experimental period, the animals were killed by cervical decapitation. Blood was collected, plasma separated and used for determination of plasma constituents. Kidneys were removed and washed with ice-cold saline and their weights recorded.

Plasma samples were collected for the estimation of LPO Basal, LPO FeSO$_4$ induced, GSH and vitamin-C.

**RESULTS AND DISCUSSION**

Kidney receives approximately one quarter of cardiac output through which it transports variety of potentially toxic substance within its parenchyma. Hence, renal glomerular and tubular epithelial cells are more susceptible to toxic insults. Presentation of noxious substances to glomerular and peritubular capillary network, therefore occurs with greater frequency than with others capillary beds.

Table I depicts the changes in levels of malondialdehyde—the end product of lipid peroxidation, (basal and ferrous sulphate induced) in both control and experimental groups. The basal level of malondialdehyde was significantly increased in the kidneys during mercuric chloride treatment (Group III) when compared to that of control (Group I). Incubation of the homogenate with ferrous sulphate, increased malondialdehyde production in both control, and mercuric chloride treated groups. A similar increase in the level of lipid peroxides during mercuric chloride administration has been reported (Kalpana devi et al., 1994);
Huang et al, 1996) supports our present observation of increase in lipid peroxidation using ferrous / ascorbate induction system. Administration of garlic extract in nephrotoxic rats, decreased the levels of lipid peroxides (Group IV and V). Prophylactic garlic treatment provided a better protection against mercuric chloride-induced lipid peroxides (Group V), rather than curative group (Group IV). The observed decrease may be attributed to the presence of ideally polysulfides, that are present in the garlic extract and have been reported to possess antioxidant like properties.

Table II depicts the levels of renal glutathione which significantly reduced during mercuric chloride toxicity (Group III), when compared to that of control (Group I). Administration of mercuric chloride to garlic extract pretreated rats (Group V) did not show any significant decline in the renal GSH levels. Ascorbic levels significantly decreased in the kidney of Group III animals. A similar decrease has been reported during inflammation during cadmium intoxication. A significant increase was observed in the levels of ascorbic acid during garlic extract administration in mercuric chloride induced nephrotoxic rats (Group IV and V). The levels of lipid peroxidation and levels of antioxidant activities were assayed in kidneys.

### Table 1

**Levels of Lipid Peroxidation in the Kidney of Normal and Experimental Rats**

(Values are Mean ± S.D for six animals)

| Particulars          | Group – I C | Group – II C+G | Group – III M | Group – IV M+G | Group – V G+M |
|----------------------|-------------|----------------|---------------|----------------|---------------|
| LPO Basal            | 2.23±0.14   | 6.12±1.19$^a$ | 24.60±6.42$^b$ | 4.43±0.16$^c$ | 3.22±0.12$^d$ |
| LPO FeSO₄ induced    | 5.33±0.21   | 6.93±0.48$^c$ | 13.17±0.54$^c$ | 9.06±0.18$^c$ | 7.32±0.16$^c$ |

C – Control, G- Garlic, M- Mercury

Treatments of groups are: Group I – control, Group II Control + Garlic (100mg/kg bw/p.o), Group III-Mercury (2mg/kg bw/i.p) thrice, Group IV – Mercury + Garlic (Curative), Group V- Garlic + Mercury (Prophylactic).

LPO is expressed as –nanomoles of MDA formed /mg protein at 37°C

Comparison is done between groups: a-Group I and Group II, b-Group II and Group III and group IV, d-Group IV and Group V.

The symbols represent statistical significance: *p<0.01; $ - p<0.05; **- p<0.001
Table 2
Levels of Non-Enzymatic antioxidants in the Kidney of control and experimental rats
(Values are Mean ± S.D for six animals)

| Particulars | Group –I C | Group –II C+G | Group –III M | Group –IV M+G | Group –V G+M |
|-------------|------------|---------------|-------------|-------------|------------|
| GSH         | 5.04±0.22  | 5.89±0.23²³  | 1.46±0.023²³ | 3.18±0.032²³ | 3.74±0.63²³ |
| Vitamin –C  | 2.18±0.13  | 2.51±0.13²³  | 0.82±0.023²³ | 1.07±0.06²³  | 1.85±0.11²³ |

C – Control, G- Garlic, M- Mercury

Treatments of groups are: Group I – control, Group II Control + Garlic (100mg/kg bw/p.o), Group III-Mercury (2mg/kg bw/i.p) thrice, Group IV – Mercury + Garlic (Curative), Group V- Garlic + Mercury (Prophylatic).

Units are expressed as: GSH-ìg/mg protein, Vitamin C-ìg/mg protein

Comparison is done between groups: a-Group I and Group II, b-Group II and Group III and group IV, d-Group IV and Group V.

The symbols represent statistical significance: *p<0.01; $ - p<0.05; **- p<0.001

REFERENCE

1. World Health Organisation (1991) Inorganic mercury: Environmentl Health Criteria., 118: 1-115
2. McDowell, E.M., Nagle, R.B., Zalme, R.C., McNeil, J.S. et al., (1976) Studies on the pathophysiology of acute renal failure. I. Corelation of ultra structure and function in the proximal tubules of rat following administration of mercuric chloride Virchows. Arch., 22:173-196.
3. Huang, Y.L., Chen, S.L. and Lin, T.H. (1996) Lipid peroxidation in rats administered with mercuric chloride. Biol. Trace. Elm. Res., 52:193-206.
4. Fenwick, G.R. and Hanley, A.B. (1985) Food. Sci. Nutr., 23:1-73.
5. Koch, H.P. and Lawson, L.D. (1996) The science and therapeutic application of allium sativum. L. and related species. Planta Med., 61:139-143.
6. Giraradi, G. and Elias, M.M (1993)] Effect of different renal glutathione levels on renal mercury disposition and excretion in the rats. Toxicology, 81:57-67.
7. Chatterjee, C.C., 1992. Human physiology, 1, 563-569, Medical Allied Agency, Calcutta.
8. Huang, Y.L., Chen, S.L. and Lin, T.H. (1996) Lipid peroxidation in rats administered with mercuric chloride. Biol. Trace Elem. Res., 52:193-206.

9. Kalpana Devi, V., Sumathi, R. And Varalakshmi, P. (1994) Evaluation of the antidotal effect of DL-α-lipoic acid against mercuric chloride induced acute renal dysfunction. Med. Sci. Res., 22: 859-862.

10. Liebert J., Murias, M. and Bloszy K. E. (1999) Effect of several sesquiterpene lactones on lipid peroxidation and glutathione levels Planta. Med., 65:320-324.

11. Horie., T., Awuzu. S., Itajura, Y. and Fuwa, T. (1992) Identified Diallyl polysulfides from an aged garlic extract which protects the membranes from lipid peroxidation. Planta. Med., 52: 468-469.

12. Zalups, R.K. and Lash, L.H. (1994) Recent advance in understanding the renal transport and toxicity of mercury J. Toxicol. Environ. Health., 42:1-44.

13. Braget, P. and Bonda. I.L. (1980) Oxidant stress during inflammation. Anti inflammatory effects of Antioxidants. Agents Actions, 10:536-539.

14. Pharikal, K., Das, P.C., Dey, C.d. and Das Gupta, S. (1988) Tissue ascorbate as a metabolic marker in cadmium toxicity. Int. J. Vitamin. Nutr. Res., 58: 306-311.