Can Liv.52 Protect Mammalian Kidney Against Toxic Substances?
– Results and Possibilities

Rathore, H.S.
School of Studies in Zoology, Vikram University, Ujjain, India.

ABSTRACT
A controlled trial was done on 24 Swiss albino mice divided in three groups – control on 50 g food daily, another on 50 g food + cadmium chloride (CdCl$_2$) daily and the third on 50 g food + CdCl$_2$ + Liv.52 daily. The morphological and histopathological findings on the 31st day after the mice were sacrificed revealed that in the Liv.52-treated group:
1. The kidneys showed normal shape and size
2. The glomeruli appeared normal and did not show any signs of damage
3. Casts were absent, the tubules compact and rounded, neither dilated nor damaged.

Thus, the protective effect of Liv.52 has been established.

INTRODUCTION
Cadmium-induced renal damage in man and animals results in proteinuria and reduced reabsorption of glucose, amino acids, phosphorus and calcium (Friberg et al. 1974). Disturbed mineral metabolism causes stone formation (Tsuchiya, 1978). Renal damage has caused death of Cadmium (Cd) industry workers (Bulmer et al., 1938; Beton et al., 1966). In a comprehensive review, Piscator (1986) suggests that Cd-induced renal damage can be prevented only if Cd does not reach toxic levels and, in this context, the role of drugs has neither been described nor recommended. In our recent experiment, it was found that Liv.52 could prevent Cd-induced histopathological and biochemical (GOT, GPT, AP) alterations in mice liver (Rathore and Verma, 1986). Cd damages the liver, kidney and spleen simultaneously (Dalhamn and Friberg, 1955, 1957). Hence, we undertook this study to test the ability of Liv.52 to protect mice kidney against Cd-intoxication.

MATERIALS AND METHODS
Four month old Swiss albino male mice obtained from the Biological Products Division, Veterinary College, Mhow (M.P.) were used. Food and water were given ad libitum. CdCl$_2$ was dissolved in distilled water to prepare a solution of 20 ppm (20 mg/litre).

Each 2.5 ml of Liv.52 syrup contains the following plant extracts:

- Capparis spinosa: 17 mg
- Cichorium intybus: 17 mg
- Solanum nigrum: 8 mg
- Cassia occidentalis: 4 mg
- Terminalia arjuna: 8 mg
- Achillea millefolium: 4 mg
- Tamarix gallica: 4 mg
The mice were divided into three groups:
Group A: 8 mice on 50 g food daily, served as controls.
Group B: 8 mice on 50 g food + 10 ml stock solution of CdCl₂ daily
Group C: 8 mice on 50 g food + 10 ml of stock solution of CdCl₂ + 5 ml of Liv.52 syrup.

The drug and/or CdCl₂ solution was thoroughly mixed in the fresh standard mice food every day. 10 ml of stock solution of CdCl₂ contained 0.2 mg CdCl₂.

The mice were killed on the 31st day. The fresh kidneys were measured; their Bouin’s fixed sections cut at 6 µ were stained in Delafield’s hematoxylin and eosin. Histopathological observations for each kidney were made according to four parameters: glomerular change, tubular dilation, interstitial change and occurrence of casts. The experiments were done thrice.

**RESULTS AND DISCUSSION**

(1) *Morphology: Table 1 shows that CdCl₂ feeding for one month caused shrinkage of the kidney (Group B) as compared to the size of the control kidney (Group A). When CdCl₂ was fed along with Liv.52 for one month, the kidney showed normal shape and size (Group C).*

<table>
<thead>
<tr>
<th>Group</th>
<th>Length of kidney (mm)</th>
<th>Width of kidney (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Controls (12)</td>
<td>13.10 ± 0.15</td>
<td>8.83 ± 0.28</td>
</tr>
<tr>
<td>B. CdCl₂ (12)</td>
<td>11.50 ± 0.20*</td>
<td>8.00 ± 0.23</td>
</tr>
<tr>
<td>C. CdCl₂ + Liv.52 (12)</td>
<td>8.60 ± 0.19</td>
<td></td>
</tr>
</tbody>
</table>

* Significant based on ‘t’ test at 5% level of significance. Numbers in parentheses indicate number of animals used.

(2) *Histopathology: Controls (Group A). Normal rounded glomeruli. Tubules are normal. No dilation, no sloughing of epithelium and no casts are seen. No inclusion. In brief, in controls the pathological signs are altogether absent (Figs.1 and 2).*
CdCl₂ + Liv.52 treatment (Group C): Glomeruli appear normal. They do not show damage at any spot. Casts are absent. Tubules are compact, rounded and at places thin-walled but neither dilated nor damaged. No inclusion (Figs. 5 and 6).

DISCUSSION
Pathological observations in mice kidney following CdCl₂ feeding agree with the findings of previous workers who have also found histopathology of the renal cortex in man (Bonell, 1955; Kazantzis et al., 1962) and in animals (Axelsson et al., 1974; Elinder et al., 1981) following Cd poisoning.

Before explaining the possible role of Liv.52 against Cd-toxicity it becomes necessary to look at the mechanism of Cd-induced renal damage. As soon as Cd enters the body, it reaches the liver where it is efficiently trapped in the form of Cd-metallothionein complex. Metallothionein is a low molecular weight protein synthesized by the liver and Cd binds with this molecule. The liver slowly releases Cd-metallothionein (Change et al., 1980; Falck et al., 1983). Reabsorption of Cd-metallothionein results in the accumulation of Cd in the kidney. The kidney does not allow rapid catabolism of Cd-metallothionein as it can also synthesize metallothionein according to the degree of exposure), and free Cd will bind with the other cytoplasmic membranes for which it has a high affinity (Teare et al., 1976) and kill the kidney cells.

Some of the known properties of Liv.52 (on the liver), which might have reduced the toxicity of cadmium, are as follows:
1. The kidneys have a limited capacity to synthesize metallothionein, and if Liv.52 stimulates its synthesis, it can stimulate protein synthesis in the liver (Subbarao and Gupta, 1978). All the cadmium is trapped in the form of Cd-metallothionein complex, which is not toxic to cells. Even if a little Cd is present and has damaged the membranes Liv.52 can repair the cytoplasmic membranes (Saxena et al., 1980). In this way Liv.52 can maintain the normal structure of the tubules in the kidney in the presence of cadmium.

2. Cd affects the activity of alkaline phosphatase (Nogawa et al., 1980) but Liv.52 can maintain its optimal activity (Qazi, 1965), which is a must for tubular function (Benedek et al., 1966).

3. Cd damages the blood vessels (Gunn et al., 1963) but Liv.52 can check it (Saini and Saini, 1985); this can prevent vascular damage to the kidney.

Further research is required to explain how Liv.52 actually protects the kidney against damage from toxicants.

ACKNOWLEDGEMENT
This research work was supported with grants from The Himalaya Drug Company, Bombay. The Head of the Department gave us departmental facilities.

REFERENCES
17. Qazi, I.H., *Probe* (1965): 1, 1