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

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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 $CdCl_2$ daily
Group C: 8 mice on 50 g food + 10 ml of stock solution of $CdCl_2$ + 5 ml of Liv.52 syrup.

The drug and/or $CdCl_2$ solution was thoroughly mixed in the fresh standard mice food every day. 10 ml of stock solution of $CdCl_2$ contained 0.2 mg $CdCl_2$.

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 $CdCl_2$ feeding for one month caused shrinkage of the kidney (Group B) as compared to the size of the control kidney (Group A) . When $CdCl_2$ was fed along with Liv.52 for one month, the kidney showed normal shape and size (Group C).

Table 1: Effect of CdCl2 alone and in combination with Liv.52 on the morphology of mice kidney after 30 days' oral treatment

Group		Length of kidney (mm)	Width of kidney (mm)
A.	Controls (12)	13.10 ± 0.15	8.83 ± 0.28
B.	$CdCl_2$ (12)	11.50 ± 0.20*	8.00 ± 0.23
C.	$CdCl_2$ + Liv.52 (12)		8.60 ± 0.19

* 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 glomruli. 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).

Fig. 1: Control: Tubules and glomerulie are normal (100 x)

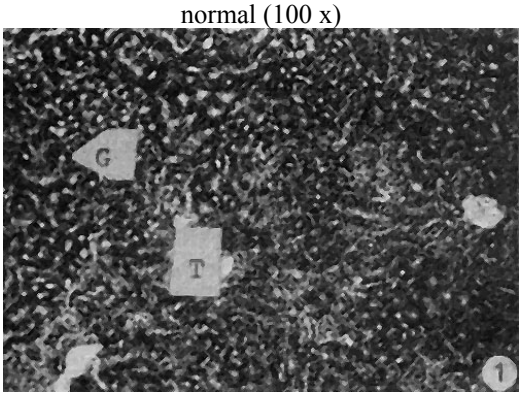
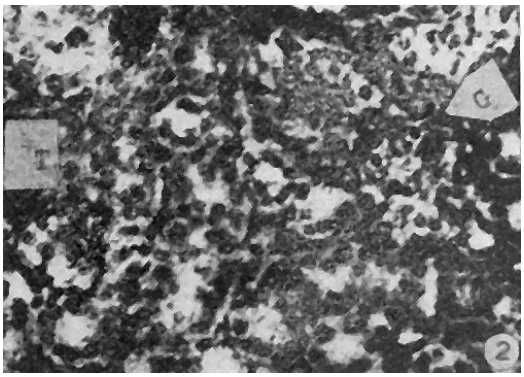


Fig. 2: Control: Magnified view (400 x)



$CdCl_2$ treatment (Group B): Dilation of tubules is evident; sloughing of epithelium indicates advanced disintegration of tubules. At places, casts (dead tubule's remains) are also seen. Glomeruli show shrinkage; however, at places they show complete disintegration. Inclusion of blood cells is evident (Figs.3 and 4).

Fig. 3: $CdCl_2$ treated: Dilated tubules, damaged glomeruli, infiltration of blood cells (100 x)

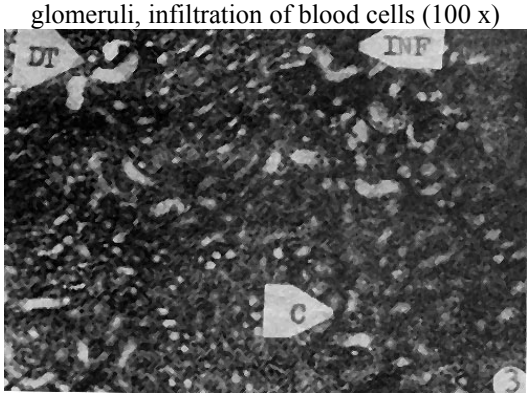
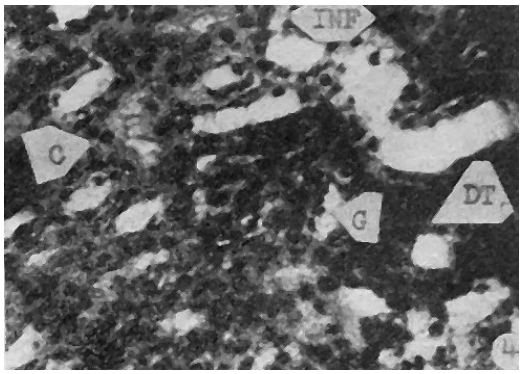


Fig. 4: Magnified view of Fig. 3 (400 x)



$CdCl_2$ + Liv.52 treatment (Group C): Glomruli 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).

Fig. 5: $CdCl_2$ + Liv.52 treatment: Tubules and glomeruli appear normal (100 x). G=Glomeruli; T=Tubules and DT=Dilated tubules

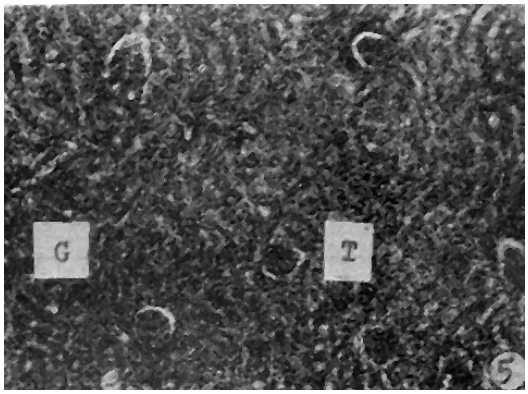
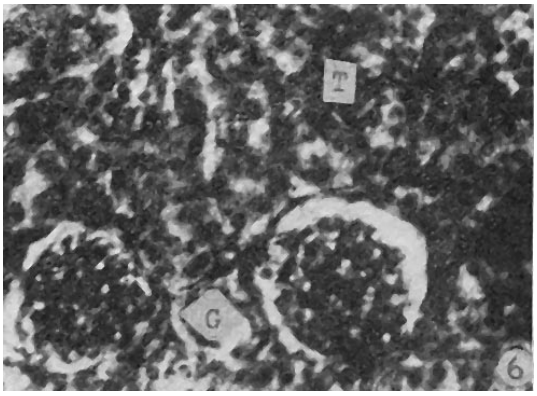


Fig. 6: Magnified view of Fig. 5 (400 x) INF=Infiltration of blood cells and C=Casts



DISCUSSION

Pathological observations in mice kidney following $CdCl_2$ 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.

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