EFFECT OF 'AROGYAVARDHINI' AGAINST CARBON TETRACHLORIDE INDUCED HEPATIC DAMAGE IN ALBINO RATS

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Summary : 'Arogyavardhini' - an indigenous formulation was evaluated for its hepatoprotective activity in rats, using two models of carbon tetrachloride (CCl_4) hepatic damage, one simulating vital hepatitis and the other simulating fatty change. The protective effect was assessed from serum aspartate transaminase (AST) and alkaline phosphatase levels and from histopathological changes in liver. The results revealed that 'Arogyavardhini' (5 *mg/100g*, PO daily) was effective in minimizing the changes in serum levels of AST and alkaline phosphatase induced by CCl. The protective effect was also evident on histopathological examination.

Key words : Arogyavardhini carbon tetrachloride hepatoprotective action

INTRODUCTION

A number of indigenous formulations have been claimed to possess hapatoprotective activity. A few of them have also been studied in experimental models (1,6). 'Arogyavardhini' is an indigenous formulation (see below) which is claimed to be hepatoprotective. This study was undertaken to evaluate its action against carbon tetrachloride (CCl_4) induced hepatic damage in albino rats.

MATERIAL AND METHODS

Drug administration : 'Arogyavardhini' was obtained as tablets (200 *mg* each) containing 1 part each of mercury, sulphur. lohabhasma, tamrabhasma and abhrakbhasma; 2 parts of Triphala churna (Terminalia chebula, Terminalia beterica and Phyllanthus emblica) ; 3 parts of Shilajit; 4 parts of Guggul (Commiphora mukul) ; 18 parts of Kutki (Picrorrhiza kurrooa) and 72 parts of the decoction of Azadirachta indica. Tablets were

crushed and the powder (50 *mg/kg*, P0 daily for 4 weeks) was given as freshly prepared suspension in gum acacia. Control animals received only the vehicle.

Experimental protocols : Male albino rats of Haffkine Strain (100 to 140 *g*) were divided into four groups. Group I (n=6) acted as normal control. Group II (n=6) was used to study the effects of administration of 'Arogyavardhini' alone (Drug control). Group III (n=12) was used to study acute hepatic damage. CCl_4 was administered once in the dose of 1.25 *ml/kg*, P0, in liquid paraffin (1.4 v/v). This group was further subdivided into group I_a (n=6), which was pretreated with 'Arogyavardhini' and group I_b (n=6) which was pretreated with gum acacia (control). Croup IV was used to study chronic reversible hepatic damage. CCl_4 (1 *ml/kg*, SC, with equal volume of liquid paraffin) was administered twice a week for 8 weeks. Later, this group was divided into three groups (n=6 each) viz. group IV_b-treated with 'Arogyavardhini' and group IV_b - treated with gum acacia and group IV_c - sacrificed 24 hr after the last injection of CCl_4.

The animals were observed daily and weighed weekly. Twenty four hr after the study period, blood samples were withdrawn by cardiac puncture under light ether anesthesia for estimating serum AST (5) and serum alkaline phosphatase (2). Later, the animals were sacrificed and their livers were removed, The weights and volumes of livers were recorded. Histopathological examination was done by an experienced pathologist, who was unaware of the treatment given to the animals. The histopathological lesions were scored as described previously (4) in 4 grades (0-no degeneration, 1 - few vacuolated cells per lession, 2 - more than 10 vacuolated cells per lession, 3 - one or two rows of vacuolated cells per lession and 4 - more than two rows of vacuolated cells per lesion),

The results were analysed by student's "t" test.

RESULTS

Effect of treatment with "Arogyavardhini" (Group I and II) : Control animals gained in body weight (108$\pm$ 4.18 g/100 g of initial wt). The drug did not significantly affect the weight gain. Control liver weight (3.41$\pm$ 0.26 g/100 g wt) and volume (2.99 $\pm$ 0.17 ml/100 g wt), serum AST (44.00 $\pm$2.80 IU/l) and serum alkaline phosphatase (20.33 $\pm$1.67 KA units %) were also essentially unaltered by drug treatment. There was no evidence of necrosis, degeneration or fibrosis in livers of both groups.

Acute hepatic damage (Group III) : None of the animals from this group died during the study period. There was no significant difference in body weight gain,

weight or volume of liver in the two subgroups. A significant rise in serum AST and alkaline phosphatase levels was noted in group III_b, which did not receive 'Arogyavardhini". This rise was less marked in group III_a (Table I). Similarly, the histopathological changes viz. necrosis and degeneration were less marked after "Arogyavardhini" pretreatment.

TABLE I : Effect of 'Arogyavardhini' on CCl_4 induced acute hepatic damage in albino rats (Mean± S.D.) (n=6 each).

No.	*Parameter*	*Control*	*Arogyavardhini pretreatment*
1.	Change in body weight (*g*/100 *g* of initial)	88.18 ± 12.85	85.92 ± 10.62
2.	Liver weight (*g*/100 *g* of BW)	4.58 ± 0.83	4.05 ± 0.88
3.	Liver volume (*ml*/100 *g* of BW)	4.39 ± 0.91	3.70 ± 0.75
4.	Serum AST (IU/l)	186.67 ± 72.14	100.33 ± 51.82*
5.	Serum alk. Phosphatase (KAU%)	46.14 ± 10.87	30.30 ± 8.57*
6.	Necrosis	1.28 ± 0.51	0.80 ± 0.34*
7.	Degeneration	1.05 ± 0.71	0.40 ± 0.34*

*$P<0.05$ in comparison with control. See text for histological scoring.

Chronic reversible hepatic damage (Group IV) : Only one animal died from group IV_b. There was no significant difference in body weight gain and weight and volume of liver in the groups IV_a, IV_b and IV_c. Group IV_c shows the effects of chronic administration of CCl_4 The rise in serum AST levels and histopathological changes viz. degeneration and fibrosis were less marked in group IV_b as compared to those in group IV_c. Serum AST and alkaline phosphatase levels were significantly less in group IV_a in contrast to those in group IV_b. The degree of necrosis was comparable in these two groups, but degeneration and fibrosis were less marked in group IV_a, treated with "Arogyavardhini", which also showed significant amount of regeneration (Table II).

TABLE II : Effect of 'Arogyavardhini' on chronic reversible hepatic damage induced by admini stration of CCr_4 in albino rats. (Mean ± S.D.) (n=6 each).

No.	*Parameter*	*Group IV*		
		a	b	c
1.	Change in body-weight (*g*/100 *g* of initial)	110.44±28.89	92.66±20.32	90.50±23.80
2.	Liver weight (*g*/100 *g* of BW)	4.25±0.51	4.12±0.91	4.00±0.80
3.	Liver volume (*ml*/100 *g* of BW)	4.00±0.85	3.52±0.98	3.60±0.98
4.	Serum AST (IU/l)	60.10±14.94*	87.20±17.48▲	110.50±19.80
5.	Serum alk. phosphatase (KAU%)	36.20±9.31*	58.70±14.94	64.25±16.10
6.	Necrosis	0.60±0.73	0.68±0.98	1.60±1.04
7.	Degeneration	0.72±0.63*	1.16±0.78▲	2.80±0.86
8.	Fibrosis	1.70±0.05*	3.02±0.98▲	1.52±0.41
9.	Regeneration	2.13±1.00*	1.00±0.63	1.00±0.80

* Comparsion between a and b
▲ Comparison between b and c
*, ▲ $P < 0.05$
a : CCl_4 (for 8 weeks) + Arogyavardhini (for 4 weeks)
b : -- " -- + Gum acacia (for 4 weeks)
c : -- " -- only.

DISCUSSION

The hepatoprotective activity of "Arogyavardhini" was studied in two models simulating acute viral hepatitis and fatty change in liver respectively.

Pre-treatment with "Arogyavardhini" was found to protect the liver against acute damage induced by administration of a large dose of CCl_4 (group III) In order to study the effect of this drug on regeneration of hepatic parenchyma a pre-cirrhotic stage was induced by administration of CCl_4 over a period or 8 weeks. When these animals were left to recover on their own, it was found that the extent of degeneration and fibrosis was reduced with decline in serum AST levels (group IV_b vs. group IV_c). Treatment with "Arogyavardhini" not only resulted in normalization of serum levels of both AST and alkaline phosphatase, but also accelerated the regeneration of hepatic parenchyma and minimized the extent of fibrosis (groups IV_a vs. group IV_b).

From this study, it is not possible to comment on the mechanism of hepatoprotective effect of "Arogyavardhini". One of the ingredients of "Arogyavardhini" viz. picrorrhiza kurrooa has been reported to exert hepatoprotective action (3). The actions of other components need to be evaluated.

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REFERENCES

1. Joglekar, G.V., G.K. Chitale and J. H. Balwani. Protection by indigenous drug against hepatotoxic effect of carbon-tetrachloride in mice. *Acta Pharmac. Toxicol. (Copenn)*, **20** : 73-79, 1963.

2. King, E. J. and A. R. Armstrong. Convenient method for determining serum and bile phosphatase activity. *Canad. Med. Ass. J.*, **31** : 376-381, 1934.

3. Pandey V. N. and G. N. Chaturvedi. Effect of different extracts of kutaki on experimentally induced abnormalities in the liver. *Ind. J. Med. Res.*, **57**: 503-512, 1969.

4. Rege, N., S. Dahanukar and S. M. Karandikar. Hepatoprotective effect of cyanidol (+) against carbon-tetrachloride induced liver damage. *Indian Drugs*, **21** : 556-568, 1984.

5. Reitman, S. and S. Frankel. A colorimetric method for the determination of serum glutamic oxalacetic and glutamic pyruvic transaminases. *Amer. J. Clin. Path.*, **28** : 56-63, 1957.

6. Srinivasan, S., V. R. Prabhu and J. H. Balwani. Effect of an indigenous drug preparation on carbon-tetrachloride hepatotoxicity. *Ind. J. Med. Res.*, **56** : 879-883, 1968.