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Comparative Efficacy of Liv.52 and *Andrographis paniculata*, (Nees.) in Experimental Liver Damage in Rabbits

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ABSTRACT

The comparative efficacy of Liv.52 vs. Andrographis paniculata was evaluated in carbon tetrachloride (CTC)-induced liver damage in rabbits divided into 4 groups. Those animals treated with these drugs showed marked clinical recovery from liver damage as compared to control animals, being seen earlier in the Liv.52-treated animals.

Aspartate aminotransferase (AST) and alanine amninotransferase (ALT) enzyme levels showed significant increases in CTC-induced liver damage. Recovery was rapid and complete in the Liv.52-treated animals following CTC damage.

Hypoglycaemia and hypercholesterolaemia that were observed in CTC-induced toxicity returned towards normalcy after Liv.52 treatment.

Histopathological changes indicative of liver damage caused by CTC were evident in three groups of animals. Liv.52-treated animals showed remarkable regenerative changes but not those treated with Andrographis paniculata.

INTRODUCTION

Several workers have reported liver dysfunction due to various injurious stimuli in experimental animals and man[1,2]. Liv.52 (Himalaya) has been used for several years in the treatment of jaundice[3], alcoholic liver damage[4], cirrhosis[5] and other liver dysfunctions[6].

Andrographis paniculata (Kalmegh) has been found to possess protective effects on experimentally induced hepatopathy in dogs[7]. The decoction of the leaves of this plant has been reported to improve sluggish liver function and biliary flow[8]. However, its therapeutic value in restoration of liver disorders in comparison to Liv.52 has not been fully elucidated. The present paper puts on record the comparative efficacy of *A. paniculata* and Liv.52 in the restoration of liver function after carbon tetrachloride-induced hepatopathy.

MATERIALS AND METHODS

Thirteen healthy New Zealand White (NW) rabbits were randomly distributed in four groups of 4, 3, 3 and 3. Animals of Group-I were kept as healthy control, while in Groups II, III and IV, liver damage was induced by oral administration of CTC @ 0.2 ml/kg body weight in paraffin for 4 consecutive days.

After CTC induced hepatopathy, Group-II animals were kept as untreated control, while Group-III received 0.5 gm/kg dried powder of leaves of *A. paniculata* orally once a day for six days. Group-IV animals were treated with Liv.52 orally @ 1 ml/kg once a day for six days. The dose of *A. paniculata* in rabbits was calculated as per the earlier prescriptions, which varies from 0.3-1.5 gm/kg body weight[7,9].

Fasting blood samples were collected for biochemical analysis one day before and 5,7 and 17 days after CTC intoxication and drug therapy. The serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) and alanine aminotransferase (ALT) were estimated by the method of Reitman and Frankel[10], glucose by the method of Folin and Wu[11], total cholesterol by the method of Zlatkis *et al.*[12] and total protein by that of Greenberg[13].

At the end of the experimental study, all the animals were sacrificed to perform gross and histopathological examinations. The statistical analysis of the data was carried out using Fisher's 't' test and paired 't' test as described by Snedecor and Cochran[14].

RESULTS AND DISCUSSION

Throughout the observation period, rabbits in Group-I remained clinically healthy. But clinical signs like depression, anorexia, rough coat, pale mucous membrane, staggering gait, loss of body weight and enteritis were, however, evident in Groups-II, III and IV animals after CTC intoxication. Similar clinical signs after CTC intoxication have also been reported in dogs[15]. But in Group-IV animals, which were treated with Liv.52, the clinical signs started to recede and by the 11th day, clinical recovery was complete.

The mean AST and ALT values before and after CTC administration are shown in Table 1. There was a significant increase (p<0.05) in the serum levels of both these enzymes by day 5 in the animals of Groups-II, III and IV after receiving CTC. Increase in the values of AST and ALT enzymes after CTC induced hepatopathy is very well documented[16]. After administration of *A. paniculata* in Group III animals and Liv.52 in Group IV animals, a significant reduction (p<0.05) was recorded by day 7 in the AST and ALT levels in comparison to Group-II liver damaged, untreated animals. However, the reduction in enzymatic levels towards normalcy was more pronounced in the Liv.52 treated, as compared to the *A. paniculata*-treated group.

Table 1: Mean changes in the values of Asparate Aminotransferase and Alanine Aminotransferase in the different groups

Groups/Days	AST (RF Units/ml)				ALT (RF Units/ml)			
	0	5	7	17	0	5	7	17
I.	$49.75^{a,A}$ ± 4.23	$51.25^{a,A}$ ± 5.15	$47.50^{a,A}$ ± 3.23	$50.25^{a,A}$ ± 4.09	$32.00^{a,A}$ ± 3.16	$32.00^{a,A}$ ± 3.16	$31.50^{a,A}$ ± 3.97	$31.75^{a,A}$ ± 3.54
II.	$47.67^{a,A}$ ± 2.60	$208.33^{b,B}$ ± 4.41	$196.67^{b,B}$ ± 6.00	$72.00^{a,A}$ ± 0.00	$35.33^{a,A}$ ± 4.63	$235.00^{b,B}$ ± 29.30	$159.33^{a,b,B}$ ± 13.86	$79.00^{a,A}$ ± 0.00
III.	$45.33^{a,A}$ ± 7.75	$199.00^{b,B}$ ± 21.00	$166.33^{b,B,C}$ ± 13.12	$64.33^{C,A}$ ± 8.57	$33.00^{a,A}$ ± 5.29	$221.33^{b,B}$ ± 15.56	$120.00^{b,c,B,C}$ ± 27.39	$42.33^{a,c,A}$ ± 7.36
IV.	$43.67^{a,A}$ ± 6.44	$180.00^{b,B}$ ± 22.91	$115.00^{a,b,C}$ ± 22.91	$48.33^{a,A}$ ± 5.55	$35.33^{a,A}$ ± 5.60	$68.87^{b,B}$ ± 29.76	$207.33^{c,C}$ ± 6.33	$36.67^{a,A}$ ± 4.33

Note: Means having the same small letters row-wise and capital letters column-wise are not significantly different, probability level (p<0.05).

There was reduction in mean glucose and increase in total cholesterol levels in the blood following CTC intoxication (Table 2). In animals of Groups-III and IV treated with *A. paniculata* and Liv.52 respectively, a trend towards 0 day value was observed. However, the rate of return towards normalcy was comparatively higher in the Liv.52-treated animals (Group-IV). Hypercholesterolaemia and hypoglycaemia have also been reported earlier in CTC liver damage[17]. Serum proteins did not show any significant variation.

Table 2: Mean changes in blood glucose and serum total cholesterol in the different groups

Groups/Days	Blood glucose (mg/100 ml)				Serum total cholesterol (mg/100 ml)			
	0	5	7	17	0	5	7	17
I.	$120.00^{a,A}$ ± 4.08	$120.00^{a,A}$ ± 7.07	$122.50^{a,A}$ ± 3.22	$126.25^{a,A}$ ± 3.14	$74.00^{a,A}$ ± 12.99	$71.50^{a,A}$ ± 12.66	$70.75^{a,A}$ ± 11.43	$72.75^{a,A}$ ± 11.98
II.	$123.33^{a,A}$ ± 8.82	$76.66^{b,B}$ ± 3.33	$85.00^{b,B}$ ± 2.09	$90.00^{b,B}$ ± 0.00	$65.33^{a,A}$ ± 6.89	$102.67^{b,B}$ ± 8.88	$97.00^{b,B}$ ± 6.24	$79.00^{a,A}$ ± 0.00
III.	$140.00^{a,A}$ ± 5.77	$83.33^{b,B}$ ± 3.33	$93.33^{b,B}$ ±4.40	$110.00^{a,A}$ ± 5.70	$58.00^{a,A}$ ± 6.03	$91.67^{b,B}$ ± 3.84	$86.67^{b,B}$ ± 1.20	$65.33^{a,A}$ ± 0.51
IV.	$116.67^{a,A}$ ± 6.67	$73.33^{b,B}$ ± 1.67	$86.67^{a,A}$ ± 7.67	$105.00^{a,A}$ ± 7.64	$61.67^{a,A}$ ± 2.03	$94.00^{b,B}$ ± 3.21	$75.33^{a,A}$ ± 3.93	$66.67^{a,A}$ ± 6.94

Note: Means having the same small letters row-wise and capital letters column-wise are not significantly different, probability level (p<0.05).

Macroscopically, the liver in CTC-treated animals was swollen, pale and mottled. Histopathology of the liver in CTC-treated animals showed extensive, diffuse, haemorrhagic parenchyma and obliteration of the normal architecture. Swollen hepatic cells constricted the sinusoids. Degeneration was of the centrilobular type. The nuclei were either pyknotic or completely lost. Similar changes have also been reported by others[15,18].

The degenerative changes were less extensive in rabbits treated with *A. paniculata*. Only 50% of the liver showed degenerative changes with granular cytoplasm. Other changes like swollen hepatic cells and pyknotic nuclei were also present.

But Liv.52-treated animals showed marked regenerative changes (Fig.2) and cell division with two nuclei in dividing stages (Fig.1) under light microscopy. This strongly suggested a protective effect of Liv.52 on the CT-damaged liver.

Fig. 1: Liver showing dividing cell with two nuclei x 3000

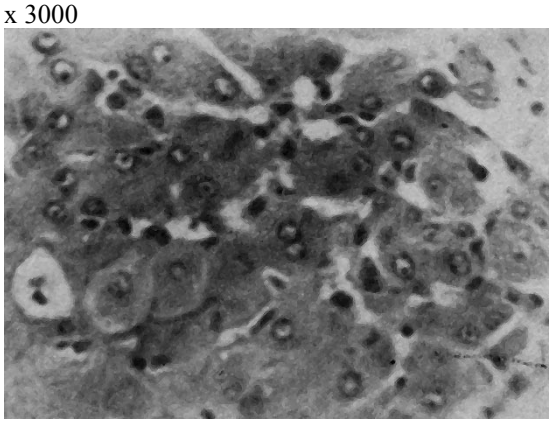
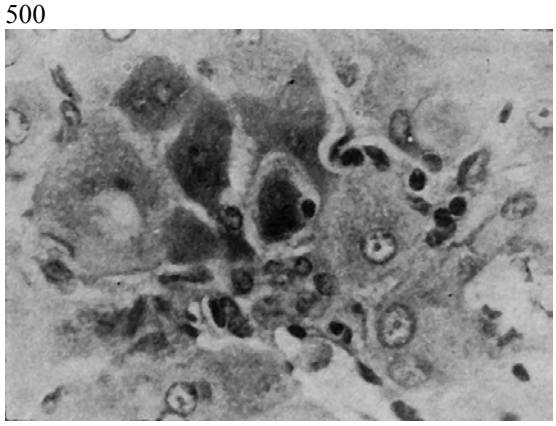


Fig. 2: Liver regenerative changes with mitosisi x 500



Our results indicate that *A. paniculata* could reduce CTC-induced liver toxicity in rabbits although the 0.5 gm/kg dose did not initiate regeneration. Liv.52 was found to be distinctly superior to *A. paniculata* as shown by rapid clinical recovery, normalization of SGOT and SGPT enzyme levels, blood glucose and serum total cholesterol, and regenerative changes in the liver following CTC-induced damage. Regeneration of liver cells with Liv.52 has also been reported by Prasad[19,20]. Liv.52 not only protects the liver from injurious effects but also accelerates regeneration in the damaged liver, which is an advantageous feature.

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