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Effect of Liv.52 on Carbon Tetrachloride - Induced Hepatotoxicity in Rabbits

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ABSTRACT

Carbon tetrachloride was administered to induce hepatotoxicity in male rabbits. The serum enzymes ALT and AST were monitored. In one group of carbon tetrachloride-treated rabbits, Liv.52 was administered orally by Ryle's tube. Observations were made for five days. Liv.52 produced marked reduction in ALT levels, whereas the effect of Liv.52 produced marked reduction in ALT levels, whereas the effect of Liv.52 on AST levels was less marked. Reasons for this differential effect of Liv.52 on ALT and AST levels are discussed.

INTRODUCTION

Viral hepatitis and alcoholic liver disease continue to be major health problems. Though good hygiene can help limit the spread of the first and abstinence from alcohol can prevent the second, both these are unlikely to be achieved in the near future. Modern medicine offers little by way of cure. Several indigenous herbs are reputed to be useful in viral hepatitis. Their clinical evaluation is difficult because of the variable and self-limiting nature of the disease. The experimental evaluation is mostly done in rats by studying the protective effect against carbon tetrachloride-induced damage. The response of the rats to carbon tetrachloride is known to be variable and specificity of enzyme changes is doubtful. Therefore, it is necessary to develop more reliable methods for testing hepatoprotective agents. Hence it was decided to use rabbits as test animals. Liv.52 is widely used as a hepatoprotective agent and therefore it was decided to test the protective effect, if any, of Liv.52.

MATERIALS AND METHODS

Twelve male rabbits weighing between 1.3 kg and 2.5 kg were used in this study. The rabbits were housed individually and fed on natural rabbit feeds. The rabbits were divided into two groups. Group I acted as control and Group II acted as test group for the protective effect of Liv.52. Blood was collected from the ear vein to estimate Alanine amino transferase (ALT-formerly SGPT) and Aspartate amino transferase (AST-formerly SGOT). Thereafter each rabbit received carbon tetrachloride in the dose of 0.5 ml/kg intraperitoneally as a single dose. Rabbits in Group I received water once daily orally for 5 days and rabbits from Group II received Liv.52 syrup in the dose of 5.0 ml/kg per day orally for 5 days. The dose of Liv.52 was calculated by extrapolating the human adult dose according to the surface area ratio[1]. Blood samples were collected from the ear vein every 12 hours on the first two days and every 24 hours on the following 3 days for serum ALT and AST estimations. The enzyme activities were determined by the method of Reitmann and Frankel[4].

RESULTS

The fasting serum enzyme levels were within the normal range for all rabbits prior to carbon tetrachloride administration[5]. After carbon tetrachloride administration in the control group ALT

levels doubled in 12 hours and were progressively rising upto 96 hours. On the other hand AST levels doubled in 12 hours, reached a peak at 48 hours, but started declining at 72 hours (Table 1). In the Liv.52 treated group ALT levels doubled in 12 hours but started declining at 24 hours, and reached normal levels at 96 hours (Fig.1). The levels of AST in the Liv.52 treated group increased at 12 hours but decreased at 24 hours, rose again to reach a peak at 48 hours and decreased after 72 hours (Fig. 2).

Table 1: ALT and AST levels in rabbits treated with carbon tetrachloride (Mean I.U. ± SD; n=6)

Time after CCl_4 (hours)	ALT	AST
0	59.9 ± 1.65	20.0 ± 6.81
12	123.4 ± 0.17	43.5 ± 6.81
24	147.2 ± 20.60	62.1 ± 3.90
48	166.0 ± 20.40	70.5 ± 7.34
72	192.8 ± 27.40	42.13 ± 8.40
96	205.8 ±19.80	44.00 ± 9.53

Note the progressive rise of ALT upto 96 hours; AST level peaks at 48 hours and then declines.

DISCUSSION

The results of this study are interesting in that the response of ALT and AST to carbon tetrachloride are different. ALT shows a much larger increase and progressive rise. AST shows a much smaller increase with a peak after 48 hours and then a decline. It is known that ALT concentrations are high in the liver and very low in the other tissues[3]. AST on the other hand is found in high concentrations in the heart, skeletal muscle and kidney apart from the liver (Table 2). Carbon tetrachloride is known to damage other tissues also. Therefore ALT levels give a reliable guide to liver cell damage, whereas AST levels are not indicative of liver damage. It is more specific for cardiac necrosis and these effects are seen after 48 hours. In the present study AST levels rose in 12 hours, reached a peak at 48 hours and fell slowly at 72 hours. The effect of Liv.52 is also remarkable, in that ALT levels were reduced from 24 hours onwards and reached normal at 96 hours. The AST levels rose at 12 hours but fell at 24 hours and rose again at 48 hours. This probably indicates that the rise in AST in the first 24 hours is due to liver damage and the delayed rise in reaching a peak at 48 hours is due to damage to other tissues. Therefore, the first peak at 24 hours is suppressed by Liv.52 but it has no effect on the second peak. The method employing rabbits therefore appears superior in studying hepatotoxic agents and Liv.52 showed hepatotoprotective action in this study.

Figure 1: Mean ALT levels (IU/Lit.) in control and Liv.52-treated animals after CCl_4 injection

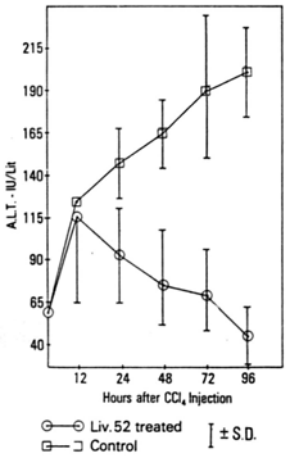

Figure 2: Mean AST levels (IU/Lit.) in control and Liv.52-treated animals after CCl_4 injection

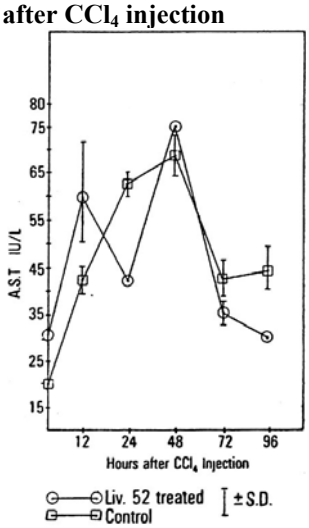

Table 2: Transaminase levels

	Heart	Liver	Skeletal muscle	Kidney	Pancreas	Spleen	Lung
AST	156	142	99	91	28	14	10
ALT	7.1	44	4.8	19	2.0	1.2	0.7

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