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Alcohol Hangover and Liv.52

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ABSTRACT
Ethanol and acetaldehyde levels in blood and urine have been evaluated in 9 volunteers following administration of Liv.52 and placebo on the evening of the study and on the following morning. On the following morning the volunteers scored their symptoms and completed visual analogue scales. Single dose and multiple dose studies were done.

Liv.52 produced a considerable reduction in blood and urine levels of ethanol and acetaldehyde after 12 hours. It is possible that Liv.52 prevents the binding of acetaldehyde, bringing about higher initial blood levels followed by rapid elimination. It reduced the hangover symptoms.

INTRODUCTION
Many epidemiological studies have established a relationship between excessive alcohol intake and liver disease[1], although there seems to be a weak relationship between the extent and duration of alcohol intake and severity of liver injury[2]. Acetaldehyde has long been suspected to be the causative agent of alcoholic liver disease[3]. For the same ethanol intake, chronic alcoholic users have been shown to have lower blood ethanol and higher blood acetaldehyde levels compared to non-alcohol users[4]. A similar change in alcohol metabolism has recently been described in moderate social drinkers[5]. In the same study, Liv.52 (The Himalaya Drug Co.), a herbal formulation of several plant principles prepared according to Ayurvedic concepts, was shown to raise the blood ethanol level and to cause rapid elimination of acetaldehyde. It was also shown to enhance the rate of absorption of ethanol.

Acetaldehyde has unpleasant effects on the central nervous system and its persistence may be responsible for hangover symptoms in moderate social drinkers[6]. The present study was designed to check the effect of Liv.52 on ethanol and acetaldehyde levels in blood and urine, and on hangover symptoms.

MATERIAL AND METHODS
Nine healthy male subjects, mean age of 39.6 years (range 31 – 57 years), and mean weight 64.4 kg (range 54 - 76 kg), volunteered for the study. All the subjects consumed moderate alcohol (40 - 100 g per week) socially and had occasionally experienced hangover effects. Chronic alcoholics and those who did not drink socially were excluded. The complete protocol of the study was discussed and written consent was obtained from each volunteer before entering the study.

One batch of a particular brand of Indian whisky was used throughout the study. The ethanol content determined by gas chromatography was 37.5 g/100 ml. On each study evening, the volunteers consumed four portions of whisky, each of 60 ml. Each portion was mixed with an equal volume of soda and ice and was consumed within 30 min. The first two portions were consumed on an empty stomach. Measured snacks were permitted with the last two portions to avoid severe gastric symptoms.

Liv.52 is an Ayurvedic formulation containing active principles of the following herbs: *Capparis spinosa, Cichorium intybus, Solanum nigrum, Cassia occidentalis, Terminalia arjuna, Achillea millefolium, Tamarix gallica* and *Phyllanthus amarus* (formerly wrongly identified as *Phyllanthus*

niruri). These ingredients are known to exert a hepatoprotective action (Subbarao, V.V. 1975, unpublished data).

Table 1: Mean blood concentrations and total urinary excretion of ethanol and acetaldehyde

	Ethanol			Acetaldehyde		
	Placebo	Liv.52 single dose	Liv.52 multiple dose	Placebo	Liv.52 single dose	Liv.52 multiple dose
Blood (mg/100 ml)						
1 hour	75.00 ± 5.25	86.2 ± 4.03	95.3 ± 3.99	5.14 ± 0.38	5.29 ± 0.38	5.96 ± 0.66
12 hours	30.7 ± 7.7	5.39 ± 1.52	4.82 ± 2.70	2.68 ± 0.38	1.59 ± 0.22	0.78 ± 0.23
Urine (μg) 4-12 hours	110 ± 20.2	69.9 ± 21.0	24.8 ± 7.38	383 ± 74.6	285 ± 61.1	142 ± 24.6

Table 2: Showing the mean distance from the hangover point on the visual analogue score and mean symptom score

	Placebo	Liv.52 - multiple dose
Mean distance (mm)	236 (± 32.7)	288 (± 29.8)
Mean score	3.81 (± 0.81)	2.44 (± 0.65)

The dose of Liv.52 was 6 tablets taken 2 hour prior to consumption of alcohol in the single dose study and 3 tablets for 14 days for the multiple dose study. Six tablets of an identical appearing placebo were given 2 hour prior to commencing the drinks on a placebo day.

The study was performed on 3 occasions: Day 1 following a single dose of placebo, Day 2 after a single dose of Liv.52 tablets and Day 3 after 15 days of Liv.52 treatment. No alcohol was permitted 24 hour before each trial day.

On each trial day, 3 volunteers reported to the Clinical Pharmacology facility (two air-conditioned bedrooms, lounge, recreation facility and pharmacodynamic test laboratory) at 17.00 hour after eating their usual lunch at 13.00 hour. The drug was administered (placebo or Liv.52) at 17.30 hour. At 20.30 hour after drinking two portions of whisky, venous blood was collected for ethanol and acetaldehyde estimation. A standard dinner was served at 22.00 hour after drinking the 4 portions of whisky (total ethanol 90 g). The volunteers retired at 23.00 hour. Blood was collected 1 hour after drinking the whisky. At 7.00 hour the next morning they were woken up and venous blood was again collected for estimation of ethanol and acetaldehyde. Urine was collected from 23.00 to 7.00 hour. They were estimated immediately after collection by head space Gas Chromatography[8]. Thereafter, the volunteers filled up the symptom scores and marked visual analogue scales.

Tests for hangover

1. A pair of words designating opposite feelings was selected and written at the two ends of a 100 mm line. The end of the line associated with the word designating hangover was called the 'hangover point'. Four such pairs of words were used. To overcome the right-hand effect, two hangover points were on the left and two hangover points on the right. The distance of the mark made by each subject from the hangover point was taken as the parameter.

2. A list of 10 symptoms commonly associated with hangover was given to the volunteers to score from '0' (zero) indicating absent, to '3' indicating severe.

RESULTS AND DISCUSSION

Unpleasant feelings in the morning following excessive alcohol consumption are commonly referred to as the hangover effect. In gross form it is estimated to occur in approximately 50% of cases[6,9], but the use of sensitive tests may detect it in the majority of persons after consumption of about 1.5 g/kg of ethanol[8,10]. In the present study approximately 1.5 g/kg ethanol was consumed.

Four visual analogue scales and scores of ten common symptoms were recorded to compare the hangover effect.
As expected, Liv.52 administration caused higher ethanol levels in the blood at 1 hour, especially after multiple doses, possibly by inhibiting the presystemic metabolism of ethanol[5]. Acetaldehyde levels were also higher (non-significant). At 12 hour, Liv.52 treatment caused a significantly reduced level of ethanol and acetaldehyde in the blood and in the 4-12 hours urine specimens. The single dose treatment had a similar but less pronounced effect.

Acetaldehyde is known to form adducts with cell proteins[9,11], which may lead to cellular damage. The results suggest that Liv.52 prevent the binding of acetaldehyde, causing a higher initial blood level and rapid elimination subsequently.

Lower levels of ethanol and acetaldehyde in the blood at 12 hours are reflected in the decreased symptom scores and the change in the visual analogue score. The last two observations are indicative of a reduced hangover after Liv.52 treatment. The differences did not reach statistical significance due to the small number of subjects, low level of the hangover effect and variability between volunteers.

Although a crude formulation has been used, the results are significant and interesting. Further work on ethanol and acetaldehyde binding and clearance, and the effects of Liv.52 on them is warranted.

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