Anti-cholestatic activity of HD-03, a herbal formulation in thioacetamide (TAA)-induced experimental cholestasis

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In the present study HD-03, a herbal formulation was investigated for its anti-cholestatic activity in TAA-induced cholestasis in anaesthetized guinea pigs. Administration of TAA at a dose of 100 mg/kg body wt significantly reduced the bile flow, bile acid and bile salt excretion. Pretreatment with HD-03 at a dose of 750 mg/kg body wt per orally for 15 days in guinea pigs significantly prevented thioacetamide-induced changes in bile flow, bile acids and bile salts excretion. Thus, HD-03 can serve as a potent choleric and anti-cholestatic agent.

HD-03 is a multi-herbal formulation consisting of Solanum nigrum L. (whole plant, 30%), Cichorium intybus L. (seeds, 20%), Picrorrhiza kurroa Benth. (roots, 20%), Tephrosia purpurea L. (whole plant, 20%) and Andrographis paniculata Nees. (leaves, 10%). Many of the individual ingredients of the formulation were earlier investigated for their protective effect against different models of experimental hepatotoxicity1-5. HD-03 is proved to be an useful hepatoprotective agent against paracetamol, thioacetamide and isoniazid-induced hepatic damage and 750 mg/kg body wt was found to be an optimum dose6. It is also found to posses free radical scavenging activity in CCl4-induced hepatotoxicity in rats7. In the present study, HD-03 a herbal formulation was investigated for its anticholestatic activity in guinea pigs.

Acute hepatic injury may be either cytotoxic, cholestatic or mixed type. Cytotoxic injury refers to the degeneration or necrosis of hepatic parenchymal cells, while cholestatic injury is characterised by stagnated bile, jaundice and minimally abnormal hepatic parenchymal cells8. Thioacetamide intoxication leads to mixed type of hepatic injury in experimental animals8. Thioacetamide-induced cholestasis in guinea pigs—Twenty-four inbred male guinea pigs weighing between 400-450 g were used for the study. The animals were maintained at 12-hr light and dark cycle, fed ad libitum with standard pellet diet (Lipton India Ltd., Mumbai) and had free access to water. The animals were divided into three groups of eight each. The animals of group I received 10 ml/kg body wt of vehicle (water) once a day orally for 15 days and served as control. Animals of group II were subjected to the same treatment as in group I and in addition on day 15 the animals were injected with 100 mg/kg body wt ip of thioacetamide to serve as positive control. Group III animals were administered with 750 mg/kg body wt of HD-03 as an aqueous suspension once a day orally for 15 days. On day 15 the animals of group III also received 100 mg/kg body wt ip injection of TAA. After 24 hr of TAA injection, animals from all the groups were anaesthetized with urethane, 1.5 g/kg body wt ip in saline. After anaesthetization, the bile duct was exposed by midline incision and cannulated with polyethylene canula. The bile was collected for 4 hr9 and bile flow was recorded. Bile juice was analysed for estimation of bile salts10 and bile acids11.

The data was analysed statistically using unpaired Student's t test to find out the difference. The minimum level of significance was fixed at P<0.05.

TAA-induced cholestasis in guinea pigs (Table 1)—Administration of TAA at a dose of 100 mg/kg body wt in guinea pigs significantly reduced bile flow, bile acids [cholic acid and deoxycholic acid] and bile salts concentration. Pre-treatment with HD-03 for 15 days at a dose of 750 mg/kg body wt significantly protected TAA induced changes on bile flow, bile acids [cholic acid and deoxycholic acid] and bile salts.

Toxic agents may interfere with bile production by selective injury or blockage of mechanism for hepatic uptake, processing or excretion of the components9. Metabolism of thioacetamide, formed by action of the

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Table I—Effect of HD-03 on TAA-induced cholestasis in guinea pigs

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<thead>
<tr>
<th>Parameters</th>
<th>Control</th>
<th>TAA</th>
<th>TAA+HD-03</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bile flow (ml/100mg/4 hr)</td>
<td>2.893 ± 0.158*</td>
<td>0.98 ± 0.10</td>
<td>2.145 ± 0.10*</td>
</tr>
<tr>
<td>Cholic acid (µg/ml)</td>
<td>4.77 ± 0.42*</td>
<td>1.79 ± 0.20</td>
<td>3.36 ± 0.458**</td>
</tr>
<tr>
<td>Deoxycholic acid (µg/ml)</td>
<td>10.40 ± 1.67**</td>
<td>3.40 ± 0.98</td>
<td>9.53 ± 0.75*</td>
</tr>
<tr>
<td>Bile salts (mg/ml)</td>
<td>3.62 ± 0.32*</td>
<td>1.28 ± 0.21</td>
<td>3.16 ± 0.24*</td>
</tr>
</tbody>
</table>

*P<0.001 and **P<0.01 as compared to TAA group.

Amine oxidase of Ziegler, is responsible for hepatic injury. In the present study, TAA intoxication reduced bile secretion which was accompanied by reduction in bile acids and salts. HD-03, a herbal formulation has been reported for its hepatoprotective activity against various hepatotoxins and a very good antioxidant in vivo. It is also evident from the present results that HD-03 may serve as a good hepatoprotective agent in the treatment of hepatic disorders.

References