Comparative study of Liv. Compound syrup and herbal formulations for hepatoprotective activity

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ABSTRACT

Traditional system of medicine recommends various crude drugs for the treatment of hepatic disorders. Liv. Compound is such proprietary polyherbal formulation which is recommended in various liver diseases. Polyherbal formulations Hep-I and Hep-II were developed for treatment of liver disorders and evaluated along with Liv. Compound syrup for hepatoprotective activity. Liver necrosis was produced by administering carbon tetra chloride (CCl4) (1:1 CCl4 in olive oil 2ml/kg subcutaneously on 2nd and 3rd day). The liver damage was evidenced by increased levels of serum glutamate oxaloacetate transaminase (SGOT), serum glutamate pyruvate transaminase (SGPT), serum alkaline phosphatase (ALP), and serum bilirubin. Liv. Compound syrup, Hep-I and Hep-II syrups showed significant hepatoprotective activity at dose of 500mg/kg which was compared with standard Liv-52 syrup. From the biochemical parameters it was found that Hep-I formulation shows excellent hepatoprotective activity followed by Liv. Compound and Hep-II formulation.

Key words: CCl4 induced hepatotoxicity, polyherbal formulation, Hepatoprotective activity

INTRODUCTION

The management of liver disease is still a challenge to modern medicine. No drug has been developed in modern system of medicine which may stimulate the liver function, protect it from damage or help in regeneration of hepatic cells. Some important hepatoprotective polyherbal formulations are Liv-52, Livol, Arogyavardhini, Stimuliv etc. Liv. Compound syrup is such a well known marketed polyherbal formulation containing 19 medicinal plants. Many ingredients of Liv. Compound syrup were earlier investigated for their hepatoprotective activity against different hepatotoxicity models. Liv. Compound is claimed to be useful in hepatitis, jaundice, and biliary dysfunctions. However the pharmacological effects need experimental evidence for their actions.

We have undertaken this study to evaluate the efficacy of Liv. Compound syrup, Hep-I and Hep-II formulation in rats in which acute hepatotoxicity was induced by CCl4.

MATERIALS AND METHODS:

All the crude drugs and material were supplied by SG-Phytopharma Pvt. Ltd., Kolhapur, Maharashtra and authenticated by Government college of pharmacy, Karad, Maharashtra.

Preparation of Formulations:

Formulation Hep-I was prepared by using hydro-alcoholic extract of Lawsonia alba1, Eclipta alba2, Berberis aristata3, Aloe vera4, Andrographis paniculata5, and Tephrosia purpuria6.

And formulation Hep-II was prepared by using hydro-alcoholic extract of Boerhavia diffusa7, Melia azadirachta8, Phyllanthus niruri9, Croton oblongifolius10, Picrorrhiza kurroa11 and Plumbago zeylanica12. The contents in dose based on traditional knowledge and reports present on these plants. Contents of crude drugs are summarized in table No. 1.

Table 1. Composition of formulations Hep-I (hydro alcoholic extract) and Hep-II (hydro alcoholic extract).

<table>
<thead>
<tr>
<th>Plants</th>
<th>Hep-I</th>
<th>Hep-II</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lawsonia alba</td>
<td>25</td>
<td>-</td>
</tr>
<tr>
<td>Eclipta alba</td>
<td>125</td>
<td>-</td>
</tr>
<tr>
<td>Berberis aristata</td>
<td>75</td>
<td>-</td>
</tr>
<tr>
<td>Aloe vera</td>
<td>75</td>
<td>-</td>
</tr>
<tr>
<td>Andrographis paniculata</td>
<td>50</td>
<td>-</td>
</tr>
<tr>
<td>Boerhavia bifusa</td>
<td>-</td>
<td>50</td>
</tr>
<tr>
<td>Melia azadirachta</td>
<td>-</td>
<td>50</td>
</tr>
<tr>
<td>Phyllanthus niruri</td>
<td>-</td>
<td>75</td>
</tr>
<tr>
<td>Croton oblongifolius</td>
<td>-</td>
<td>75</td>
</tr>
<tr>
<td>Tephrosia purpurea</td>
<td>50</td>
<td>-</td>
</tr>
<tr>
<td>Plumbago zeylanica</td>
<td>-</td>
<td>75</td>
</tr>
<tr>
<td>Picrorrhiza kurroa</td>
<td>-</td>
<td>50</td>
</tr>
</tbody>
</table>

Choice of Animals:

Male Albino Rats (Wistar strain) with weight range 150-180 gms and mice with weight range 25-30 gms were...
obtained from KLES’s college of pharmacy Hubli, Karnataka. All the animals were maintained on 12 hour light and 12 hour dark cycle and received standard diet and water ad Libitum.

Carbon tetrachloride induced hepatotoxicity in Rats:

The rats were divided in to six groups containing five animals in each group.

**Group A**: Serve as normal control received 4% gum acacia 1ml/kg orally for 4 days with 2ml of olive oil given subcutaneously on second and third day.

**Group B**: serve as a toxicant received 4% gum acacia 1ml/kg orally for 4 days with 1:1 CCl₄ in olive oil 2ml/kg subcutaneously on second and third day.

**Group C**: serve as a standard received Liv-52 syrup 1ml/kg orally for 4 days with 1:1 CCl₄ in olive oil 2ml/kg subcutaneously on second and third day.

**Group D**: received Liv. Compound syrup 1ml/kg orally for 4 days with 1:1 CCl₄ in olive oil 2ml/kg subcutaneously on second and third day.

**Group E**: received Hep-I syrup 500 mg/kg orally for 4 days with 1:1 CCl₄ in olive oil 2ml/kg subcutaneously on second and third day.

**Group F**: received Hep-II syrup 500 mg/kg orally for 4 days with 1:1 CCl₄ in olive oil 2ml/kg subcutaneously on second and third day.

The rats were anaesthetized with ether on fifth day and blood was collected from retro-orbital plexus. Then scarified by cervical dislocation. The liver was carefully isolated and preserved in 10% formalin. The serum was separated by centrifugation and used for estimation of different biochemical parameters like SGOT, SGPT, ALP and Bilirubin. The weight of each liver was recorded and then subjected to histopathological studies.

**Assessment of hepatoprotective activity:**

The hepatoprotective activity of all the above formulations was assessed by using following parameters.

1) Morphological parameters: change in color, weight.
2) Biochemical parameters: Blood samples were examined for change in SGOT, SGPT, ALP and serum bilirubin.
3) Histopathological parameters: histological changes in the liver architecture like focal necrosis, fatty changes, inflammatory cell infiltration etc.

**RESULTS:**

The rats treated with CCl₄ alone developed significant hepatocellular damage as evidenced from increase in serum levels of SGOT, SGPT, ALP and serum bilirubin when compared with the normal control group. There was increase in liver weights and livers appeared pale reddish brown.

Treatment with Liv. Compound, Hep-I and Hep-II syrup at dose of 500mg/kg caused reduction in increased serum levels of SGOT, SGPT, ALP and serum bilirubin. The value for SGOT, SGPT, ALP and Bilirubin are nearly normal for Hep-I formulation.

Graph 1. Effect of Hep-I, Hep-II and Liv. Compound syrup compared to Liv-52 (Standard) on CCl₄-induced rise in SGOT, SGPT and ALP. The values represents Mean± SEM., n=5, Positive control (B) differ from all at p<0.001 in case of SGPT, SGOT and ALP, Normal control (A) differ from Liv. Comp. at P<0.05 and from HEP-II at P<0.01 in case of SGPT, *P<0.05,**P<0.01.
Significant difference in enzyme levels (Graph-1.) in normal, positive and test groups indicate the hepatoprotective activity of formulations. Among the new formulations, Hep-I formulation exhibits highest hepatoprotective activity followed by Liv. Compound and Hep-II. Serum bilirubin levels also confirmed that Hep-I formulation have high hepatoprotective activity. (Graph-2.) In comparison of liver weights, rats treated with Hep-I, exhibit lowest liver weight among the other formulations this may be due to high hepatoprotective activity of Hep-I which prevent liver necrosis. (Graph-3.)

Graph 2. Effect of Hep-I, Hep-II and Liv. Compound compared to LIV-52 (Standard) on CCL₄-induced rise in Total and Direct Bilirubin. The values represents Mean±SEM, n=5. Positive Control differ from all groups at P<0.01, Normal control (A) differ from Liv.- 52  at P<0.05 in case of total bilirubin. *P<0.05, **P<0.001.

Graph 3. Effect of Hep-I, Hep-II and Liv.compound compared to LIV-52 (Standard) on CCL₄-induced rise in liver weights of rats. The values represents Mean±SEM, n=5
Histopathology:
Histological section of normal control group A showed normal hepatic cells with well preserved cytoplasm, prominent nucleus and conspicuous central vein (figure 1).

Group D, E and F showed liver tissue and hepatocytes showing regenerative activity. (figure 4,5,6.)

Histological sections of Group B showed high degree of damage characterized by congestion of central vein and portal triads, presence of prominent Kupffers cells and cloudy degeneration indicating fibrosis. (figure 2).

Histological section of Group C showed the recovery against CCl₄ induced damage as compared to normal control. (figure 3).
There is mild lymphocyte infiltration in the hepatic lobule. Portal triads are normal. This is indication of regenerative activity of the liver.

**DISCUSSION:**

The toxic effect of CCl₄ is due to free radical generation (CCl₃⁻), which may cause lipid peroxidation thus altering the permeability of liver cell membrane. Herbal principles are coming up as an most effective sources of disease treatment. Polyherbal formulations Hep-I, Hep-II and proprietary formulations Liv. Compound syrup contain the extract of several medicinal plants that contains specific therapeutically active principles and are used in liver disorders. The combined synergistic action of all the ingredients helps to normalize the liver function and thus cure complex liver disorders. From the results it is concluded that the formulation Hep-I which is a hydroalcoholic extract of 6 medicinal plants can be preferred for various liver disorders.

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**REFERENCES**


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