A perspective botanical drug: Hepatoprotective activity of dry extract prepared from the aerial part of chicory plant (Cichorium intybus L.)

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Introduction
Intoxication alcohol, heavy metals, pesticides, and other xenobiotics is a leading cause of liver damage. Milk thistle (Silybum marianum L. Gaertn.) is one of the best-known medicinal herbs with hepatoprotective properties. Silymarin, a mixture of flavonoids extracted from fruits, displays antioxidant and membrane-stabilizing activity. Numerous phyto drugs (e.g., Carl, Legalon) and dietary supplements are currently marketed worldwide.

Chicory (Cichorium intybus L.) is a well-known plant cultivated in Europe, Asia, Canada, the eastern part of the U.S., northern Africa, and Australia. Unlike milk thistle, chicory is not widely used as a hepatoprotective phyto drug or dietary supplement. However, chicory is a part of a multi-component phytodrug Liv-52 introduced to the pharmaceutical market by the Himalaya Drug Company in 1955 to treat various liver injuries.

The primary purpose of the presented preclinical study is to investigate the hepatoprotective properties of the brand-name botanical drug prepared from the aerial part of chicory (Silymarin).

DEC Chemical Composition
The primary constituents present in DEC are phenolic carboxylic acids (e.g., esters of caffeic, ferulic, coumaric acids with organic acids (quinic and tartaric)), flavonoids (isoorcisin, astragalin, rutin, luteolin, and kaempferol), and oxycoumarins (esculetin, chlorochin). The mixture used in the studies contained 9.20 ± 0.43% of phenolic constituents and was calculated as chicoric acid.

DEC was standardized by the sum of phenolic compounds. The extraction yield of DEC was 10.3 ± 1.0% and 55.2 ± 0.4% of the dry weight.

Milk thistle (Silybum marianum L. Gaertn.) extracts were prepared from the aerial part of the plant by cold extraction in 90% ethanol. The extracts were separated into fractions according to their polarity and were used for the phytochemical analysis of the chicory.

Methods
Highly purified dry extract was obtained from the aerial part of wild chicory (DEC). DEC was developed at the All-Russian Research Institute of Medicinal and Aromatic Plants (VILAR). DEC was standardized by the sum of phenolic compounds. The extraction yield of DEC was 10.3 ± 1.0% and 55.2 ± 0.4% of the dry weight.

Results
• Serum levels of triglyceride, total cholesterol, total bilirubin, and glucose significantly increased in the HgCl2-treated group compared with the control group (Table 1).
• The difference in the levels of triglyceride, total cholesterol, total bilirubin, and glucose between HgCl2 and HgCl2-DEC groups were statistically significant (p<0.05) (Table 1).
• Activities of γ-glutamyl transferase, alkaline phosphatase, aspartate aminotransferase, and alanine aminotransferase increased following HgCl2 treatment (Table 2).
• The administration of DEC in the doses 100 and 500 mg/kg significantly reduced serum levels of γ-glutamyl transferase, and alanine aminotransferase, the statistically significant reduction of alkaline phosphatase and aspartate aminotransferase was observed in animals receiving 500 mg/kg DEC (Table 1).
• The treatment with HgCl2 resulted in a hydrol-droplet degeneration of hepatocytes (Figure 1A). Treatment with DEC 500 mg/kg led to a more normal liver appearance (Figure 1B). The lobules were formed correctly, and the hepatocytes have a pale eosinophilic cytoplasm, the nuclei are preserved.
• The hepatoprotective effects of DEC, 500 mg/kg, were comparable with the effects observed in the group receiving 100 mg/kg of Silimar (Tables 1 and 2).

Conclusions
• DEC demonstrated significant hepatoprotective properties.
• The DEC treatment of rats receiving HgCl2 reduced serum levels of the studies biomarker of liver function. Moreover, these changes were more noticeable in animals receiving maximal DEC dose, 500 mg/kg.
• The hepatoprotective effects of DEC, 500 mg/kg, were comparable with the effects observed in the group receiving 100 mg/kg of Silimar.
• After assessment of DEC safety profile, it can be evaluated in clinical trials as a promising botanical drug for the therapy of the hepatobiliary system.

Table 1. Effect of DEC and Silimar on total protein and lipids serum levels

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>Control</th>
<th>HgCl2 treated</th>
<th>DEC 100mg/kg</th>
<th>DEC 500mg/kg</th>
<th>Silimar 100mg/kg</th>
<th>Silimar 500mg/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total protein, g/L</td>
<td>74.7 ± 1.0</td>
<td>83.7 ± 1.4**</td>
<td>75.3 ± 0.7**</td>
<td>76.3 ± 0.9**</td>
<td>75.3 ± 1.1</td>
<td>75.3 ± 1.1</td>
</tr>
<tr>
<td>Glucose, mmol/L</td>
<td>7.04 ± 0.7</td>
<td>9.01 ± 0.16**</td>
<td>7.25 ± 0.14**</td>
<td>7.55 ± 0.13**</td>
<td>7.45 ± 0.18</td>
<td></td>
</tr>
<tr>
<td>Total cholesterol, mg/dl</td>
<td>1.72 ± 0.04</td>
<td>2.80 ± 0.08**</td>
<td>2.10 ± 0.06**</td>
<td>1.85 ± 0.05**</td>
<td>1.91 ± 0.07**</td>
<td></td>
</tr>
<tr>
<td>γ-glutamyl transferase, U/L</td>
<td>0.18 ± 0.11</td>
<td>1.55 ± 1.12**</td>
<td>1.20 ± 1.55**</td>
<td>1.20 ± 1.55**</td>
<td>1.40 ± 1.16**</td>
<td></td>
</tr>
<tr>
<td>Total bilirubin, mg/dl</td>
<td>4.92 ± 0.2</td>
<td>7.80 ± 0.1**</td>
<td>4.60 ± 0.11**</td>
<td>4.80 ± 0.11**</td>
<td>4.70 ± 0.2**</td>
<td></td>
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