Effects of Liver Extract from the Ocean Sunfish (Mola mola) on Acute Gastric Lesions in the Rat

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Liver extract (Liver-E) from the Ocean Sunfish (Mola mola) has been employed as a crude remedy for the treatment of human gastric ulcers in a particular local area of Japan. However, the actual value of the anti-ulcer effect of Liver-E has not yet been fully investigated. Concerning the Liver-E of ocean sunfish there is only analytical report [1, 4]. Therefore, we examined the effects of Liver-E on three different types of experimental acute gastric lesions and on the gastric secretion, including a comparative evaluation with cimetidine. Rats were subjected, in this experiment, to a variety of damaging agents and stress designed to elicit gastric lesions.

Male, 7–9 weeks old standard Wistar rats (150–200 g) were used in this study. Fresh liver from the Ocean Sunfish (Mola mola) was boiled down without additional water and subjected to a five hour extraction process using a gentle flame. This liver extract (Liver-E) is an oily fluid and has an opaque, orange color and potent, fishy odor. Distilled water was used as our placebo and cimetidine (Sigma Chem. Co., Ltd.) was also used as the positive control in our experiments. Table 1 lists the dosage schedule for each of these drugs as well as the number of rats used in each part of this experiment.

Stress induced gastric lesions: Liver-E, the placebo and cimetidine were orally administered 30 minutes prior to the experiment. After the completion of a 24 hour period of stress exposure [8], the animals were sacrificed employing an overdose of ether anesthesia. The Ulcer Index (U.I.) for each rat was calculated and expressed as the sum of the lengths of the gastric lesions. Evaluations of the efficacy of each of the drugs were based on the U.I. and comparisons between the control and subject groups were made.

Indomethacin induced gastric lesions: Liver-E, cimetidine and the placebo were given orally for a 30 minute period, prior to the beginning of the experiment. Seven hours post indomethacin administration, the rats were sacrificed and the U.I. was obtained by the method as described above.

HCl-ethanol induced gastric lesions: Thirty minutes after the oral administration of Liver-E, cimetidine and the placebo, HCl-ethanol (60% ethanol in 150 mM HCl) was given orally at a dose of 1 ml/rat. The stomachs of these rats were surgically removed an hour after the administration of the HCl-ethanol and then processed by the method as described above.

Estimation of the gastric secretion: Under ether anesthesia, the stomach of each rat was ligated at the pylorus and Liver-E, cimetidine and the placebo were injected into the duodenum. Four

Table 1. Experimental design

<table>
<thead>
<tr>
<th>Group</th>
<th>Drug</th>
<th>Dosage</th>
<th>Stress</th>
<th>Indomethacin</th>
<th>HCl-ethanol</th>
<th>gastric secretion</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>D.W.</td>
<td>1.0 ml/rat</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>II</td>
<td>cimetidine</td>
<td>200 mg/kg</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>III</td>
<td>Liver-E</td>
<td>0.1 ml/rat</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>IV</td>
<td>Liver-E</td>
<td>0.5 ml/rat</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>V</td>
<td>Liver-E</td>
<td>1.0 ml/rat</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>5</td>
</tr>
</tbody>
</table>

D.W.: Distilled water.
Liver-E: Liver extract from the Ocean Sunfish.
hours after this operation, the rats were sacrificed and the gastric juice present in the stomach was collected. The volume [8], acidity [8] and pepsin activity [10] of the gastric juice were estimated. All of the data was subjected to the ANOVA and Tukey's q-test or the method of Least Significant Difference (LSD).

The effects of Liver-E and cimetidine on stress-, indomethacin- and HCl-ethanol-induced gastric lesions are shown in Fig. 1.

**Effect of Liver-E on stress induced gastric lesions:** The U.I. of the placebo control group was $51.9 \pm 9.8$ mm (Group I). The U.I. of the Liver-E administration groups were $38.8 \pm 5.6$ mm (Group III), $30.3 \pm 8.8$ mm (Group IV) and $38.3 \pm 5.4$ mm (Group V), respectively. The U.I. of the cimetidine treated rats was $20.4 \pm 1.6$ mm (Group II). It is apparent that Liver-E significantly diminished, dose dependently, the formation of gastric lesions. Cimetidine also had a significant suppressive effect on the development of gastric lesions.

**Effect of Liver-E on indomethacin induced gastric lesions:** For the Liver-E treatment groups, a suppressive effect on gastric lesion formation was only observed for Group V (U.I. of $4.8 \pm 3.8$ mm). Also, a significant suppressive effect was detected for Group II (U.I. of $4.9 \pm 4.0$ mm) compared to Group I (U.I. of $16.8 \pm 6.8$ mm). From the data obtained in this part of our experiment, the highest dosage of Liver-E (1.0 ml), Group V, had a significant preventive effect on the development of indomethacin induced gastric lesions as effective as cimetidine.

**Effect of Liver-E on HCl-ethanol induced gastric lesions:** As indicated in Fig. 1, Group V exhibited the smallest U.I. ($23.8 \pm 15.9$ mm) of all the treatment groups in our experiment. Also, Group IV (U.I. of $40.3 \pm 16.8$ mm) was effective in suppressing the development of HCl-ethanol induced gastric lesions as well as the cimetidine treatment group (Group II, U.I. of $38.9 \pm 13.2$ mm). The U.I. ($70.3 \pm 19.0$ mm) for the lowest dosage Liver-E treatment group (Group III, 0.1 ml) was not statistically significant from that ($85.9 \pm 17.0$ mm) of our control group (Group I).

**Effect of Liver-E on the gastric secretion (volume, acid output and pepsin output) of pyloric ligated rats:** The average volume of gastric juice collected for Group II (1.5 ml), Group IV (1.5 ml) and Group V (1.5 ml) was significantly suppressed compared to Group I (3.0 ml) (Fig. 2). The average volume of gastric juice collected for Group III (3.1 ml) did not differ significantly from the control group (3.0 ml). The acid output was calculated from the volume of the gastric juice collected multiplied by the acidity of the gastric juice and expressed as $\mu$Eq per hour (Fig. 2). The mean acid output for Group I was $44.3 \mu$Eq/hr, while the mean acid output for Group II was $22.3 \mu$Eq/hr. The average acid outputs for the Liver-E treatment groups were, for Group III $36.9 \mu$Eq/hr, for Group IV $42.2 \mu$Eq/hr and for Group V $27.6 \mu$Eq/hr. Thus the highest Liver-E dosage group, Group V, exhibited a comparable suppressive effect on the acid output of the
gastric secretion to the cimetidine group. The pepsin output was significantly depressed for Group II, Group IV and Group V compared to Group I (Fig. 2).

It is apparent from the data collected from the evaluations of the three different types of acute gastric lesions in the rat, that the liver extract from the Ocean Sunfish possesses both preventative and suppressive properties against acute gastric lesion formation. The mechanism for acute stress induced gastric lesions is attributed to poor circulation in the gastric mucosa, related to sympathetic and the exasperation of gastric secretion due to vagotonia [2, 7, 11]. Also, the increased HCl concentration of the gastric juice can induce gastric lesions [3]. Cimetidine is an H2-receptor antagonist and is employed as the drug of choice for the treatment of gastric ulcer which caused by stress and acid output in humans [9]. Liver-E, as effective as cimetidine, prevented the formation of gastric lesions which were caused by the administration of stress, indomethacin and HCl-ethanol. The suppressive effects of Liver-E on gastric secretion, acidity and pepsin output were also similar to the previously documented action of cimetidine. However, the administration of Liver-E at a dose of 1.0 ml/rat proved to be more effective for the prevention of gastric lesions induced by HCl-ethanol than cimetidine in this study. Cimetidine did not prevent the lesion formation by acidified ethanol [5], and is not cytoprotective [6]. Cytoprotection is unrelated to the inhibition of gastric acid secretion [6]. Although the oral administration of Liver-E at a dose of 0.5 ml/rat did not depress the acid output, treatment with the same dosage (0.5 ml/rat) of Liver-E prevented the formation of gastric mucosal lesions produced by HCl-ethanol in a dose-dependent manner. These results suggest that the active mechanism of Liver-E may be due to its cytoprotective activity. Under these circumstances, the Ocean Sunfish liver extract (Liver-E) may prove to be as useful and effective as cimetidine for the treatment of acute gastric lesions in man.

REFERENCES