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# Application of Iranian Medicinal Plants to the Treatment of Liver Injury

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***ABSTRACT*** *: Matricaria Chammomillal L., Foemiculum Vulgare mill, and Plantago Psylium L. have been screened for their hepato protective activities against liver damge induced by $CCl_4$ intoxication in mice. Hydroalcoholic extractions (2:8) of herbal drugs were concentrated in vacuo and concentrated crude extracts of Matrica Chammomilla L. and Foeniculum Vulgare mill were orally administered at doses of 100 mg/kg, 200 mg/kg, 400 mg/kg, and 800 mg/kg. Plantago Psyllium was given at doses of 50 mg/kg, 100 mg/kg, 200 mg/kg, and 400 mg/kg. Liver protective activities of these herbs were determined after administration of $CCl_4$. Liver size, serum enzyme activities, sleeping time, and histopatology of the liver were examined one hour after administration of $CCl_4$. ALT and AST activities, liver weight and sleeping time decreased in groups that received 400 mg/kg of Matricaria Chammomilla L. or Foeniculum Vulgare. Histological investigation showed significant increase in hepatic cell regeneration and reduction in liver injury. The group that received 100 mg/kg Plantago Psylium showed liver protection but protection was not significant in other doses.*

***Key Words*** *: Liver, Carbontetrachloride toxicity, Hepatoprotection.*

## INTRODUCTION

Hepatitis viruses, drugs, chemicals, and many other factors cause liver injuries. For this purpose many efforts have been made to produce and find therapeutic remedies for liver damage (Yoshinobu *et al.*, 1983).

Regarding protection of the liver, a new era was opened by the introduction of the natural constituents isolated from the seed of Silybum Marianum (compositae), commonly called the milk thistle (Vogal *et al.*, 1977). Special attention was paid in searching for other liver protective and therapeutic agents from various medicinal plant sources as well (Chang and Choi, 1978; Kalantari *et al.*, 1995; Oshima *et al.*, 1995).

Recently, Chinese scientists have extracted some hepatoprotective compounds from herbs which traditionally used for hepatic disorders (Liu *et al.*, 1994). Our search for potential liver protective agent has led to Iranian medicinal plants such as *Matricaria Chammomilla L., Foemiculum Vulgare mill* and *Plantago Psylium L.* which have been traditionally used for liver disease.

## MATERIALS AND METHODS

### 1. Materials

Plant materials were purchased from the local market at Ahwaz, Iran. Outbred Albino Swiss white female mice were supplied by the Razi Research Center in Hasarak Karaj, Iran and used under proper light and diet control.

Carbon tetrachloride, formaldehyde, and sodium hydroxide were purchased from Merck (Germany). Alanine transaminase (ALT) and aspartate transaminase (AST) kits were purchased from Zist Shimi Co. (Iran).

Centrifugae Beckmon Model Tj.6 (U.S.A.). Microtom Model 2045, Sakura Tissue Passage Medel RH. 12EP-2 (Japan). Spectrophotometer pharmacia (England).

### 2. Method

Plant materials were placed in flask and refluxed with 80% ethanol (v/v) for 6 hours. Then it was filt-

**Table 1.** Dose schedule

| Group | Day 1 | Day 2 | Day 3 | Day 4 | Day 5 |
|---|---|---|---|---|---|
| -Ve control | Saline | Saline | Saline | Saline | Hexobarbital Sodium and one hour later blood colletion |
| +Ve control | Saline | $CCl_4$ | $CCl_4$ | Saline | Hexobarbital Sodium and one hour later blood colletion |
| $CCl_4$+ Extract | Extract | $CCl_4$+ Extract | $CCl_4$+ Extract | Extract | Hexobarbital Sodium and one hour later blood colletion |

ered off and the filtrate was concentrated under vacuum. Concentrated crude extracts of *Matrica Chammillal* and *Foemiculum Vulgare* mill were administered orally at doses of 100 mg/kg, 200 mg/kg, 400 mg/kg, and 800 mg/kg. Plantago Psyllium was given at doses of 50 mg/kg, 100 mg/kg, 200 mg/kg, and 400 mg/kg.

The negative control group received normal saline and olive oil, and the positive control group received normal saline and $CCl_4$. Each group consistsed of 10 mice (20-22 g). $CCl_4$ was dissolved in olived oil and each extract was dissolved in physiological saline. According to the method described by Chang and Choi (1978) the dose schedule is listed in Table 1.

On the fifth day, 0.2 m*l* hexobarbital sodium was intraperitoneally administered to measure sleeping time.

One hour later blood was collected from the jugular vein for the measurment of liver enzyme activities. Livers were then removed and weighed and their macroscopic appearance documented. Some were photographed. Representative slices of the lives were fixed in 10% neutral buffered formalin for histopathological examinations (Pauline *et al.*, 1994).

## RESULTS AND DISCUSSION

It has been reported that an important aspect of the liver injury is necrogenic activity of $CCl_4$ in liver. In this activation stage, $CCl_4$ is metabolized to a powerful destructive free radical form that leads to auto-oxidation of polyenic fatty acids presented in the cytoplasmic membrane (Lin *et al.*, 1995).

In order to evaluate the liver protective activities of *Matrica Chammilla L.*, doses of 100 mg/kg, 200 mg/kg, 400 mg/kg, and 800 mg/kg were studied. The results showed that one hour after $CCl_4$ administration ALT AST, liver weight, and sleeping time were decreased in the group received 400 mg/

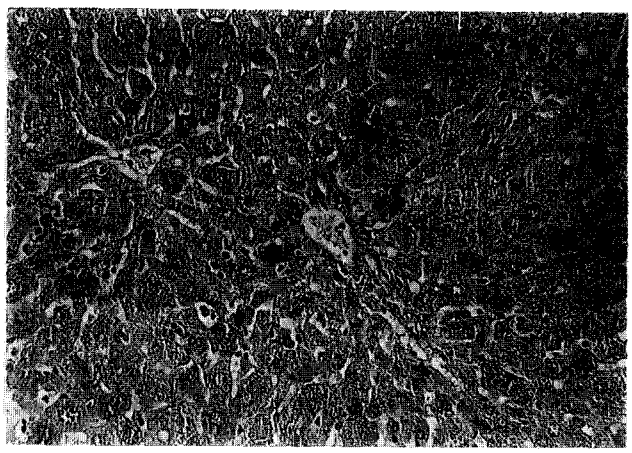

**Fig. 1.** The liver protective effect of *Chammonilla L.* at dose of 400 mg/kg in mice.

**Table 2.** Effect of *Matricaria C.L.* extract on serum aminotransferases activities, liver weight and sleeping time induced by $CCl_4$

| Treatment | ALT activities (U/L) | AST activities (U/L) | Liver weight (g) | Sleeping time(min) |
|---|---|---|---|---|
| -Ve control | 45 ±0.79 | 110.3±1.34 | 1.31±0.04 | 22.4±0.5 |
| +Ve control | 64.9±1.97 | 154.4±3.05 | 1.4 ±0.04 | 41.3±2.6 |
| $CCl_4$+Matricaria C.L. 100 mg/kg | 61.2±1.61 | 135.8±2.42 | 1.33±0.048 | 30 ±1.8 |
| $CCl_4$+Matricaria C.L. 200 mg/kg | 57.2±1.45 | 133 ±2.2 | 1.32±0.049 | 24.4±2.7 |
| $CCl_4$+Matricaria C.L. 400 mg/kg | 55.2±1.22 | 125.2±1.61 | 1.31±0.033 | 22.6±0.8 |
| $CCl_4$+Matricaria C.L. 800 mg/kg | 63.8±2.08 | 144.7±2.99 | 1.45±0.048 | 37.5±1.7 |

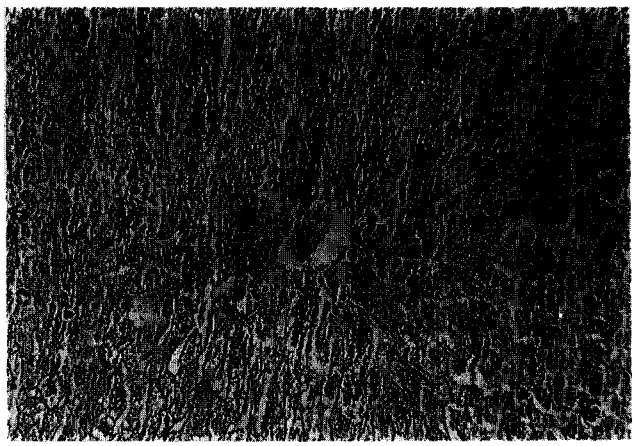

**Fig. 2.** The liver protective effect of *Foeniculum Vulgare* mill at dose of 400 mg/kg in mice.

**Fig. 3.** A severe necrosis of the liver in mice treated with $CCl_4$

kg in compared with the control group (Table 2). The histopathological investigation showed hepatic cell regeneration significantly increased and liver injury reduced (Fig. 1) as compared with the _Ve control group (Fig. 3).

Gorup received 400 mg/kg of *Foenicuhum Valgare* mill showed that one hour after $CCl_4$ administration ALT and AST activities, liver weight and sleeping time were decreased in compared with control group (Table 3). The histopatological investigation showed hepatic cell regeneration significantly increased and liver damage reduced (Fig. 2).

The crude extract of *Plantago Psylium* showed liver protection at dose of 100 mg/kg but at the other doses protection were not significant (Table 4).

In histopathological examinations of the crude

**Table 3.** Effect of *Foeniculum V.M.* extract on serum aminotransferases activities, liver weight and sleeping time induced by $CCl_4$

| Treatment | ALT activities (U/L) | AST activities (U/L) | Liver weight (g) | Sleeping time(min) |
|---|---|---|---|---|
| -Ve control | 45 ±0.79 | 110.3±1.34 | 1.31±0.04 | 22.4±0.5 |
| +Ve control | 64.9±1.97 | 154.4±3.05 | 1.4 ±0.04 | 41.3±2.6 |
| $CCl_4$+Matricaria V.M. 100 mg/kg | 60.3±1.6 | 147.2±3.05 | 1.4 ±0.05 | 35.3±2.8 |
| $CCl_4$+Matricaria V.M. 200 mg/kg | 57 ±1.1 | 131.2±2.4 | 1.34±0.05 | 29.2±2.5 |
| $CCl_4$+Matricaria V.M. 400 mg/kg | 53 ±0.69 | 123.5±1.7 | 1.31±0.024 | 22.1±0.9 |
| $CCl_4$+Matricaria V.M. 800 mg/kg | 64.9±1.95 | 150 ±2.59 | 1.37± 0.04 | 37.5±1.6 |

**Table 4.** Effect of *Plantogo Psylium* crude extract on serum aminotransferases activities, liver weight and sleeping time induced by $CCl_4$

| Treatment | ALT activities (U/L) | AST activities (U/L) | Liver weight (g) | Sleeping time(min) |
|---|---|---|---|---|
| -Ve control | 45 ±0.79 | 110.3±1.34 | 1.31±0.04 | 22.4±0.5 |
| +Ve control | 64.9±1.97 | 154.4±3.05 | 1.4 ±0.04 | 41.3±2.6 |
| $CCl_4$+*P.Psylium* 50 mg/kg | 59 ±1.8 | 151.7±2.4 | 1.38±0.04 | 38.4±1.49 |
| " " $CCl_4$+100 mg/kg | 55 ±0.92 | 125.7±1.49 | 1.32±0.039 | 24.3±0.95 |
| " " $CCl_4$+200 mg/kg | 59 ±1.26 | 137.5±1.94 | 1.35±0.045 | 32 ±1.67 |
| " " $CCl_4$+400 mg/kg | 60 ±1.27 | 140.6±2.3 | 1.36± 0.05 | 35 ±1.63 |

extracts at the effective doses 400 mg/kg, there were not any abnormal fats, necrosis in the liver cells and also liver structure was recovered to normal shape (Fig. 1, Fig. 2) as compared with the positive control group (Fig. 3). Therefore it seems that these crude extracts are good enough for treatment of liver damage caused by $CCl_4$. Groups administered 400 mg/kg of *Matricaria Chammomilla L.* Foeniculum vulgare mill and 100 mg/kg of *Plantago Psylium* showed significant protection, 1 hr after $CCl_4$ administration.

## CONCLUSION

We investigated some of the Iranian medicinal plants for their liver protective activities, and we found that *Matricaria Chammomilla L.* at dose of 400 mg/kg was able to protect liver from damage induced by $CCl_4$ in mice. The plant *Foeniculum Vulgare* and *Plantago Psylium* also at a dose of 400 mg/kg showed the same effect. Hence it is worthwhile to find the active agent from these medicinal plants especially focusing on *Matricaria Chammomilla L.*

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