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Hepatoprotective activity of the whole plants of *Fumaria indica*

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Whole plants of *Fumaria indica (fam. Fumariceae)* were studied for their hepatoprotective activity against carbontetrachloride, paracetamol and rifampicin-induced heptatotoxicites in albino rats. The petroleum ether extract against carbonetrachloride, total aqueous extract against paracetamol and methanolic extract against rifampicin-induced hepatotoxicities showed similar reductions in the elevated levels of some of the serum biochemical parameters in a manner similar that of silymarin indicating its potential as a hepatoprotective agent.

WHOLE of plant of *Fumaria indica* (Hausk.) Pugsley, (fam *Fumariaceae)*, commonly known as parpat, pitpada and shahterah, forms a constituent of many Ayurvedic, Unani and common household medicinal preparation. The drug is used to purify blood[1], dyspepsia and in obstructions of liver[2]. Although the drug is used as one of the components of many liver formulations[3], no systematic study to assess these claims was carried out yet. The present investigation was therefore carried out to evaluate the drug for its hepatoprotective activity.

EXPERIMENTAL

Plant Material

Whole plants of *Fumaria indica* were purchased from the local market and their indetity was confirmed by comparing with herbarium specimen preserved in the museum of Botany Departments of M.S. University of Baroda, Vadodara and Central Drug Research Institute, Lucknow. The drug, dried and powdered (60 mesh), was subjected to preliminary phytochemical screening[4] and proximate analysis[5]. The acid soluble ash was analysed for different inorganic metal ions using Atomic Absorption Spectrophotometer (GBC-901). The powder was then successively extracted with petroleum ether (60-80°) (2.38%) and methanol (14.63%) using a soxhlet extractor while successive aqueous (16.82%) and total aqueous (14.54%) extracts were prepared by decoction method. These extracts, dried under reduced pressure using a rotary flash evaporator at 50°, were subjected to TLC studies using various solvent systems[6]. The powered drug (120 mesh) and the different extracts mentioned above were then screened for hepatoprotective activity.

Albino (Wistar) rats (150-200 g) of either sex maintained under standard animal housing conditions (temperature: 23±2°, relative humidity: 55±10% and 12 h light and dark cycle) were used for all sets of experiments comprising of six rats each. The rats were allowed access to take standard laboratory feed and water *ad libitum.*

Toxicity studies

The rats were divided into control and test groups. The control group received the vehicle (5% w/v acacia mucilage, 1 ml/kg, p.o.) while the test

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group received various test substances orally. The powder and different extracts were subjected to acute toxicity and hepatotoxicity studies using reported methods[7], to findout whether these pre hepatotoxic.

Hepatoprotective Activity

The rats were divided into control, hepatotoxin and test (test sample + hepatotoxin) groups. The control and the hepatotoxin groups received the vehicle while the test groups received test samples orally.

Carbontetrachloride-induced hepatotoxicity[7]

The test suspensions were administered orally three times at 12 h intervals. $CC1_4$ (2.5 ml/kg, p.o.) was administered 30 min after the first dose of test suspensions. After 36 h of CCl_4 treatment, 2 to 3ml of blood was collected by purcturing the retroorbital plexus and was allowed to clot for 45 min at RT. Serum was separated by centrifugation at 2500 rpm and analysed for various biochemical parameters.

Paracetamol-induced hepatotoxicity[8]

All the groups received a single oral dose of test suspensions daily for 3 days. On the 3rd day,the paracetamol and test groups received a single oral dose of paracetamol (3 g/kg) 30 min. after the administration of third dose of test suspensions. After 48 h of paracetamol treatment, blood was collected and serum was analysed for various biochemical parameters.

Rifamipicin-induced hepatotoxicity[8]

The test suspensions were administered orally four times at 12 h interval. Rifampicin (1 g/kg, p.o.) was administered 30 min. after the first dose of test suspensions. After 48 h of rifampicin treatment, blood was collected and the serum was analysed for various biochemical parameters.

Assessment of liver functions

Biochemical parameters such as serum glutamic oxalacetic transaminase[9] (SGOT), serum glutamic pyruvic transaminase[9] (SGPT), alkaline phosphatase[10] (ALKP), total bilirubin[11] (T Bil), and direct bilirubin[11](D Bil) which give an idea regarding the functional state of the liver were analysed. The estimations were carried out on Ames RA-50 Chemistry analyser of Miles India Ltd., Baroda.

Statistical analysis

The mean value ± SEM was calculated for each parameter[12]. Percent reduction against the hepatotoxin by the test samples was calculated by considering the enzyme level difference between the hepatotoxin-treated and the control group as 100% level of reduction. For determination of significant intergroup differences one way analysis of variance and Dunnett's test[13] was carried out.

RESULTS AND DISCUSSION

The whole plant of *Fumaria indica* was selected for the present investigation since this plant parts have been used in the indigenous system of medicine and literature[14].

The various successive extractive values were found to be petroleum ether (60-80°) (0.86), benzene (0.61), chloroform (0.52), acetone (1.26), methanol (9.48) and water (17.17)% w/w. The qualitative chemical examination showed the presence of carbohydrates, alkaloids, steroids, fixed oils, fats, saponins, phenolic compounds, tannins, gums and mucilages. The TLC studies confirmed the presence of these constituents in addition to amino acids. Development of finger prints may serve as markers in identification of the drug as a whole or when

Table 1

Effect of the Whole plant of Fumaria indica on Carbon Tetrachloride Induced Hepatotoxicity

Group	Biochemical Parameters Mean ± SEM (% Reduction)				
	SGPT (U/ml)	SGOT (U/ml)	ALKP (U/l)	T Bil (mg/dl)	D Bil (mg/dl)
Control	56.96±3.24	137.53±12.28	169.06±4.66	1.23±0.03	0.20±0.01
CCl_4	725.51±38.03	1160.77±52.08	456.70±13.15	3.55±0.11	1.50±0.03
Silymarin	65.45±1.54* (98.73)	152.95±2.47* (98.49)	150.63±1.54* (106.40)	0.71±0.01* (122.41)	0.24±0.01* (96.92)
Powder	567.84±9.46* (23.58)	941.24±11.73* (21.45)	187.83±4.08** (93.47)	1.75±0.03* (77.16)	0.41±0.01* (83.85)
Pet. ether extract	119.35±11.57** (90.67)	405.22±24.69* (73.84)	198.25±21.89** (89.85)	1.32±0.14* (96.12)	0.30±0.01** (92.31)
Methanolic extract	377.41±43.41* (52.07)	503.85±46.44* (64.20)	206.85±9.95* (86.86)	1.04±0.04** (108.19)	0.37±0.01** (86.92)
Aqueous extract	291.88±24.41 (64.86)	551.77±33.99* (59.52)	165.45±9.96** (101.25)	2.04±0.14* (65.09)	0.63±0.01* (66.92)
Total aq. extract	56.68±1.87** (100.04)	705.08±3.83* (44.53)	206.70±3.46* (86.91)	0.64±0.02** (125.43)	0.43±0.01* (82.31)

Significantly different reduction compared to: Carbon Tetrachloride=*, Similar reduction compared to Silymarin=** ($P<0.01$)

incorporated in the polyherbal formulations. The proximate analysis of the whole plants showed foreign organic matter (10.99), moisture content (8.27), total ash (16.13), acid insoluble ash (1.56), water soluble ash (7.15), sulphated ash (27.39), alcohol soluble extractive (4.48) and water soluble extractive (10.02)% w/w. The acid soluble ash showed the presence of sodium (0.007207), potassium (0:060280), calcium (0.006000), coblalt (0.000300), copper (0.000038), magnesium (0.006720) and zinc (0.010167) % w/w. Lead and nickel were found to be absent.

Acute toxicity studies indicated that the powder as well as the extracts of the whole plant was found to be practically non toxic. These were also found to be non hepatotoxic at the selected dose levels, since the serum biochemical parameters are within the normal levels.

Carbontetrachloride treatment in normal rats elevated the levels of serum biochemical parameters significantly ($p<0.001$) indicating acute hepaticellular damage and biliary obstruction (Table 1). Out of the different test samples, the petroleum ether extract showed maximum, significant, ($p<0.01$) reduction in the elevated levels of serum biochemical parameters followed by the total aqueous extract, aqeous extract, methanolic extract and the powdered drug when arranged in descending order in terms of activity. This indicates that the petroleum ether extract of the whole plant of *F. indica* protected the liver from carbontetrachloride toxicity of a greater extent than the other test samples. The group of rats treated

Table 2

Effect of the Whole plant of *Fumaria indica* on Paracetamol Induced Hepatotoxicity

Group	Biochemical Parameters Mean ± SEM (% Reduction)				
	SGPT (U/ml)	SGOT (U/ml)	ALKP (U/l)	T Bil (mg/dl)	D Bil (mg/dl)
Control	58.98±0.63	137.53±1.27	182.67±0.79	0.88±0.02	0.25±0.01
Paracetamol	265.28±3.14	356.00±5.17	313.49±7.40	3.42±0.17	0.57±0.03
Silymarin	36.47±1.16* (110.91)	139.06±1.42* (99.30)	66.20±0.57* (189.93)	1.00±0.01* (95.28)	0.30±0.01* (84.38)
Powder	219.94±9.44 (21.98)	339.82±8.77 (7.41)	83.15±3.13** (176.07)	1.31±0.03* (83.07)	0.49±0.01* (25.00)
Pet. ether extract	50.24±0.51** (104.24)	241.69±2.06 (52.32)	189.05±2.25* (95.12)	0.99±0.01** (95.67)	0.47±0.01* (31.25)
Methanolic extract	35.53±0.56** (111.37)	230.08±1.11 (57.64)	135.40±1.11** (136.13)	1.10±0.02** (91.34)	0.22±0.01*** (109.38)
Aqueous extract	163.47±1.06* (49.35)	241.62±3.53 (52.36)	138.55±1.83** (133.73)	1.12±0.02** (90.55)	0.19±0.01*** (118.75)
Total aq. extract	104.47±1.76** (77.95)	156.59±3.13** (91.28)	110.67±2.31** (155.04)	0.99±0.02** (95.67)	0.33±0.01** (75.00)

Significantly diffrent reduction compared to: Paracetamol=*, Silymarin=***; Similar reduction compared to Silymarin = ** ($P<0.01$)

with petroleum ether extract also showed reduction in the elevated levels of SGPT, ALKP and DBil comparable to those of silymarin. The hepatoprotective activity of the drug may be due to scavenging effect of free radicals or stimulatory activity on liver[15].

Paracetamol when administered in over dose resulted in liver damage in albino rats as evidenced by the significant elevation in serum biochemical parameters (Table 2). Among the test samples the total aqueous extract showed maximum, significant reduction ($p<0.01$) in the elevated levels of serum biochemical parameters followed by methanolic extract, aqueous and petroleum ether extracts, and powdered drug when placed in the descending order of activity. The total aqueous extract showed similar reductions in all the biochemical parameters in a manner similar to that produced by silymarin. The hepatoprotective activity of the drug may be due to their inhibitory effects on cytochrome p_{450} or promotion of its glucuronidation or due to stimulatory effects on hepatic regeneration[16].

The rats treated with rifampicin elevated significantly ($p<0.01$) the serum biochemical parameters (Table 3). The methanolic extract showed maximum, significant decrease ($p<0.01$) in the elevated levels of serum biochemical parameters followed by petroleum ether extract, aqueous extract, powdered drug and total aqueous extract when placed in the descending order of activity. The total aqueous extract showed significant reduction ($p<0.01$) in all the other serum biochemical parameters except in those of SGPT and ALKP levels and significantly better activity ($p<0.01$) in terms of reduction in SGOT and

Table 3 : Effect of the Whole plant of Fumari indica on Rifampicin Induced Hepatotoxicity

Group	Biochemical Parameters Mean ± SEM (% Reduction)				
	SGPT (U/ml)	SGOT (U/ml)	ALKP (U/l)	T Bil (mg/dl)	D Bil (mg/dl)
Control	76.24±1.61	85.69±2.16	76.17±1.66	1.01±0.03	0.19±0.01
Rifampicin	195.53±3.50	265.46±2.27	141.05±2.91	2.81±0.05	1.21±0.03
Silymarin	41.00±0.66 (129.54)	135.07±1.30* (72.53)	76.03±2.26* (100.22)	1.59±0.02* (67.78)	0.87±0.04* (33.33)
Powder	118.76±3.46* (64.35)	168.15±2.71* (54.13)	105.95±3.02* (54.10)	1.95±0.03* (47.78)	0.65±0.02*** (55.57)
Pet. ether extract	42.55±1.28** (128.24)	103.64±1.27*** (90.02)	70.97±0.81** (108.01)	1.95±0.01* (47.78)	0.83±0.01** (37.25)
Methanolic extract	35.16±1.55** (134.44)	93.13±0.74*** (95.86)	80.87±0.80** (92.76)	1.74±0.02* (59.44)	0.71±0.02*** (49.02)
Aqueous extract	46.43±0.73** (124.99)	110.05±1.72*** (86.45)	102.43±0.82* (59.53)	2.01±0.01* (44.44)	0.98±0.01* (22.55)
Total aq. extract	51.61±1.47* (120.65)	178.77±0.90* (48.27)	81.00±1.28** (92.56)	2.14±0.01* (37.22)	1.23±0.01 (-)

Significantly different reduction compared to: Rifampicin=*, Silymarin=***, Similar reduction compared to Silymarn=** ($P<0.01$)

DBil levels when compared to those of silymarin. The hepatoprotective activity of the drug may be due to its inhibitory effects on the formation of an active metabolite, 25- desacetylrifampin[17]. The administration of different extracts of the drug alone to normal rats produces slight reduction in the normal levels of SGPT which is more prominant after the administration of paracetamol and rifampicin than CCl_4. This may be due to the availability of enzyme level of due to its physiological inertia before maintaining the body homeostasis or it may be due to the inhibitory activity on mitochondrial enzyme levels. The mechanism of action of the drug can be established only after further detailed investigations.

These studies, therefore, instigate further detailed investigations on this drug in order to justify the claims and incoporatoin in traditional medicines against liver disorders.

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