The Effects of Long-term Use of *Fumaria parviflora* extract on Some Serum Biochemical Parameters of Rats

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ABSTRACT

The effects of long term use of *Fumaria parviflora* on serum concentrations of total protein, glucose, cholesterol, triglyceride, aspartate aminotransferase (AST), alanine aminotransferase (ALT) and blood urea nitrogen (BUN) were investigated. Three groups of rats (7 rats in each group) were sampled 15 and 30 days after the oral administration of 100, 200 and 300 mg kg⁻¹ of hydroalcoholic extract of the plant and one group (7 rats) was sampled as control. There was no significant difference between treatment and control groups at day 15. At day 30, administration of 300 mg kg⁻¹ of the extract caused a significantly higher serum concentration of AST than other groups (p<0.05). This group also have higher serum ALT than the group which received 100 mg kg⁻¹ of the extract (p = 0.043). The rats that received 300 mg kg⁻¹ of the extract had significantly higher serum total protein than the group which received 100 mg kg⁻¹ of the extract (p = 0.04) and had a marginally higher total protein than the control group (p = 0.08). According to the results of the present study, it seems that long-term administration of *F. parviflora* extract with lower doses than that reported by other authors may cause hepatic damage.

Key words: *Fumaria parviflora*, long-term use, hepatic damage, serum concentrations, rat

INTRODUCTION

Treatment with herbal drugs has been in use since ancient times and in modern medicine, medicinal herbs are an integral part of alternative therapy (Karim et al., 2011; Nabavizadeh et al., 2009).

*Fumaria parviflora* Lam. (Fumariaceae) is an annual creeper plant that grows in a wide variety of areas of Iran, the Indo-Pakistan subcontinent and Turkey. It has been reported to be used traditionally in the folk medicine of various countries for treatment of hepatobiliary disorders, dermatological diseases and as a blood purifier, diuretic, diaphoretic, anthelmintic, antipyretic, appetizer and laxative (Akhtar et al., 2000; Heidari et al., 2004; Khalighi et al., 2005; Githiori et al., 2006; Rao et al., 2007; Tripathi et al., 2010).

Several studies have been conducted regarding the effects of short-term, up to 4 days, administration of *F. parviflora* on different organs. Some previous studies showed the beneficial effects of the *F. parviflora* in the treatment of the hepatobiliary system diseases (Adewusi and Afolayan, 2010; Nabavizadeh et al., 2009). On the other hand, the hepatotoxic effects of this plant have been reported by Heidari et al. (2004) and Gilani et al. (1996). This herb has been widely used as a drug in different countries such as Iran (Nabavizadeh et al., 2009) and to the best of our
knowledge, there is no previous study about the effects of the long-term use of F. parviflora. Therefore, this study was undertaken to investigate the effects of long-term use of F. parviflora on hepatic related biochemical parameters (total protein, glucose, cholesterol, triglyceride, aspartate aminotransferase, alanine aminotransferase and blood urea nitrogen) in the blood serum of rats.

MATERIALS AND METHODS

From April 2010 to June 2010, aerial parts of Fumaria parviflora were collected and after taxonomical authentication, drying in shade and grinding, hydroalcoholic extract was obtained by the Medical and Natural Products Chemistry Research Center, Shiraz, Iran. In summary, 100 g of powdered dried plant was extracted with 70% ethanol. The solvent was evaporated and the residue was dissolved in distilled water to obtain various concentrations (Sa et al., 2006).

Twenty eight male Sprague-Dawley rats (180-200 g) were obtained from the Razi Serum Research Institute, Shiraz, Iran. The animals were acclimatized to the animal room condition 4 days before the beginning of the experiment. The rats were kept under constant conditions of temperature (25-27°C), relative humidity (20-30%) and a 12-h light/dark cycle with free access to food (standard laboratory rodent pellet diet, Razi, Iran) and water. The experiment was performed according to the suggested European ethical guidelines for the care and use of laboratory animals in experimental investigations.

The animals were randomly divided into 4 groups (7 rats for each group) as follows: group 1 (control), groups 2, 3 and 4 receive normal saline, 100, 200 and 300 mg kg⁻¹ of the extract, respectively. The normal saline and the extract were administrated daily by gavage.

At days 15 and 30 of the experiment, animals were sacrificed using ether anesthesia. Blood samples (2-3 mL) were collected by heart puncture and the serum was separated after centrifugation at 750 g for 10 min and stored at -18°C until analysis.

Serum biochemical analysis was done for measuring total protein (TP) by Biuret method, glucose by glucose oxidase method, cholesterol by a modified Abell-Kendall/Levey-Brodie (A-K) method, triglyceride by the enzymatic procedure of McGowan et al. (1983). Also, aspartate aminotransferase (AST) and alanine aminotransferase (ALT) activities by the colorimetric method of Reitman and Frankel and blood urea nitrogen (BUN) by diacetyl monoxime method (Burtis and Ashwood, 1994) were measured.

Statistical analysis: Statistical analysis was performed using SPSS12 (Illinois, Chicago). One-way analysis of variance (ANOVA) tests with a post hoc Bonferroni test were used for comparison of the measured factors between different groups in each sampling occasion. Differences were considered significant at \( p < 0.05 \).

RESULTS AND DISCUSSION

Table 1 shows the results of the measurements at days 15 and 30. No significant differences were observed among treatment and control groups at day 15. However, at day 30, there were significant differences between treatment and control groups in the serum concentration of AST \( (p = 0.029) \), ALT \( (p = 0.03) \) and there was a marginally significant difference about the TP \( (p = 0.067) \). A post hoc Bonferroni test showed that the group 4 had significantly higher serum AST than that of control and groups 2 and 3 \( (p = 0.023, p = 0.032 \) and \( p = 0.023 \), respectively). Serum concentration of ALT in the group 4 was significantly higher than that of group 2 \( (p = 0.043) \). Group 4 had significantly higher TP than that of group 2 \( (p = 0.04) \) and a marginally higher TP than the control group \( (p = 0.08) \).
Fumaria species contain different organic acids and isoquinoline alkaloids such as fumaric acid, protopine, cryptopine, sinactine, dihydrofumarilaine, parfumidine and dihydrosoanguirine (Suau et al., 2002). Protopine is the main alkaloid of the *F. parviflora*. It has been shown that protopine has antiarrhythmic, antibacterial, antianalgesic, anticholinergic, antihistaminic, antiinflammatory, antihemostatic, hypotensive, vasodialatory and hepatoprotective activity (Wada et al., 2007; Yu et al., 1999).

Our results showed that 100 and 200 mg kg⁻¹ daily doses of *F. parviflora* extract had no significant effects on the measured factors and the effects of 300 mg kg⁻¹ daily doses were significant. Because toxicity occurrence in rats due to 400 mg kg⁻¹ of *F. parviflora* extract has been reported, 100, 200 and 300 mg kg⁻¹ daily doses were selected in the current research. However, there are some contradictory reports about the toxic dose of the *F. parviflora*. Appearance of clinical signs of toxicity and histopathological signs of hepatotoxicity in rats due to the use of 400 mg kg⁻¹ of hydroalcoholic extract (Heidari et al., 2004). Gilani et al. (1996) reported prolongation in pentobarbital-induced sleep as well as increased strychnine-induced lethality in mice with a single dose of 500 mg kg⁻¹ of aqueous-methanolic extract of the plant. On the other hand, no obvious toxic effects for hexane, chloroform and water-soluble extracts of *F. parviflora* up to a dose of 1.6 g kg⁻¹ have been reported (Heidari et al., 2004). Heidari et al. (2004) proposed a different method of extract preparation, different animals and experimental methods as the probable causes of the controversial findings about the effects of the *F. parviflora*.

Aspartate aminotransferase is present in different tissues including liver, heart, muscle, kidney and brain. Damage to any of these tissues causes the release of the AST into serum. On the other hand, ALT is mainly found in the liver and an increase in ALT values in serum is a sign of liver disease (Orhan et al., 2010). In the current study, the significant increase of serum AST and ALT in group 4 can be signs of hepatic damage, which is due to long term use of the extract.

According to our results, the administration of *F. parviflora* hydroalcoholic extract in the selected doses did not cause a significant decrease in serum concentrations of cholesterol, glucose...
and BUN. Previous researches showed that other plants from this genus such as *F. indica* have no hypcholesterolemic effects (Mehrotra *et al*., 2007). However, Jelodar and Nazifi (2000) reported that a 15 day period of the addition of *F. parviflora* whole plant to the ration of diabetic rats can decrease the increased serum levels of cholesterol, glucose, AST, ALT and creatinine.

We found that long term use of *F. parviflora* caused TP increment in the group 4. It has been shown that *F. parviflora* has laxative and diuretic effects. Partial dehydration can be proposed as a probable cause of increase in the serum TP. Although, the group 4 had higher BUN than the control group and group 2, the differences were not statistically significant. The liver is the main site of BUN production and hepatic damage in this group may be the cause of non occurrence of simultaneous increase in BUN. Similar to our results, it has been found that consumption of *F. parviflora* plant causes a numeral increase in the serum TP (Nabavizadeh *et al*., 2009; Jelodar and Nazifi, 2000). Jelodar and Nazifi (2000) also believe that *F. parviflora* increases glomerular filtration in the kidney, which may be the other probable cause of non occurrence of the BUN increment.

**CONCLUSION**

The results of the current study confirmed that the *F. parviflora* affects the hepatic function, however, our results were partially different from previous researches. It seems that the toxic doses of different extracts of the plant may not be the same and long-term administration of *F. parviflora* extract with lower doses than that reported by other authors can cause hepatic damages. Although, more work is required on a larger number of animals before the importance of these findings can be assessed, it can be recommended that in long-term administration of *F. parviflora* for the prevention of hepatic damage, besides the use of the therapeutic effects of the plant, low doses should be used.

**REFERENCES**


