Effect of fumaria officinalis hydroalcoholic extract on blood urea nitrogen and creatinine in New Zealand rabbits

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ABSTRACT

Fumaria officinalis is one of the herbal medicines used in Iran extensively. There are many useful properties recognized for this plant, but there is no information about its side effects especially in long term and at high doses. The objective of the present study was to investigate the effects of F. officinalis hydroalcoholic extract on the Blood Urea Nitrogen (BUN) and serum creatinine concentrations as indicators of kidney function. Thirty adult males of New Zealand rabbits were chosen randomly and were divided into three groups of ten. The control group did not receive any drug. Two experimental groups received 200 and 400 mg/kg of F. officinalis extract for 28 days (groups two and three, respectively). In day 28, blood samples were taken and samplings were done, (BUN) and creatinine concentrations were assayed by enzymatic methods with spectrophotometer. In the present study, F. officinalis hydroalcoholic extract administration increased BUN and serum creatinine concentrations significantly in group 1, but BUN decreased and serum creatinine increased significantly in group 2 (P<0.05). It was concluded that high doses of hydroalcoholic extract of F. officinalis can have detrimental effects on renal and hepatic function (the effects of this plant on herpetic function needs to more researches) but in medium doses cause renal failure.

Key words: Blood Urea Nitrogen (BUN), creatinine, Fumaria officinalis, rabbit.

INTRODUCTION

Herbal remedies at their proper dosages are unlikely to be a threat to the human health. Since the crude herbal medicines are mostly used without accurate dosage, taking the overdose of these products is dangerous and could lead to toxicity. The herbal medicines might also cause mild toxic effects which are not evident in short period of time. Long term traditional usage of a herb might justify the faith that they are safe and there is no need to use it at proper dosage (De Smith, 1995, 1997).

Seven species of the annual plants of genus Fumaria grow in Iran. Fumaria officinalis is the medicinal species of this genus which do not grow in Iran (Khalilighi-Sigaroodi et al., 2005). Some species of Fumaria family have been used in the Iranian traditional medicine for treatment of several diseases (Amin, 1991).

Urinary system is one of the most important systems of the body and its main functions are to control the elimination of waste and toxins from the body and to reabsorb all of the necessary nutrients back into the bloodstream. Experiments are usually done in order to study the renal function, especially glomerular filtration, and considerable changes in the measured parameters can represent renal and non-renal diseases.

The most common tests in this field include blood urea, serum creatinine and urinalysis. The kidney filters urea plasma through the glomerulus and in natural conditions nearly 25 to 40% of the filtrated urea is reabsorbed while passing through the urinary tubules (Coles, 1986).

Creatinine is an excreted material produced in the body during normal muscle metabolism and its measurement is a
useful indicator for anticipating the kidney performance (Guyton, 1991). The serum concentration of creatinine is the reflection of glomerular filtration rate.

To the best of our knowledge, there is no study about the side effects of *F. officinalis* hydroalcoholic extract on kidneys. In the present study, the changes in Blood Urea Nitrogen (BUN) and serum creatinine concentrations were studied after administration of *F. officinalis* hydroalcoholic extract in rabbits in order to find the side effects of this plant on kidney.

**MATERIALS AND METHODS**

Thirty (30) New Zealand white male rabbits at six-month age and 1.5 to 2 kg weight were purchased from Razi Institute, Shiraz, Iran. The rabbits were kept in separate cages at 20 ± 2°C with the cycle of 12 h light and darkness period for two weeks for adaptation. Rabbits were fed with commercial pellets made for laboratory animals and had free access to fresh water.

**Fumaria officinalis** extract administration

Thirty (30) male rabbits were distributed into three groups randomly. The control group did not receive *F. officinalis* hydroalcoholic extract in terms of this study. Groups 1 and 2 (experimental groups) received 200 and 400 mg/kg of *F. officinalis* hydroalcoholic extract daily, respectively based on their weight for 28 days. The extracts were given to the animals orally by polyethylene tube. The animals did not show any clinical or toxic signs throughout the study period.

**Biochemical analysis**

Blood samples were taken from the ear vein of all rabbits using insulin syringe. The samples were centrifuged at 750 g for 15 min. The sera were harvested and used for blood urea nitrogen and serum creatinine measurements. BUN and creatinine concentrations were measured by enzymatic (Tietz, 1987) and Jaffe methods (Bonsnese and Taussky, 1945), respectively using spectrophotometer (Shimatzo, Japan) and commercially available kits (Pars-Azmoon, Iran). The animals were kept at the animal house of Kazeroun University and were monitored until were euthanized for anatomic studies.

**Statistical analysis**

All the data were analyzed using SPSS statistical software, version 17 (SPSS Inc., Chicago, Illinois). One-way ANOVA was used to analyze the data. Duncan test was used for determination of significant differences between groups at the P < 0.05 level. All values were presented as mean ± standard error (SE).

**RESULTS AND DISCUSSION**

The mean ± SE concentration of BUN and serum creatinine in different groups is shown in Table 1. The statistical analysis showed the mean concentrations of BUN and serum creatinine in group 1 and the mean concentration of creatinine in group 2 had increased significantly when compared to the control group (P<0.05), but the mean concentration of BUN reduced significantly in group 2 compared to the control group (P<0.05).

The results of the present study showed that the oral administration of *F. officinalis* hydroalcoholic extract at daily doses of 200 and 400 mg/kg B.W., induce changes in BUN and serum creatinine concentrations in rabbits. There was a significant (P<0.05) increase in BUN and serum creatinine in the group which received 200 mg/kg B.W of *F. officinalis* hydroalcoholic extract (group1) compared to the control group.

Increases in BUN and creatinine in group 1 revealed kidney disorders due to kidney damage, moreover, higher BUN and creatinine can result in lower renal blood supply. In group 2, BUN decreased and creatinine increased, respectively. Reduction in BUN concentration might have different causes including increased GFR due to flavonoids, diuresis and serious liver injury, but none of the aforementioned causes affect serum creatinine, therefore, the main cause of decreased creatinine concentration could be attributed to the glomerular disorders.

Liver is the major place for BUN production and liver damage in group 2 might be the cause of lack of simultaneous increase in BUN concentration. It is possible that *F. officinalis* has alkaloidal fraction that increase BUN or it may have a chemical fraction that increases BUN and creatinine.

The clinical signs of toxicity and histopathological signs of hepatotoxicity in rats which consumed *F. officinalis* at 400 mg/kg BW are due to the hydroalcoholic extract consumption (Heidari et al., 2004). The zingiber extract resulted in BUN reduction and creatinine increase in rats (Modaresi et al, 2001). The researchers reported that significant decrease in BUN to creatinine ratio in experimental groups compared to the control group could be attributed to the liquid. Another possibility is hepatic disorder.

Some contradictory results were achieved in recent investigations with different types of the plant.

It has been reported that *Fumaria parviflora* decreased BUN - creatinine ratio and increased GFR in rat kidneys (Jelodar and Nazifi, 2000).

Determination of BUN-creatinine ratio is valuable since these two compounds have different tubular reabsorption.
The distribution of these two compounds, the influence of diet on them, effect of protein metabolism and their diagnostic value in the recognition of varieties of azotemia are different. *Zataria multiflora* extract affect the renal function at high doses (300 and 400 mg/kg BW) as being evident by significant changes in the serum creatinine concentration (Khoshvaghti, 2012). The plants of *Phyllanthus* spp increased BUN-creatinine ratio in rats suffer from diabetes and as a result, decreased GFR (Munish et al, 2010).

The toxic doses of gentamicin causes impairment of renal microcirculation and glomerular hemodynamics, thus, decreases glomerular filtration rate and thereby increases serum urea and creatinine levels (Stojiljkovic et al, 2008; Patil et al, 2010).

The gentamicin-induced toxicity may cause excessive formation of Reactive Oxygen Species (ROS) such as O$_2^*$, OH$^-$ and H$_2$O$_2$ that stimulate mesangial cells contraction which result in decreased GFR and increased serum urea and creatinine levels (Maldonado et al, 2003; Jeyanthi et al, 2009).

*Bryophyllum pinnatum* plants increased BUN and decreased creatinine level in serum of the studied rabbits and the chemical analysis of this plant showed that it had alkaloidal fraction that increased BUN (Ghiasi et al, 2011). *F. parviflora* increases glomerular filtration in the kidney, which may be the other probable cause of the absence of BUN increase (Jelodar and Nazifi, 2000).

Ashwagandha has the ability to decrease serum urea and creatinine levels by increasing glomerular filtration rate due to some of its active components like phenolic compounds and flavonoids (Harikrishnan et al, 2008).

Cyclosporine causes coagulative necrosis and fatal renal tubular cell inflammation (Mohammadian et al, 2005). *Capparis spinosa* in high dose has toxic effects on kidney (Heidari et al, 2010). Turnip root alcoholic extract protects rats against renal degeneration (Bahram and Dariush, 2011). The higher doses of *Dorema acheri* have more effects on serum proteins and BUN concentrations than the lower doses do (Mirzaei et al, 2005).

*F. parviflora* extract at the 100 and 200 mg/kg daily doses had no significant effect on the measured factors but the effects of 300 mg/kg daily dose were significant resulting in toxicity (Tajik et al, 2011). The prolongation in pentobarbital-induced sleep as well as, increased strychnine-induced lethality in mice with a single dose of500 mg/kg of aqueous-methanol extract of *F. officinalis* (Gilani et al, 1996).

A different method of the extract preparation, animals and experimental methods as the probable causes of the controversial findings showed the effects of the *F. parviflora* (Heidari et al, 2004).

**Conclusion**

The results of the present study showed that 200 mg/kg BW of *F. officinalis* hydroalcoholic extract influences glomerular function, especially in a long period and 400 mg/kg of this extract can induce renal and hepatic failure (due to decrease in BUN level). Therefore, the *F. officinalis* hydroalcoholic extract should be administered with caution especially at high doses and long term usage.

**REFERENCES**


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