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The Effect of Ginger Extract on Blood Urea Nitrogen and Creatinine in Mice

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Abstract: The present study is going to determine whether ginger has positive or negative effects of kidney. A hydro alcoholic extract of ginger was administered intraperitoneally (IP) every 48 h to male mice for a period of 20 days. Control group received saline containing equal volume of ethanol. Blood Urea Nitrogen (BUN) and creatinine were measured spectrophotometrically. Administration of ginger extract markedly decreased the BUN concentrations in experimental mice in a non linear fashion with regard to the administrated dosages. However, little changes were observed in the levels of creatinine in these animals as compared with control group. It is concluded that ginger may have a beneficial effect for removal of urea from plasma and it may be considered as a therapeutic herb to manage renal function in patient with uremia.

Key words: Herbs, ginger, kidney, blood urea nitrogen, creatinine

INTRODUCTION

Zingiber officinale Roscoe (ginger) has been used from two thousand years ago as a medicine in several Asian countries. Powdered Ginger called ginger spice has hot taste and strong smell has been used for flavoring food from old times. Traditional Iranian medicine claims the use of ginger as moisture absorbance of head, throat and stomach and with eating or using it as eyeliner it was cure of eye darkness made of moisture (Ghahreman, 1995; Tan and Vanitha, 2004). In recent studies it has been found that because of various active agents in ginger it has different pharmacological effects. Evidence from several line of studies indicated that ginger exhibit antioxidants (Lako *et al*., 2004; Murcia *et al*., 2004; Halvorsen *et al*., 2002; Jagetia *et al*., 2003) anti-inflammatory (Thomson *et al*., 2002) and antimicrobial activities (Akoachere *et al*., 2002; Polasa *et al*., 2003) and antifungal (Ficker *et al*., 2003a, b).

However, if ginger contains pharmacologically useful and active compounds such as *Zingiberene*, *Ar-curcumene*, *Beta-sezquiphellandrene*, *Gingerols andshogaols* which eliminate certain health problems not surprisingly (Halvorsen *et al*., 2002), it may also contain toxic substances which may accumulate in body or excrete through the kidneys (Bagnis *et al*., 2004; Gabardi *et al*., 2003). The kidneys are routinely exposed to high concentrations of medications and toxic substances or their metabolites. Several factors, such as active uptake by tubular cells, passive reabsorption and high concentration in the medullary interstitium (Green *et al*., 1981) make the kidneys particularly vulnerable to toxic insults. Thus, it is likely that prescribed medications and many dietary supplements might be associated with nephrotoxicity, either as a direct toxic effect, or secondary to liver dysfunction (Bagnis *et al*., 2004; Gabardi *et al*., 2003). Since an important function of the kidneys is the removal of substances from plasma and the effects of ginger in renal function is not very well elucidated, the present study was undertaken to examine the effects of ginger extract on the concentration of Blood Urea Nitrogen (BUN) and serum creatinine in mice.

MATERIALS AND METHODS

Extraction of ginger: Although eating a whole ginger and ginger extract are different in order to determine the amount of active compounds given to each animal in the present study a hydro alcoholic extract was used. A dried rhizome of ginger *Officinale roscoe* was powdered and an ethanol extract was prepared by the modified method of Fuhrman (Frondoza *et al*., 2004). Briefly, Ginger powder (1.2 g) was suspended in 3 mL of ethanol in a glass tube-stoppered and was agitated vigorously for 10 min. The mixture was allowed to stand in room temperature for 24 h and after shaking for another 10 min it was filtered trough

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a fluted filter paper into a 100 mL flask. The volume of the filtrate was then raised up to 100 mL by addition of sterile saline. The filter paper was then dried and the amount of the remaining powder on the filter paper was weighed and subtracted from 1.2 g to determine the concentration of the ginger in the extract.

Animals and experiments: At the animal laboratory room of Payame Noor University of Isfahan, Iran (2004-2005), healthy. Adult male *Var. albino* mice (Souris), weighing 28-42 g were housed in cages, with food and water *ad libitum*, maintained on a natural light: Dark cycle. The animals were acclimatized to the laboratory conditions at least one week before the start of experiment at a room temperature of 23-25°C. All the experiments were conducted between 11.00-14.00 h. The animals were divided into four groups each consisting of 4 to 8 animals. Three groups (I, II, III) were injected interaperitonealy with 2 mL of the ginger extract in doses of 10, 20 and 40 mg kg^{-1} body weight 48 h^{-1}, respectively for 20 days. Control group (IV) was injected with saline containing equal volume of ethanol as in the extract filtrate. The animals were then anesthetized and killed by decapitation. Blood samples were collected and were measured using standard diagnostic kits.

Statistical analysis: Results were expressed as mean±SEM. The intergroup variation was measured by one way analysis of variance (ANOVA) followed by Tukey's LSD test. Statistical significance was considered at $p<0.01$, 0.05 and 0.01. The statistical analysis was done using the statistical package for the social sciences (SPSS).

RESULTS

The effect of different doses of ginger extract on the mice BUN is demonstrated in Fig. 1. Mean level of BUN in the control group was 37±5 mg dL^{-1}, which decreased significantly with the administration of different doses of ginger (approximately 50%, $p<0.05$). The concentrations of BUN in the three experimental groups varied between 20 and 26 mg 100^{-1}, which was statistically insignificant.

With analyzing and comparing means of creatinine concentrations in serum of mice in control and experimental groups, little differences were observed between control and experimental groups. The results are shown in Fig. 2. Although the concentrations of creatinine measured in the experimental groups were slightly higher than creatinine level of control group, the differences were not statistically significant.

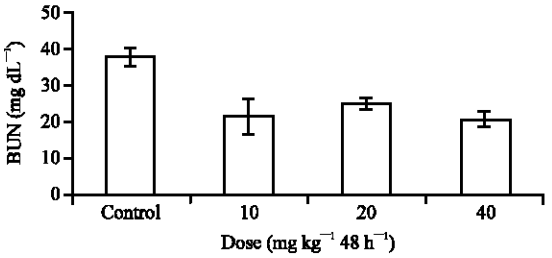

Fig. 1: Effect of different doses of ginger on BUN concentrations in mice; Four groups of mice were injected (IP) ginger extract with doses of 0, 10, 20 and 40 mg kg^{-1} 48 h^{-1} and BUN was measured after 20 days using standard diagnostic kits. Results are mean±SD of 4-8 separate determinations. Differences are significant as compared to control group, $p<0.05$

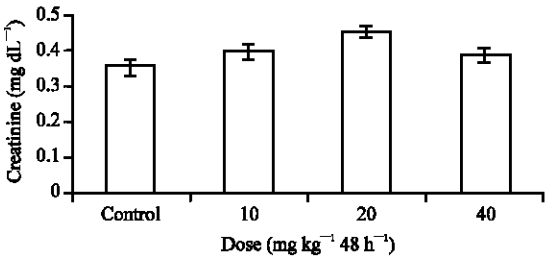

Fig. 2: Effects of different doses of ginger on serum creatinine of mice; Four groups of mice were injected (IP) ginger extract with doses of 0, 10, 20 and 40 mg kg^{-1} 48 h^{-1} and serum creatinine was measured after 20 days using standard diagnostic kits. Results are mean±SD of 4-8 separate determinations. Differences are not significant as compared to control group

DISCUSSION

Although the effects of ginger on different body systems have been extensively investigated, few studies have examined its effect on renal function. Findings of this study is the first one to be reported in this field. Because the major pathway of nitrogen excretion is as urea synthesis in the liver which released in to the blood and cleaned by the kidney, the reduction of in animals receiving ginger extract may be either due to lower rate of urea synthesis in the liver, or higher rate of urea excretion in kidney. Since a number of studies indicated that ginger exhibit antioxidants activity and anti-free radicals abilities (Polasa *et al*., 2003) thus, it may stimulate the liver performance and urea synthesis. Therefore, having

considered renal function, it is appropriate to note that the kidneys have an important role in excretion of substances from plasma. The renal handling of urea represents an important example of the excretion of a substance in urine. Since in the nephrons, urea will be passively reabsorbed (Seel and Levy, 1981; Kawamura and Kokko, 1976; Green *et al*., 1981), the reduction of BUN in animals receiving ginger extract is interpreted as suggesting a mechanism of reabsorption inhibition of urea in the nephrons.

As shown in Fig. 1 maximum effect of ginger extract was seen with the dose of 10 mg kg^{-1} 48 h^{-1}, but injection of ginger extract even in higher than effective doses has not an adverse effect on kidney. It is suggested that ginger may contain some effective compounds that influence removing certain waste products from plasma.

However, as demonstrated in Fig. 2, concentrations of creatinine in serum of these animals did not changed significantly as compared with that of the control group. It could be explained by instructive to compare the effects of urine flow rate on the renal eliminating of a substance such as creatinine to the effects of flow on urea. It is very well known that urea reabsorption occurs as a consequence of the reabsorption of water, in another word, urea reabsorption varies markedly with the rate of urine flow and depends to the volume of water that is not reabsorbed (Frondoza *et al*., 2004). While, creatinine is an organic base formed during muscle protein metabolism as a degradation product of creatine phosphate (Mayes, 1988). Lick many other organic bases, creatinine is filtered at the glomerulus and eliminated from plasma by the kidney. It means that creatinine is filtered only but is not reabsorbed, therefore ginger might have little influence on its excretion, whereas urea is filtered and reabsorbed partly in the nephrons. In addition the relation of urea to the water reabsorption may cause extra cellular contraction, which consequently resulted higher concentration of substances such as creatinine in plasma. This may be the reason for higher although insignificant level of creatinine in the animals receiving ginger (Fig. 2).

In contrast to other herbal remedies and dietary supplements that may cause some kind of renal dysfunction (Bagnis *et al*., 2004; Seel and Levy, 1981), results of the present study indicate that ginger has not any adverse effect on kidney, but it has a beneficial effect for removal of urea from plasma. In conclusion, it is of interest therefore to investigate whether ginger could be used as a therapeutic herb to manage renal function in patient with uremia.

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