THE PROTECTIVE EFFECT OF GINGER (ZINGIBER OFFICINALE) ON SOME BIOCHEMICAL PARAMETERS IN RATS

ABSTRACT:
The aim of the present study is to investigate the effect of daily injection of ginger Zingiber officinale extract on the physiological parameters, as well as the histological structure of the liver of adult rats. Adult male rats were divided into four groups: (G1, G2, G3, and Control groups). The first group received 500 ml/kg b. wt/day of aqueous extract of Zingiber officinale i.p. for four weeks, G2 received 500 ml/kg b wt/day of aqueous extract of Zingiber officinale for three weeks and then received carbon tetrachloride CCl4 0.1ml/150 g b. wt. for one week, G3 received 500 ml/kg body weight/day of aqueous extract of ginger Zingiber officinale i.p. for three weeks and then received CCl4 for one week combined with ginger. The control group (C) received a 500 ml/kg B WT/day of saline water i.p. for four weeks. The results indicated a significant decrease in the total protein and increase in the albumin/globulin ratio in the third group compared with first and second group. Also, the results reported a significant decrease in the body weight in the third and the fourth groups compared with the first and the second groups. A significant decrease in the globulin levels in the third and the fourth groups were detected compared with the first and the second groups. The obtained results showed that treating rats with ginger improved the histopathological changes induced in the liver by CCl4. The study suggests that ginger extract can be used as an antioxidant, free radical scavenging and protective action against carbon tetrachloride oxidative damage in the liver.

KEY WORDS:
Zingiber officinale, carbon tetrachloride, total proteins, albumin, globulin, albumin/globulin ratio, liver histology, rat.

INTRODUCTION:
Ginger root Zingiber officinale has been used for thousands of years in the Far East. It is an important cooking flavour food and herbal medicine around the world, the ginger family (Zingiberaceae). The Zingiber officinale rhizome contain numerous of chemical compounds, including [6] gingerol, α-zingeriberene, gingerone, camphene, neral, camphene and a host of other chemical constituents (Ojewole, 2006). Gingerols are the major components of ginger (Kato et al., 2006), and it has a strong anti-oxidant actions, antitumor, anti-inflammatory properties and prevent generation of free radicals, it is considered as a safe herbal medicine without side effects (Chun et al., 2002; Shen et al., 2003;Verma et al., 2004; Ali et al., 2008) . The aim of the present study is to investigate the effect of daily injection with ginger Zingiber officinale on the total protein, albumin, globulin, the albumin/globulin ratio, the liver weight, the body weight, and the liver/ body weight ratio in male rats.

Carbon tetrachloride (CCl4) is a potent hepatotoxic agent including liver cirrhosis (Ulicná et al., 2003; Manna et al., 2006; Botsoglou et al., 2008). CCl4 metabolism produces a profound oxidative stress through its metabolism to trichloromethylperoxy (CCl3OO) and to trichloromethyl (CCl3) causing damage of cell membrane (Slater, 1982; Kalf et al., 1987; Recknagel et al., 1989; Plaa, 1991). Lu et al. (2003) studied the antioxidation activity and the protective effect of ginger oil on DNA damage and reported that ginger oil has dominative protective effect on DNA damage induced by H2O2. They suggested that ginger oil might act as a scavenger of oxygen radical and might be used as an antioxidant.

The hepatoprotective activity of aqueous ethanol extract of Zingiber officinale was evaluated against single dose of acetaminophen-induced acute hepatotoxicity in rat (Ajith et al., 2007). The authors concluded that the hepatoprotective effect of aqueous ethanol extract of Z. officinale against acetaminophen-induced acute...
toxicity is mediated either by preventing the decline of hepatic antioxidant status or due to its direct radical scavenging capacity.

Al-Naqeeb *et al.* (2003) studied the effects of administration of ginger in rats and observed that serum proteins were unaffected by ginger treatment, while liver protein content was decreased. Al-Amin *et al.* (2006) mentioned that streptozotocin injected rats exhibited hyperglycaemia accompanied with weight loss. These ginger-treated diabetic rats sustained their initial weights during the treatment period. York *et al.* (2007) studied the effectiveness of Chinese herbal extract Number Ten (NT). This extract is a dietary formulation prepared from rhubarb, ginger, astragalus, red sage and turmeric. The authors demonstrated that NT reduced the weight gain in rodents. Moreover, Roberts *et al.* (2007) demonstrated that NT combined with Gallic acid was ineffective in causing weight loss or in suppressing food intake. While Islam and Choi (2008) found that final body weight and liver weight were not influenced by the ginger containing diet.

**MATERIAL AND METHODS:**

Aqueous ginger extract was prepared from locally available ginger roots. Adult male albino rats weighing approximately 200-250 g, obtained from the Animal House of King Fahd Medical Research Centre, Jeddah, Saudi Arabia, were randomly divided into four main groups.

The first group served as control and received 500 ml/kg b.wt/day of saline solution i.p. for four weeks. The second group received 500 ml/kg b.wt/day of aqueous extract of ginger *Zingiber officinale* i.p. for four weeks according to Thomson *et al.* (2002). The third group received 500 ml/kg b.wt/day of aqueous extract of ginger *Zingiber officinale* i.p. for three weeks and then received carbon tetrachloride CCl4 0.1ml/150 g b.wt according to Kaneyuki and Shohmori (1981) for one week. The fourth group received 500 ml/kg b.wt/day of aqueous extract of ginger *Zingiber officinale* i.p. for three weeks and then received 0.1ml/150 g b.wt CCl4 for one week with 500 ml/kg b.wt/day of aqueous extract of ginger.

The level of total protein, albumin, and globulin were determined using the spectrophotometer method. The albumin/globulin ratio, the liver weight, the body weight and the liver/body weight ratio were calculated.

**Statistical analysis**

Analysis of data was carried out by Student’s *t*-test for comparing the means of experimental and control groups (Spiegel, 1981).

**RESULTS AND DISCUSSION:**

The result showed that 500 mg/kg/day b.wt. of aqueous extract of ginger *Zingiber officinale* affected the serum total protein, albumin, globulin and the albumin/globulin ratio. A significant decrease in total protein in the third group (treated with CCl4) was recorded compared with first and second group. Significant decrease in the globulin levels in the third and the fourth groups (treated with CCl4 + ginger + CCl4) were detected compared with the first and the second groups. In addition, ginger caused a significant increase in albumin/globulin ratio in the third and the fourth groups compared with the first and the second groups (Figs 1-4).
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The result showed that 500 mg/kg/day b.wt of aqueous extract of ginger *Zingiber officinale* affected the body weight and the liver/body weight ratio. Significant decreases in body weight in the third group compared with the first and the second groups, and in the fourth group compared with the first group were detected. Moreover, a significant decrease in the liver weight in the third group compared with the second group was observed. Besides, a significant decrease in the liver/body weight ratio in the third and the fourth group compared with the second group. However, the results indicated that no changes in the body, liver weight and the liver/body weights ratio in the second group compared with the control one (Figs 5-7).

The present results exhibited a significant decrease in total protein levels in the group treated with CCl₄ compared with the control and the ginger supplemented groups. There was a significant decrease in globulin level in the third and the fourth groups (treated with CCl₄ + ginger + CCl₄) compared with the first and the second groups. Treatment with ginger caused a significant increase in albumin/globulin ratio in the third and the fourth groups compared with the first and the second groups. These results are in agreement with those of Mandal *et al.* (1992) who reported the effect of Mikania Cordata root extract on the rate of hepatic protein synthesis *in vivo* in CCl₄-induced liver damage. Pre-treatment with the root extract showed enhancement in the levels of hepatic protein content that were adversely affected with CCl₄ treatment. Increase in the total protein mass, fractional rate of protein synthesis, total rate of protein synthesis in response to the pretreatment of the root extract in hepatic tissue indicated the tissue repair leading to a functional improvement of the hepatocytes that were disorganised with CCl₄ intoxication. Also, Mandal *et al.* (1998) reported the effect of the Trianthema portulacastrum L. on the CCl₄-induced chronic hepatocellular damage. The CCl₄ administration alone caused alterations of plasma albumin and globulin. The administration of plant extract restored parameters to the normal level. Gole and Dasgupta (2002) suggested that Aphanamixis polystachya shows a beneficial effect on toxic liver injury. The antihepatotoxic activity was evaluated on carbon tetrachloride (CCl₄)-induced liver injury. The leaf extract ameliorated the depressed value of serum albumin caused by CCl₄. Bhandarkar and Khan (2003) found that administration of *Lawsonia alba* afforded good hepatoprotection against CCl₄ induced reduction in total serum protein. They suggested hepatoprotective and antioxidant activity of extract of *L. alba* bark. Manjunatha and *et al.* (2005) resulted that leaf extracts of *Leucas hirta* demonstrated hepatoprotective activity against CCl₄ induced liver damage and recorded a significant
decrease in total protein level caused by CCl₄, the authors suggested that Leaf extracts showed a significant increase in total protein. Shih et al., (2005) studied the effects of Anoectochilus formosanus (AFE) on liver fibrogenesis in carbon tetrachloride (CCl₄)-induced cirrhosis. CCl₄ led to the drop of serum albumin concentration, the AFE increased the albumin concentration and the albumen and the protein levels in the liver of rats.

Lin and Lin (2006) investigated the effects of Reishi mushroom, *Ganoderma lucidum* extract (GLE), on liver fibrosis induced by carbon tetrachloride (CCl₄). CCl₄ caused decrease in plasma albumin, albumin to globulin ratio (A/G ratio) and hepatic protein level. Compared with CCl₄ group, GLE treatment significantly increased plasma albumin level and A/G ratio but increased hepatic protein level. They found that administration of GLE significantly reduces CCl₄-induced hepatic fibrosis in rats, probably by exerting a protective effect against its free-radical scavenging ability.

The present investigation showed no change in the total protein, albumin, globulin, and the ratio of albumin/globulin in the ginger treated group compared with the control one. These results agree with those of Al-Naqeeb et al., (2003) and Ugwu et al., (2008) who reported that serum protein levels are unaffected by ginger extract administration.

From the present results it is clear that increment in body weight in the fourth group was detected. This agrees was agreement with Al-Naqeeb et al., (2003) who studied the Biochemical and histopathological toxicity of an aqueous extract of ginger in female rats. The authors reported that administration of ginger extract did not cause any apparent adverse gastrointestinal effects among the rats. The weight gain is attributed to the normal growth of the rats and supports the conclusion that ginger treatment did not affect the health of the animals.

Gowda et al., (2008) conducted the efficacy of turmeric *Curcuma longa* to ameliorate the adverse effects of a flatoxin in broiler chicks. The addition of turmeric (curcuminoids) to the flatoxin diet significantly improved feed intake and weight gain of chicks.

The present results recorded an increase in the liver weight in the fourth group. This agrees with Shih et al., (2005) who studied the effects of Anoectochilus formosanus extract (AFE) on liver fibrogenesis in carbon tetrachloride (CCl₄)-induced cirrhosis. The CCl₄-induced liver atrophy, while AFE increased the liver weight.

The animals of the first and second groups showed normal liver structure (Fig. 8).

Fig. 8. Photomicrographs of liver sections of control rats showing normal histological appearance of the liver, including central vein (CV), blood sinusoids, hepatic cells, kupffer cell and centrally located nuclei.

Examination of liver sections obtained from rats of G₁ and G₂ showed obvious histopathological alterations of the liver. Liver section of the rat treated with ginger supplemented demonstrated normal arrangement of hepatocytes, although no significant difference was observed between control and ginger group (Fig. 9).

Fig. 9. Photomicrographs of liver sections of the rat supplemented with ginger s showing normal arrangement of hepatocytes. The structural pattern is similar to control.

The normal structural organization of the hepatic lobules was impaired and the characteristic cord-like arrangement of the normal liver cells was almost lost. Liver sections revealed that a considerable number of damaged hepatic cells that lost their characteristic appearance while others showed a marked cytoplasmic vacuolization which was so extensive in some cells to the extent that only slight remnants of the cytoplasmic mass cells – frequently forming a narrow peripheral rim was left. The nuclei of these cells were pyknotic. In addition, congestion of the intrahepatic blood vessels and inflammatory leucocytic infiltrations were observed. Some liver cells were degenerated and suffered from fatty infiltrations (Fig. 10).
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Fig. 10. Photomicrographs of liver sections of rats received aqueous extract of ginger for three weeks and then received CCl4 (0.1mg/150g) for one week showing hydropic degeneration associated with inflammatory leukocyte infiltrations. The Kupffer appear spread on the sinusoids. Periportal round cell infiltration appears.

In animals treated with CCl4 combined with ginger (G4), the majority of these histopathological changes were diminished but some of the intrahepatic vessels were congested and some hepatocytes appeared with vacuolized cytoplasm and Kupffer cells were activated (Fig. 11).

Yemitan and Izegbu (2006) studied the Protective effects of Zingiber officinale (Zingiberaceae) against carbon tetrachloride and acetaminophen-induced hepatotoxicity in rats. The protective effect of the extract on CCl4 and acetaminophen-induced damage was confirmed by histopathological examination of the liver. These results indicated that the oil from the rhizome of Zingiber officinale could be useful in preventing chemically induced acute liver injury. Patrick-Iwuanyanwu et al. (2007) investigated the hepatoprotective effects of garlic (Allium sativum), ginger (Zingiber officinale) and vitamin E pre-treatment against carbon tetrachloride-induced liver damage in male wistar albino rats were. Carbon tetrachloride was administered after feeding animals with diets containing ginger, garlic, vitamin E and various mixtures of ginger and garlic. Histological examination of the liver revealed severe infiltration of inflammatory cells in rats treated with CCl4 alone. However, the observed alteration in the normal architecture of the hepatic cells decreased remarkably in pre-treated rats. Mallikarjuna et al. (2008) investigated the influence of ginger on hepatic antioxidant enzymes system in ethanol treated rats. Ethanol significantly decreased the superoxide dismutase, catalase, glutathione peroxidase, glutathione reductase and glutathione content while an increase of malondialdehyde levels was estimated in the hepatic tissue. This effect was reversed by a treatment with dietary ginger in rats by improved antioxidant status which suggests that treatment of ginger may have protective role against the ethanol induced hepatotoxicity.

El-Sharaky et al. (2009) investigated the effect of ginger (Zingiber officinale Roscoe) extract in alleviating hepatotoxicity caused by bromobenzene in male albino rats. They found that Pre-treatment with different doses of ginger extract prior to bromobenzene-treatment alleviated its toxic effects on the tested parameters in the animal.

Shati and Elsaid (2009) studied the effect water extracts of thyme (Thymus vulgaris) and ginger (Zingiber officinale Roscoe) on alcohol abuse and reported high significant increase in nitric oxide and malondialdehyde levels in liver and brain and high significant decrease in the total antioxidant capacity and glutathione peroxidase activity in alcoholic group. In addition, the liver function enzymes such as l-gamma-glutamyl transpeptidase and butyryl cholinesterase activities showed highly significant increase in alcoholic group. In contrast, the water extracts of thyme and ginger showed significant amelioration on these changes both in liver and brain tissues. They concluded that water extracts of thyme and ginger performed detoxifying and antioxidant effects. Therefore, it is recommended to use them to avoid alcoholic toxicity.

The present investigation suggests that ginger extract my used as antioxidant, free radical scavenging and protective action against carbon tetrachloride induced oxidative damage in liver.
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