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Ameliorative Effect of the Aqueous Extract of *Zingiber officinale* on the Cadmium-Induced Liver and Kidney Injury in Females Rats

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Abstract

The present study was carried out to determine the protective effect of the orally administered aqueous ginger extract (*Zingiber officinale*) against hepatotoxicity and nephrotoxicity induced by high dose of cadmium bromide in adult female albino rats (*Rattus norvegicus*). A total of twenty rats were used in the study. The animals were divided into four groups: Control rats received tap water, second group received cadmium as cadmium bromide at a dose (100 mg Cd^{+2}), third group received Cd^{+2} plus 2g/L aqueous ginger extract, while the last group received only 2g/L ginger extract for 40 days. The result analysis showed that there were several histological changes in the liver and kidney tissue of cadmium treated rats in comparison to control. The cadmium bromide caused degeneration of hepatocytes, inflammatory infiltrated leucocytes and dilation of blood sinusoid lumens in treated rat liver. In kidney, dilatation of tubules, congestion of blood vessels with RBCs and inflammation in cortex of cadmium treated rats were also observed. After administration of aqueous ginger extract to the cadmium treated group, the liver and kidney have approximately returned to the normal histological features. In conclusion, the aqueous extract of *Z. officinale* showed an ameliorative effect against cadmium bromide induced hepatotoxicity and nephrotoxicity.

Keywords*:* Ginger; Cadmium; Liver; kidney, *Zingiber officinale***.**

1. Introduction

Cadmium (Cd) is one of the most toxic heavy metals. This metal is a serious environmental and occupational contaminant and may represent a serious health hazard to humans and other animals (Kikuzaki and Nakatani 1993 and Mustafa *et al.,* 1993). Several studies have demonstrated the effect of cadmium (Cd) on various organ-systems in the body. It has been reported that Cd induced nephrotoxicity, testicular damage, lung damage, hepatotoxicity, and body weight loss (Ige *et al.,* 2011). Absorption of ingested Cd is only about 5% and after absorption it accumulates in the liver and then in the kidney (Smalinskienel *et al.,* 2006) and its half-life is very long, exceeding 10 yr (Kramarova *et al*., 2005).Cadmium can accumulates and cause a number of lesions in the body tissues, such as the liver, kidney and testis (Egwurugwu *et al.,* 2007, Stoilova *et al.,* 2007). Liver of rats treated with $CdCl_2$ showed that there were degenerative changes in numerous hepatocytes; the cells were enlarged and had light and foamy cytoplasm filled with numerous vacuole-like spaces and in the kidney showed that there were many areas of tubular damages were observed in all treatment animals. These renal damages appeared as hypertrophy and degeneration of epithelia of renal tubules with distinct of mononuclear cells infiltration. The walls of the blood sinusoids were dilated and showed numerous Kupffer cells (Mahran *et al.,* 2011). The toxic effects of cadmium on organisms include nephrotoxicity, carcinoegenicity, hepatotoxicity and endocrine disruption (Serafim and Bebianno, 2007).

Ginger (*Zingiber officinale*) is one of the world's best known spices, and it has also been universally used throughout history for its health benefits. The main constituents of ginger include volatile oil, phenolic derivatives (zingerone) and oleoresin (gingerols and shogaols) are main antioxidant compound in ginger (Kikuzaki and Nakatani, 1993). Ginger extract possesses antioxidative characteristics, since it can scavenge superoxide anion and hydroxyl radicals. Z. *officinale* was found to inhibit the activity of lipoxygenase and peroxidation (Topic *et al.,* 2002). Barakat and Mohamed (2011) showed ability of ginger to protect the liver against

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the oxidative stress and hepatocellular injury that follows a supra therapeutic dose of acetaminophen.

The aim of the present study was to evaluate the effect of ginger water extract in protecting against the toxic effect of cadmium bromide on kidney and liver of rats.

2. Materials and Methods

2.1. Animals and Housing

The study was carried out on twenty adult female Wistar albino rats (*Rattus norvegicus*). All rats were weighing about (271.55 ± 8.3738 gm) and (10) weeks of age at the time the experiment was started.

The animals were bred and housed in plastic cages (56 x 39 x 19 cm) bedded with wooden chips. The animals were purchased from the Animal House of the Department of Biology, College of Science, Salahaddin University-Erbil. Climate controlled conditions were maintained and temperature was set as (22± 2^{o}C). Regular 12-hours diurnal cycles were kept using an automated light-switching devise, The rats were given standard laboratory chow containing 0.5% NaCl, 22% protein and 4-6 dietary fat and allowed drinking water *ad libitum.*

2.2. Experimental Design

Albino rats used in this experiment (were) grouped into the following groups:

2.3. Control Group

The rats of this group received standard rat's diet containing 0.5% NaCl, 22% protein and 4-6% dietary fat and tap water *ad libitum* (Krinke 2002).

Group 1: Cadmium bromide solution

The rats of this group received Cadmium bromide solution daily in the drinking water 100 mg (Cd^{+2}) for 40 days (Benoff *et al.*, 2008).

Group 2: Cadmium bromide & aqueous Ginger extract.

The rats of this group received Cadmium bromide (100 mg) and ginger (2 g/L) daily in the drinking water for 40 days (Hasanabad *et al.*, 2005).

Group 3: Dose of aqueous Ginger extract.

The rats of this group received ginger daily in the drinking water (2 g/L) for 40 days.

2.4. Collection of Liver and Kidney Samples

At the end of the experiment, the rats after being starved over night were anesthetized with ketamine hydrochloride (100mg/Kg) and then decapitated. Liver and kidney isolated after dissecting the animals into tubes with fixatives (chromaid), allowed to fix for 24 hours and then stored at 70% ethanol for histological analysis. The tissues were processed and embedded in paraffin wax. Thick sections(6µm) were obtained and stained by hematoxylin and eosin (H&E) and examined under light microscope to determine the morphological changes.

3. Results

The present investigation showed several histological alterations in the liver and kidney of cadmium treated rats in comparison to control (Figure 1-3). As shown in Figure 1b and c, cadmium bromide caused degeneration of liver cells especially hepatocytes, in which these cells were seen shrunken with condensed nuclei. Inflammatory infiltrated leucocytes forming foci were detected around blood vessels (Figure 1b). Blood sinusoid lumens were seen dilated in most regions of cadmium treated rat liver (Figure 1c). After given ginger to the cadmium treated group, the liver tissue restored most of its normal histological features (Figure 1d).

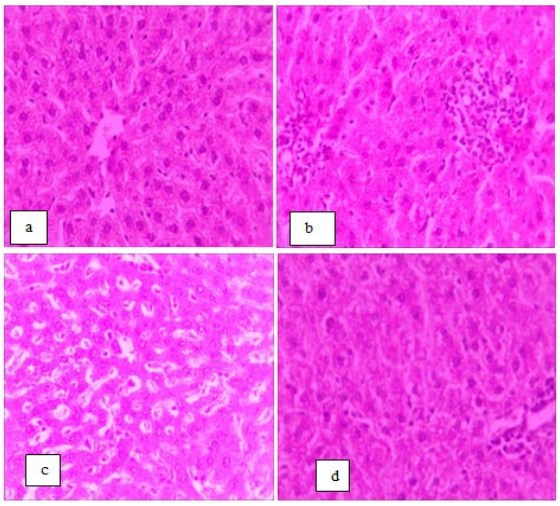

Figure1. Sections through liver, A)control showing normal structure of liver,400X,H&E,B) cadmium treated rat liver showing inflammatory leucocytes infiltration near the blood vessel, 400X, H&E, C) cadmium treated rat liver showing blood sinusoid dilatation, 100X, H&E, D) cadmium plus ginger showing approximately normal structure, 400X,H&E.

As shown in Figure 2a and b, the kidney of control group showed normal histological structure, while when cadmium bromide was given to the rats, it caused dilatation of kidney tubules, congestion of blood vessels with RBCs (Figure 2c) and inflammation in certain regions of the kidney cortex (Figure 2d). When ginger was administered in combination consequence with cadmium bromide, it has caused attenuation of the nephrotoxicity caused by cadmium (Figure 3).

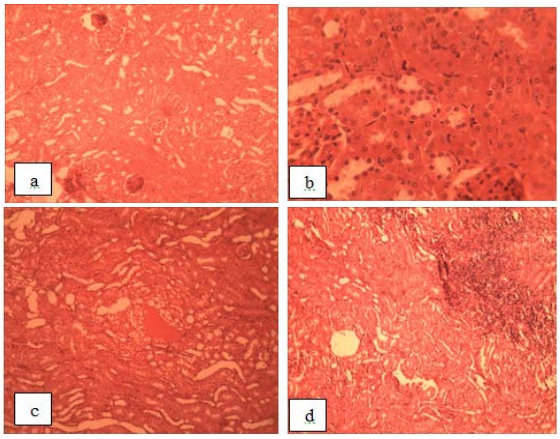

Figure 2. Sections through kidney, A) & B) control showing normal structure of kidney, 100X & 400X respectively, H&E, C) cadmium treated rat kidney showing dilatation of kidney tubule and congested blood vessel,400X,H&E, D) cadmium treated rat kidney showing Inflammatory foci in the cortical region, 100X H&E.

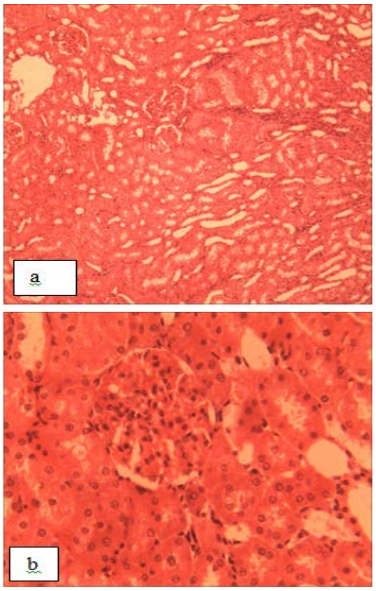

Figure 3. Sections through kidney of cadmium plus ginger treated rats showing approximately normal structure of kidney, A) 100X b) 400X.

4. Discussion

Histopathological studies revealed that alterations occurred in the hepatic and kidney architecture of cd treated rats. The kidney has been recognized as a critical target organ of Cd toxicity. Cd-treated rats showed severe cellular degeneration, necrosis, and hepatocytes and localized fatty degenerations. This agrees with earlier studies (Ige *et al.*, 2011; Mahran *et al.*, 2011). They showed that there were changes in liver including, a blurred trabecular structure, vacuolar degeneration and increased density of nuclear chromatin with very compact nuclear structure of hepatocytes. Moreover; mononuclear cell infiltrations and necrosis of single cells were also observed. These morphological hepatic changes may be due to the decline activities of hepatic Superoxide dismutases (SOD) and an increase hepatic Malondialdehyde (MDA**)** seen in Cd-treated rats (Mohammad 2011).

These changes may also be due to direct toxic effects of the toxicants on hepatocytes since the liver is the site of detoxification of all types of toxins and chemicals (Soufy *et al.*, 2007). The liver is the organ most associated with the detoxification and biotransformation of foreign compounds that enter the body. However, its regulating mechanism can be impaired by accumulated toxicants which could result in structural damage (Camargo and Martinez, 2006). Furthermore, the liver is one of the critical target organs after chronic exposure to cadmium (Sobha 2007). The liver accumulates substantial amounts of cadmium after both chronic exposures.

In kidney tubules, degeneration and hypertrophy of epithelial cells and dilation of glomeruli and massive local haemorrhage of the renal tissues were observed (Obianime and Roberts 2009). The mechanism of Cd-induced kidney damage is considered to be related to increased oxidative status. Increasing of oxygen of free radicals production seem to be induced by the interaction of Cd with mitochondrial structure (Tang and Shaikh 2001).

In ginger co-treated animals, we noticed an improvement in the Cd-induced damage in the liver and kidney. Our results were in agreement with published data by Gehan and Ayman (2010) who observed that ginger expressed an antagonistic action on cadmium toxicity. This protective effect could be attributed to the fact that ginger contains high content of antioxidants that makes it a free radical scavenger (Krishnakanta and Lockesh, 1993). Moreover, another study by Yuki Masuda *et al.* (2008) reported that the antioxidant activity of ginger might be due to not only radical scavenging activity of antioxidants but also their affinity to the substrates. Egwurugwu et *al.* (2007) reported that ginger therapy was more effective as more Cd intake was avoided. We assumed that ginger through the said antioxidant activities, first improved the blood balance with the confirmed results improving the liver functions followed by improving the kidney functions. This is the first hypothesis explaining the role of ginger in improving liver and kidney functions. Finally, our results demonstrated the ameliorative effect of aqueous ginger extract (*Zingiber officinale*) administration on the Cd induced toxic structural changes in the liver and kidney tissues of the rats. These results validate the hypothesis that the metabolism and toxic action of Cd may be modulated by aqueous ginger extract supplementation.

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