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Research Article

Study on the Efficacy of Garlic Extract Against Cadmium Toxicity of Liver and Kidney in Rats

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Abstract

Background: Cadmium (Cd) is widespread pollutant that affected human health.

Objective: The present study aimed to investigate the possible protective effect of Garlic (Allium sativum) against hepatorenal toxicity of cadmium in rats.

Methods: 32 adult male rats were used and divided equally into four groups each with 8 rat: Group I: Control group, the rats of this group were given normal diet and water for four weeks, Group II: Garlic group, the rats of this group received garlic extract 350 mg/kg bw by stomach tube every second day for four weeks, Group III: Cadmium group, the rat of this group received 60 mg/kg bw Cadmium by stomach tube every second day for four weeks, and Group IV: Garlic + Cadmium group, the rat of this group received garlic extract 350 mg/kg bw then 60 mg/kg bw Cadmium by stomach tube every second day for four weeks. At the end of the experiment, samples of blood were taken for biochemical analysis. Then rats were sacrificed and dissected, and samples of liver and kidney were collected for histological studies. Body weight was measured at the beginning and the end of the experiment. Blood samples were collected at experiment end. Sera prepared to measure activities of liver and kidney functions.

Results: It was observed that weight gain was significantly decreased in Cd group and Garlic + Cd group versus control and Garlic groups. Percentage changes in body weight were significantly decreased in Cd group and Garlic + Cd group versus control and Garlic groups. Cadmium administration caused significant increases in the activities of ALT, AST and ALP enzymes, and in the values of CRE, URE, UA, TG, CHOL, LDL-c and VLDL-c, but HDL-c was significantly decreased. These changes were ameliorated with administration of garlic.

Conclusions: Cadmium administration produces toxic effects that partially improved after garlic administration due to its antioxidant and anti-inflammatory effects.

Keywords: Cadmium; Garlic; Liver; Kidney; Protective Effects; Physiology; Histology

Introduction

Pollution of the environment is one of the most significant issues confronting humans and other living forms on our planet today. Environmental pollution is defined as the contaminating of the earth's atmospheric system's physical and biological constituents to the point that common environmental functions are significantly disrupted [1]. Valko., *et al*. [2] declared that heavy metal poisoning was associated with immunotoxicity, neurotoxicity, and carcinogenic potential, which are hypothesized to arise as a consequence of the formation of oxygen radicals, resulting in changes in physiological and biochemical features as a result of oxidative stress.

Vinodini., *et al*. [3] reported that cadmium (Cd) is one of the essential toxic metals that occur naturally. Cadmium can affect various organs in the body. The liver is the most affected organ by cadmium toxicity (either acute and/or chronic). Cadmium can affect the liver through multiple mechanisms, such as the formation of reactive oxygen species (ROS), oxidative stress, and/or disruption of cellular antioxidant systems.

Albasha and Azab [4] investigated the effects of Cd on liver function and their amelioration by aqueous extracts of fenugreek seeds, rosemary, and cinnamon in guinea pigs. The activities of ALT, AST, ALP, and γ-glutamyl transferase (γ-GT) were significantly higher in $CdCl_2$ treated rats with respect to the normal groups ($P < 0.05$). $CdCl_2$ lowered enzyme activity when combined with fenugreek, rosemary, and cinnamon, with statistically significant changes ($p < 0.05$). Renugadevi and Prabu [5] discovered that Cd-treated rats significantly elevated AST, γ-GT, ALT, ALP, and total bilirubin levels. Cd-related hepatotoxicity was characterized by reduced hepatic biomarker functions (transaminases) [6,7]. These findings might point to liver degeneration and hypofunction [8].

According to Mantur., *et al*. [9] Cadmium is one of the pollutants in the environment that affects a lot of different parts of the body, like the liver, kidney, and testis. Cd changed the liver's lipid profile and histopathology. They found essential elevation in triglycerides (TG), total cholesterol (CHOL) and low-density lipoprotein cholesterol (LDL-c), while high density lipoprotein cholesterol (HDL-c) was significantly decreased.

Garlic and its formulations have long been known as effective remedies for the prevention and treatment of cardiovascular disease. Garlic consumption reduces blood pressure, protects atherosclerosis, decreases serum cholesterol and triglycerides, inhibits platelet aggregation, and boosts fibrinolytic activity, according to a growing body of scientific research [10]. These heart-healthy advantages have been shown in both clinical and experimental studies on various garlic formulations. Garlic has been shown in several studies to protect liver cells against a variety of toxic chemicals. In many countries, acetaminophen is a commonly prescribed painkiller and antipyretic. In humans and rats, overdoes have been associated to hepatotoxicity and nephrotoxicity. While the majority of acetaminophen is converted to sulphate and glucuronide conjugates and excreted in the urine, a small amount is metabolized by various liver enzymes [11]. Garlic has been found to protect against the hepatotoxicity caused by acetaminophen.

The goal of the present study was to assess the protective effect of Garlic administration for 6 weeks on hepatorenal toxicity induced by Cadmium in adult male Albino mice.

Materials and Methods

Materials

Experimental animals

Adult male albino rats, weighing between 180-220g were used in the present study. The experimental animals were obtained from Mansour scientific foundation for research and development (MSF), Jeddah, Saudi Arabia. The rats were housed in standard plastic cages and maintained under controlled laboratory conditions of temperature (24 ± 1°C) and 12:12 h light: dark cycle for a week for acclimatization before subjected to experiments. The rats were fed *ad libitum* on normal commercial chow and had free access to water. The experimental treatments were conducted in accordance with the Ethical Guidelines of The Animal Care and Use Committee of King Abdulaziz University.

Garlic extraction

Single clove garlic were purchased from a local commercial market, Jeddah, Saudi Arabia. The dried sample was extracted three times by maceration with methanol at room temperature. The extract was filtered, and the solvent was evaporated under reduced pressure at low temperature does not exceed 40°C using a rotavapor until dryness. Then the extract kept in glass container.

Cadmium chloride ($CdCl_2$)

Cadmium chloride ($CdCl_2$) was purchased from Bayouni Trd. Co. Ltd., which is a chemical company in Jeddah market.

Methods

Experimental groups

The experiment was designed to carry out the treatments (orally) at the level of 350 mg/kg body weight garlic extract and 60 mg/kg body weight Cadmium. Thirty-two male albino rats weighing 180-220 g were randomizing divided into four groups 8 rats each as follows, Group I: Control group, the rats of this group were given normal diet and water for four weeks, Group II: Garlic group, the

rats of this group received garlic extract 350 mg/kg body weight by stomach tube every second day for four weeks, Group III: Cadmium group, the rats of this group received 60 mg/kg body weight Cadmium by stomach tube every second day for four weeks, and Group IV: Garlic + Cadmium group, the rats of this group received garlic extract 350 mg/kg body weight then 60 mg/kg body weight Cadmium by stomach tube every second day for four weeks.

At the end of the experiment, samples of blood were taken for biochemical analysis. Then rats were sacrificed and dissected, and samples of liver and kidney were collected for histological studies.

Body weight determinations

The body weights of rats were determined at the start of the experimental period and at the end, after six weeks, using a digital balance. These weights were measured at the same time during the morning [12]. Moreover, the experimental animals were observed for signs of abnormalities throughout the period of study.

Blood serum analyses

At the end of the experiment, all animals were fasted for 12 hours, water was not restricted, and then anaesthetized with diethyl ether. Blood samples were collected from orbital venous plexus in non-heparinized tubes, centrifuged at 2500 rpm for 15 minutes. The blood sera were then collected and stored at 4°C prior immediate determination of Alanine aminotransferase (ALT) [13], Aspartate aminotransferase (AST) [14], Alkaline phosphatase (ALP) [15], Creatinine (CR) [16], Urea (UR) [17], Uric acid (UA) [18], Triglycerides (TG) [19], Total cholesterol (CHO) [20], High-density lipoprotein cholesterol (HDL-c) [21], Low-density lipoprotein cholesterol (LDL-c) and Very Low-density lipoprotein cholesterol (VLDL-c) [22].

Histological examination

The rats were dissected immediately after taking blood samples from them, and the organs liver and kidney were cut and the sections were stained with Hematoxylin and Eosin [23]. Then the sections were examined by using light microscope (Olympus BX61-USA) connected to motorized controller unit (Olympus BX-UCB-USA). The examined sections were then photographed by a camera (Olympus DP72- USA).

Statistical analysis

The data were analyzed using IBM SPSS Statistics for Windows, version 23 (IBM SPSS, IBM Corp., Armonk, N.Y., USA). Collected data presented as means ± standard deviation (SD). Statistical comparisons were performed by One-Way analysis of variance followed by least significance difference (LSD) test for comparison between different groups. All statements of significance were based on probability.

Results

Weight changes in different studied groups

There were insignificant differences between studied groups regarding initial body weights. Final body weights were insignificantly decreased in all groups versus control group. Weight gain was significantly decreased in Cd group and Garlic + Cd group ($P < 0.05$) versus control and Garlic groups. Percentage changes in body weight were significantly decreased in Cd group and Garlic + Cd group versus control and Garlic groups (Figure 1).

Results of the activities of the enzymes ALT, AST and ALP in different studied groups

In Garlic treated group (GII), the activities of the enzymes ALT, AST and ALP were approximately the same when compared with the control group (GI). In cadmium treated group (GIII), the activities of ALT, AST and ALP enzymes significantly increased ($P < 0.05$) when compared with the control group GI. When using Garlic + cadmium (GIV), the mean values for CRE, URE and UA were significantly decreased when compared with the control group GII and the cadmium group GIII) Figures 2-4).

Results of creatinine, urea and uric acid in different studied groups

In Garlic treated group (GII), the mean values ±SD of Creatinine (CRE), Urea (URE) and Uric acid (UA) were approximately the same when compared with the control group (GI). In cadmium treated group (GIII), the values of CRE, URE and UA were significantly increased compared with the control group GI ($P < 0.05$). When using Garlic + cadmium (GIV), the mean values for CRE, URE and UA were significantly decreased ($P < 0.05$) when compared with the control group GI and the cadmium group GIII (Figures 5-7).

Results of triglycerides (TG), total cholesterol (CHOL), high density lipoprotein cholesterol (HDL-c), low density lipoprotein cholesterol (LDL-c) and very low-density lipoprotein cholesterol (VLDL-c) in different studied groups

In Garlic treated group (GII), the mean values ±SD of Triglycerides (TG), Total Cholesterol (CHOL), High Density Lipoprotein Cholesterol (HDL-c), Low Density Lipoprotein Cholesterol (LDL-c) and Very Low-Density Lipoprotein Cholesterol (VLDL-c) were approximately near the values of the control group (GI). In cadmium treated group (GIII), the values of TG, CHOL, HDL-c, LDL-c and VLDL-c were significantly increased ($P < 0.05$) when compared with the control group GI. When using Garlic + cadmium (GIV), the mean values for TG, CHOL, HDL-c, LDL-c and VLDL-c were significantly decreased ($P < 0.05$) when compared with the control group GII and cadmium group GIII (Figures 8-12).

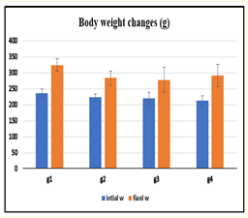
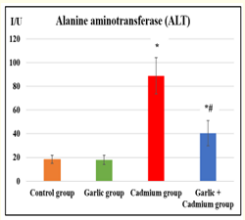


Figure 1



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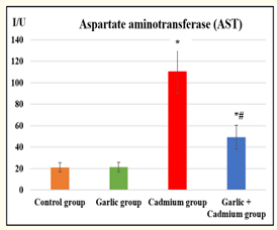

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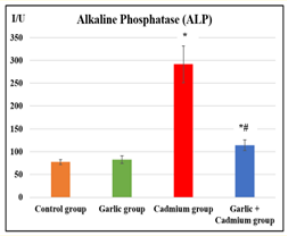
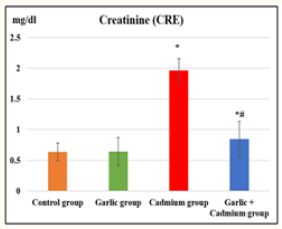


Figure 4



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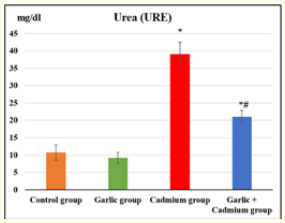

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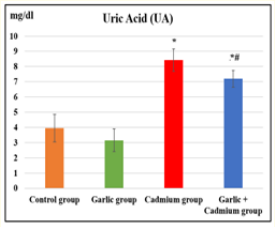

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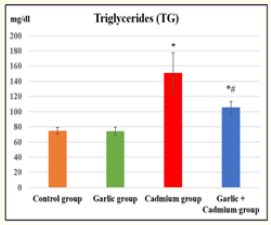
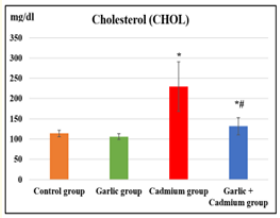


Figure 8



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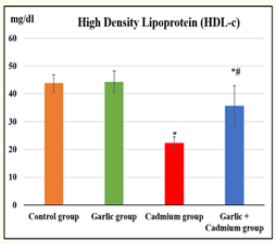

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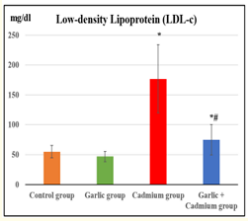

Figure 11

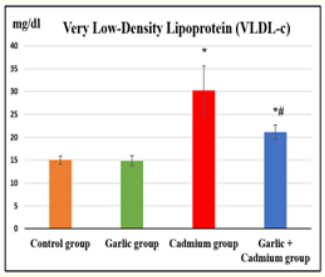

Figure 12

Histological results

Histological results of liver

Liver sections of the control group (GI)

The liver tissue of the control group (GI) was normal. Hepatocytes showed a healthy and intact structure, with no signs of cell necrosis. The hepatic sinusoids (blood sinusoids) between the hepatic cords, lined by endothelial cells, appear as flattened cells with flattened nuclei. Kupffer (K) cells were readily identified by Hematoxylin and Eosin staining and were found among sinusoidal endothelial cells (Figure 13).

Liver sections of garlic extract group (GII)

In the Garlic extract group (GII), the liver part revealed the same standard structure as the control group (GI), where blood sinuses appeared between the hepatic cords and the hepatocytes appeared typical with centrally located round nuclei, arranged in lines. Kupffer (K) cells have dark nuclei (Figure 14 and 15).

Liver sections of cadmium group (GIII)

In the cadmium (GIII) group, histological observations of liver tissue revealed some hepatocellular changes, such as cytoplasmic vacuoles with pycnotic nuclei. Dilation of liver sinusoid, Kupffer cell activation, hydropic degeneration in some hepatocytes, monocular cell infiltration of the hepatic tissue. The central veins appear filled with blood. The cross-section shows degeneration and necrosis in some cells. In addition, there is an aggregation ofchromatin materials inside the nuclear envelope and some hepatocytes showed apoptotic changes nuclear pyknosis and some hepatocytes and dilation and congestion of the central vein (Figure 16 and 17).

Liver sections of garlic + cadmium group (GIV)

In the Garlic + cadmium group (GIV), hepatocytes appeared almost normal, like those in the control g group. The liver cords were normal with a round nucleus (N) in the center of his cytoplasm. The cross-section shows degeneration and necrosis in few cells. In addition, the blood sinuses (S) appeared normal and Kupffer (K) cells were evident with dark nuclei. There are mild cytoplasmic vacuoles in some parts (Figure 18 and 19).

Histological observations of the Kidney

Kidney sections of the Control group (GI)

The kidney sections of the control group (GI) shows normal structure of the kidney, as it is divided into the outer cortex and the inner medulla. Millions of functional units, nephrons, are found in each kidney. Each nephron has major divisions of renal corpuscles, which are an initial dilated portion in the cortex, proximal convoluted tubule, and distal convoluted tubule. Bowman's capsule, the inner layer (visceral layer) of the capsule, envelops the capillaries of the glomerulus. The outer layer forms the outer boundary of the renal capsule. Between the two layers of Bowman's capsule is the urinary opening. The parietal layer of Bowman's capsule consists of a simple squamous epithelium resting on a basement membrane. Cortical nephrons are located almost entirely in the cortex (Figure 20 and 21).

Kidney sections of garlic extract group (GII)

The observations of the Garlic extract group (GII) by light microscopy revealed normal kidney structure in both the cortex and medulla, where there were no changes in the glomerular or medullary rays (Figure 22). In addition, observations showed that the structure of the collecting ducts, thin and thick branches of the loop of Henle remained normal (Figure 23)

Kidney sections of cadmium group (GIII)

Kidney sections of cadmium-treated mice group (GIII) revealed certain changes, such as the aggregation of hemolytic blood (HB) cells between the tubes. Bowman capsule of glomerulus were observed to be enlarged whereas some parts of it was found to be narrowed. Marked hyperplasia of glomerular mesangial cells in many glomeruli. The onset of cellular damage is also present, including alteration of some nuclei (double-headed arrows), as well as leakage of blood cells from the blood vessels. Some blood vessels appear to be congested and blocked by blood cells. Some sections show cytoplasmic vacuum suction and the appearance of tubular plaster. In some tubules, there are swollen cells, and the appearance of cytoplasmic vacuoles. tubular dilatation and interstitial inflammation, some tubules had necrotic cells with pycnotic nuclei (PN). The epithelia were disrupted in the proximal and distal convoluted tubules. Some of renal tubules showed casts in their Lumina. Severe congestion was observed in renal interstitial (Figure 24 and 25).

Kidney sections of garlic extract + cadmium group (GIV)

Histological examination of the kidneys of rats in the Garlic extract and cadmium (GIV)-treated group revealed more or less normal structures in the glomeruli (G). In addition, the proximal tubules (TP) appear normal. Simultaneously, a number of alterations were observed in the distal tubules (DTs), which appear lined by cellswith vacuolated cytoplasm and the nuclei (N) in the proximal tubules appeared in contact with no changes. In addition, blood vessels appeared with blood inside (Figure 26 and 27).

(Figure 13-27)

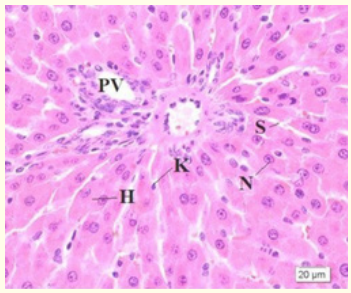

Figure 13: Section of the liver in the control group (GI) showing hepatocytes (H) appeared normal with rounded nuclei (N) hepatocytes arranged in cords which are separated by liver sinusoids (S), also seen branch of the portal vein (PV) in the portal area. Notice also normal Kupffer cells (K), (H & E stain X = 600).

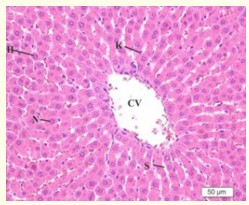

Figure 14: Liver section in Garlic extract group (GII) showing the central vein (CV) with some congestion and normal Kupffer cells (K). Also, the normal arrangement of hepatocytes in cords (H) with rounded nuclei is found in the middle of the cytoplasm (N). In addition, blood sinusoids appeared between hepatic cords (S), (H & E stain X = 400).

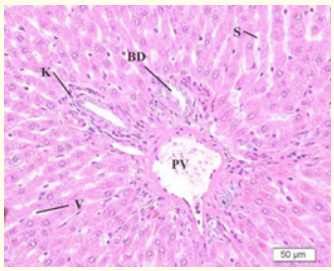

Figure 15: Liver section in Garlic extract group (GII) showing a normal arrangement of hepatocytes rounded nuclei. Notice cytoplasmic vacuolation (V). Also, appeared blood sinusoids between hepatic cords (S), branch of the portal vein (PV), branch of the bile duct (BD), and Kupffer cells (K) and showed marked dilated blood sinusoids, (H & E stain X = 400).

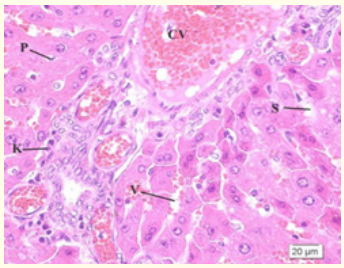

Figure 16: Liver section in cadmium group (GIII) showing the blood sinusoids between hepatic cords (S) and Kupffer cells (K). Also, it appeared the central vein (CV) was congested and hemorrhagic changes, some hepatocytes with cytoplasmic vacuolation (V), apoptotic changes, and nuclear pyknosis (P), (H & E stain X = 600).

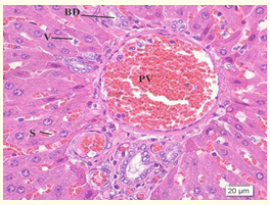

Figure 17: Liver section in cadmium group (GIII) showing portal vein (PV) fil Also, it appeared the portal vein (PV) was congested and hemorrhagic changes. The hepatocytes appeared with cytoplasmic vacuolation (V), depicting distortion of architecture with poorly defined hepatocytes. Also appeared a branch of the bile duct (BD), blood sinusoids between hepatic cords (S), and some hepatocytes showed apoptotic changes in nuclear pyknosis, (H & E stain X = 600).

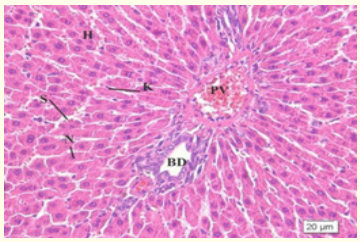

Figure 18: Liver section in a group of Garlic extract + cadmium group (GIV) showing hepatic cords and hepatic cells (H), with rounded centrally located nuclei (N). Also, Kupffer cells (K) and blood sinusoids (S) are clear. Also appeared normal the portal vein (PV) and branch of the bile duct (BD), (H & E stain X = 400).

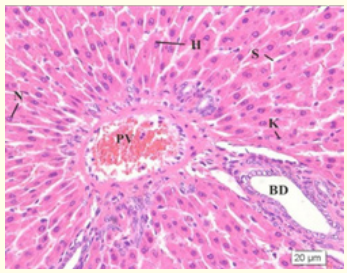

Figure 19: Liver section in a group of Garlic extract + cadmium (GIV) showing the normal structure of the liver tissues. The hepatocytes (H) appeared with rounded centrally located nuclei (N). Kupffer cells (K) and sinusoids (S) are clear. The branch of the portal vein (PV) appeared with some blood inside and an extension of the bile duct (BD), (H & E stain X = 400).

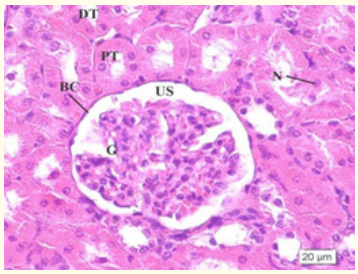

Figure 20: Kidney section of rat from the control group (GI) showing the normal structure of the cortex with renal corpuscles (glomerulus) (G) inside the Bowman's capsule (BC). Also, the urinary space (US), proximal, and distal convoluted tubules appeared normal with normal nuclei (N), (H & E stain X = 400).

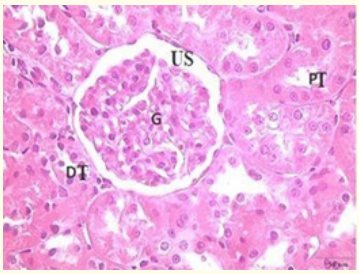

Figure 21: Kidney section of rat from the control group (GI) showing normal proximal (PT) and distal (DT) convoluted tubules, which appeared with normal nuclei. Also, the cortex with renal corpuscles (glomerulus) (G) inside the Bowman's capsule (BC) and the urinary space (US) appeared normal (H & E stain X = 400).

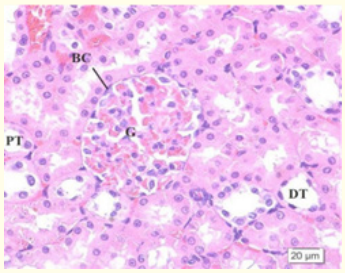

Figure 22: Kidney section of rat from Garlic extract group (GII). From the section, notice the appearance of the cortex with renal corpuscles (glomerulus) (G) inside the Bowman's capsule (BC). Also, the proximal (PT) and distal (DT) convoluted tubules appeared normal, (H & E stain X = 400).

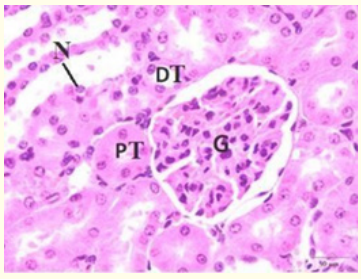

Figure 23: Kidney section of rat from Garlic extract group (GII) showing a normal pattern of renal architecture. The glomerulus (G), proximal (PT), and distal (DT) convoluted tubules appeared normal with normal nuclei (N), (H & E stain X = 600).

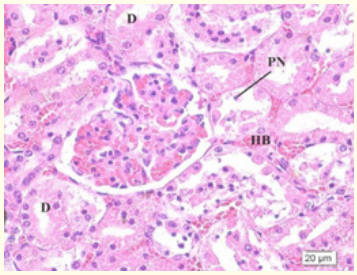

Figure 24: Kidney section of rat from cadmium treated group (GIII) showing aggregations of hemolytic blood cells (HB). In between the tubules appeared some damaged cells (D) and nuclear pyknosis (PN), (H & E stain X = 400).

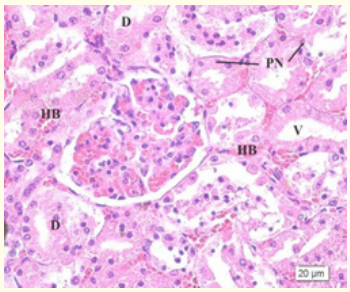

Figure 25: Kidney section of rat from cadmium treated group (GIII) showing cytoplasmic vacuolation (V). Also noted hemolytic blood cells (HB) in between the tubules. Some damaged cells (D) and pyknotic nuclei (PN) appeared in the section (H & E stain X = 400).

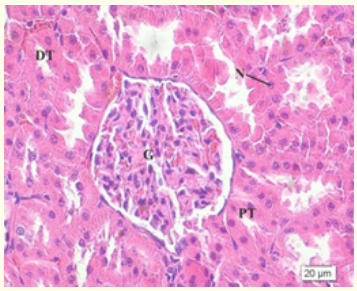

Figure 26: Kidney section from rats of Garlic extract + cadmium treated group (GIV). The section showed the approximately normal structure of the kidney. Note the presence of normal glomeruli (G), proximal convoluted tubules (PT), and some affected distal convoluted tubules (DT), and also normal intact nuclei (N), (H & E stain X =400).

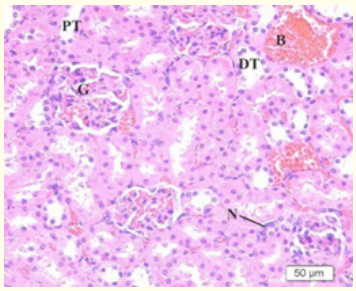

Figure 27: Kidney section from rats of Garlic extract + cadmium treated group (GIV). The section illustrated the approximately normal structure of the kidney. Note the presence of normal glomeruli (G), proximal convoluted tubules (PT), blood vessels filled with blood (B). The distal convoluted tubules (DT) and also nuclei (N) appeared normal (H & E stain X = 400).

Discussion

The purpose of the present study was to find out the protective values of using Garlic extract to protect the rats against hepatorenal toxicity of cadmium. Cadmium toxicity is linked to a number of clinical consequences, including hepatic and renal dysfunction [24]. Cadmium exposure can cause acute and/or chronic tissue damage [25]. Cadmium toxicity can affect human health through repeated exposure to low doses over long periods of time. The use of a whole plant or a portion of a plant as herbal cure, such as *Ginkgo biloba* echinacea, peppermint oil, and garlic was increased [26]. Garlic is considered to possess preventive and therapeutic characteristics for a number of ailments, including hypertension and diabetes [27,28].

In the present study, weight gain and percentage changes in body weight were significantly decreased in Cd group and Garlic + Cd group ($P < 0.05$) versus control and Garlic groups. Percentage changes in body weight were significantly decreased in Cd group and Garlic + Cd group versus control and Garlic groups. These results were consistent with previousstudies of rats [29] and chicken [30]. The cadmium reduction in body weight was reversed using Garlic, although the effect did not return to control. The use of antioxidants prevented cadmium from causing body weight loss in chickens. The reversal of body weight by Garlic supplementation may be due to its antioxidant properties [30].

The present study results are in accordance with those of Al-Baqami and Hamza [31] who studied the protective effect of resveratrol which is considered an important polyphenol and is a secondary plant metabolite against hepatotoxicity of cadmium in male rats. Their results indicated that Cd increased liver enzymes AST, ALT, ALP and γ-GT, while reducing the total protein level, they added that resveratrol played a major role in alleviating histopathological injuries and hepatic oxidative damage due to its antioxidant content which has the ability to minimize the hepatotoxicity induced by Cd in male rats.

Same results were noted by Rao., *et al*. [32] who postulated that after continuous exposure to cadmium, its bioaccumulation is well-known to be dangerous for the health of human and animals. Cadmium exposure significantly increased the levels of serum AST, ALT, ALP, bilirubin and glucose along with higher level of MDA in kidney, liver and intestine of rats. They found significant lower levels of these parameters after administration of quercetin and curcumin in combination as compared to individual treatment. Also, they added that, various histological changes following exposure to cadmium were noticed in the architecture of kidney, liver intestine of rats were improved when administered quercetin and curcumin and their combination.

A study was made to investigate the effect of different doses of cadmium on some biochemical, hormonal and histopathological parameters of the liver, kidney and testes of rats. Cadmium decreased serum levels of alkaline phosphatase (ALP) while increased serum concentration of the acid and prostatic acid phosphatases (ACP). Cadmium also caused positively destruction of the histology of the liver, kidney and testes, which were characterized by vascular congestion, vacuolation, destruction of the seminal epithelial layers, focal necrosis of nucleus, oedema of the seminal epithelia layers, focal necrosis of nucleus, oedema of the seminiferous tubules and reduction of spermatogenesis. CD also caused granular and eosinophilic cytoplasm, enlargement of sinusoids with Kupffer cells, hemorrhage, and apoptosis of cells. Finally, pre-treatment with the antioxidants; vitamin C, vitamin E and selenium, which caused a reversal of the cadmium-induced biochemical, hormonal and histological toxicities of the liver, kidney and testes. These results may be explained by the properties of oxidation/antioxidation of these xenobiotics and their mechanisms of actions [33].

In the present study, histological observations of the livers of the cadmium group (GIII) showed some changes in hepatocytes, such as cytoplasmic vacuolization by pyknotic nuclei. Some hepatocytes showed degeneration and necrosis, and there were chromatin masses in the nuclear membrane. These findings come in accordance with those of Mantur., *et al*. [9] who found that in the liver, cadmium showed changes in normal architecture, swollen hepatocytes, Kupffer cells hyperplasia, dilation, and congestion of central vein. Also, the central vein appeared engorged with blood. Cadmium is transported to the liver; in which way it can cause damage and disturbed function. The liver is the next most vital organ to be affected by cadmium poisoning after the kidney. Increased lipid peroxidation and alterations in critical components were seen after prolonged cadmium exposure of the liver.

As a result of cadmium poisoning, different pathologic alterations in hepatocytes were seen, including nodular hyperplasia, apoptosis, cellular proliferation, granulomatous inflammation and necrosis. Liver damage can be confirmed by histopathological findings and is often accompanied by elevated blood liver enzyme levels [34]. After examining the liver sections in the garlic + cadmium group it was found that hepatocytes appeared somewhat normal. The hepatic cords appeared normal with rounded nuclei in the center of its cytoplasm. Also, the Kupffer cells and sinusoids were clear with darkly stained nuclei. These findings are in agreement with the findings documented by Yildirim., *et al.* [35].

It was reported that the main nephrotoxic effect of cadmium is to enhance low molecular weight proteinuria [36]. Most of the filtered cadmium (70%) is absorbed in the proximal tubules and concentrated in the cerebral cortex, leading to kidney damage [37] and reducing the likelihood of tubular damage [38]. The damage of the kidney led to elevated levels of serum urea and creatinine. Similarly, elevated albumin excretion supports the hypothesis that cadmium exposure caused renal proximal tubule dysregulation, preventing albumin reabsorption of glomerular-filtered albumin [39]. From the present study results it could be concluded that histological changes in kidneys were due to cadmium intoxication that caused tissue damage via gradual tubular destruction [40].

In cadmium treated group (GIII), in the present study, the values of creatinine (CRE), urea (URE) and uric acid (UA) were significantly increased when compared with the control group GI. When using Garlic + cadmium (GIV), the mean values for CRE, URE and UA were significantly decreased compared with the cadmium group GIII. These results come in agreement with those of Gulnaz., *et al*. [41] who postulated that serum urea and creatinine were increased due to administration of acetaminophen induced nephrotoxicity and causes damage to kidney architecture. They added that garlic restored the levels of urea and creatinine to approximately their normal levels.

Cadmium deposition primarily occurs in the kidney proximal tubules, leading to tissue damage by inhibiting glucose, bicarbonate, protein, amino acids, and phosphate reabsorption in proximal tubules. It caused oxidative stress in transport proteins and mitochondria in tubular cells, resulting in apoptosis [42]. In this illness, intense pain is caused by renal tubular failure, calcium absorption problems, anemia, and osteomalacia [43]. The present study showed that, one of the frequently affected organs by cadmium poisoning is the kidney as cadmium can accumulate in the kidneys and cause serious kidney damage. Microscopic examination of the kidneys of cadmium-treated rats (group GIII) revealed the development of cellular damage of some nuclei and hemolytic blood cell aggregation between the tubules. Also, some blood cells were leaking from the blood vessels [44]. Cytoplasmic vacuolization, cessation of some vessels, and tubular dressings were noted. In some tubules, expanded cells with cytoplasmic vacuoles were observed, and there were also necrotic cells with pyknotic nuclei. Kidney sections from the garlic + cadmium (GIV) group showed approximately normal glomerular and proximal tubular structures. However, there were some changes in the distal tubule lined with cells with vacuolar cytoplasm. Toxic effectson the kidneys are indicated by alterations in excretory function and structural damage to the kidneys [34].

The results of the present work showed significant elevation in serum levels of triglyceride (TG), total cholesterol (CHOL), low-density lipoprotein cholesterol (LDL-c) and very low-density lipoprotein cholesterol (VLDL-c), but considerable decrease of high-density lipoprotein cholesterol (HDL-c) in cadmium group versus control and garlic + cadmium groups. Administration of garlic with cadmium group GIV improved dyslipidemia observed in the group treated with cadmium only GIII. Other studies showed similar elevations in serum levels of TG, CHOL and LDL-c after high dose administration of cadmium to rats. Liver disorders resulting from exposure to cadmium decreased HDL-c content and caused dyslipidemia [45].

The results of the present work showed that the hepatic and renal protection by garlic against Cd-induced toxicity was evident, particularly when administered in combination with Cd. The alterations in the serum levels of ALT, AST, ALP, urea and creatinine, besides the creatinine- clearance levels in urine induced by Cd were close to the normal values by the garlic extract administration, especially in group IV. The lowered trend in liver and renal functional parameters implicated that garlic alleviated the hepatic and renal damage. Similar results were reported by many researchers [46].

It was postulated that kidney tubular damage along with bone damage are known to occur due to cadmium toxicity, either via a direct effect on bone tissue or indirectly as a result of renal dysfunction. *Moringa oleifera* was administered to animals which is a well-known medicinal plant for the treatment of a wide variety of conditions. In cadmium exposed adult Wistar Albino rats, pretreatment with aqueous leaf extract has been found to play a protective role. The leaves of this plant have antioxidant properties which facilitates it to combat cadmium induced toxicity on kidneys, liver, blood, testis and also on lipid profile, like HDL-c, LDL-c and VLDL-c levels. These findings are consistent with the present study results, in which garlic showed antioxidant properties which prevented cadmium toxicity [47].

Conclusion

The present study results showed that Cd intoxication resulted in several structural changes in the liver and kidneys, where the hepatic cells suffered vacuolar and hydropic degenerations, fatty change and coagulative necrosis. The renal tubular epithelium showed hyaline droplet formation, cloudy swelling and coagulative necrosis. Moreover, leukocytic infiltration and multiple hemorrhagic foci were frequently observed in the liver and kidneys [48]. Also, the histopathological results in the present work are coincided with the findings of many investigators [48-50], where they concluded that hepatic coagulative necrosis was absent and the congestions, sinusoidal widening and leukocytic infiltrations were markedly reduced. The kidneys showed few swollen glomeruli and proliferation of the mesangial cells with minimal mononuclear cells in the interstitial tissue.

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