Study the adverse role of histological and oxidative effects of ginger (Zingiberaceae) and cadmium chloride in liver tissue of rabbits

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Abstract:

In this study, was investigate the ability of Ginger to adversely histological and physiology effect of cadmium in the liver tissue of rabbit, Ginger is source of antioxidants was administered orally to prevent the adverse effects of cadmium (cd). Twenty four male rabbits were randomized into 3 groups (n = 8), were used for this study. Animals in group (1) served as the control and were drinking distilled water. Animals in groups (2) were drinking2% cadmium chloride. Group (3) animals were, in addition to drinking cadmium, treated with 250 mg/kg of ginger. All treatments were for 12 weeks.

The results showed that cadmium caused a significant ($p<0.05$) reduction in plasma superoxide dismutase and catalase activity, but a significant increase ($p<0.05$) in plasma malondialdehyde concentration with histological changes in liver cell such as necrosis, hemorrhage with aggregation of some toxic spot as (black spot),protein cast with epithelial cell in group 3 comparison with control and other group , using ginger cause to modified these harmful effects. These findings lead to the conclusion that ginger significantly decreased ($p<0.05$) the adverse toxic harmful effects of cadmium exposure on the liver as oxidative stress.

دراسة الدور النسيجي والتأكسدي السلبي لنبات (الجرجير) وكلوريد الكادميوم في نسيج الكبد للأرانب

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الخلاصة:

في هذه الدراسة تم بحث قدرة نبات الجرجير السلبية للتأثيرات الفسلجية والنسيجية للكادميوم في نسيج الكبد في الأرانب .ونبات الجرجير مصدر لمضادات التأكسد التي تعطى فمويا والتي تعكس فعل للكادميوم.ثمانية عشر أرنبا استخدمت في هذه الدراسة وقسمت عشوائيا إلى ثلاث مجاميع 6 لكل مجموعة الحيوانات، المجموعة الأولى أبقيت كمجوعة سيطرة وأعطيت ماء الشرب الاعتيادي دون أية معاملة ولمجموعة الثانية أعطيت كلوريد الكادميوم بنسبة 2% في الماء والمجموعة الثالثة أعطيت نبات الجرجير بجرعة 250 ملغم/كغم مع كلوريد الكادميوم يوميا ولمدة 12 أسبوع .

أشارت النتائج إلى إن الكادميوم سبب وجود انخفاض معنوي 5%في إنزيم السوبر اوكسيد

دسميوتيزوالكاتيلز وزيادة معنوية في تركيز إنزيم ميلون–دي الديهايد وحدوث تغيرات نسيجه كالتنخر والنزف مع تجمع المادة السامة بشكل بقع سوداء وتجمع مادة بروتينية مع خلايا ظهارية في بعض خلايا الكبد في المجموعة الثانية مقارنة مع مجموعة السيطرة والمجموعة الثالثة، كما أن استخدام الجرجير سبب تغيرات في معظم التاثيرات المؤذية للكادميوم وسبب انخفاض معنوي على مستوى 5% في أنزيمات التأكسد وبالتالي يعمل عمل مضاد ضد الإجهاد التاكسدي للكادميوم .

Introduction:

Cadmium is risk trace metal and harmful effects in with chronic toxic in small amounts. Nevertheless, humans get exposed to cd through their environment and diet [1,2]. The manifestations of cd poisoning in humans are non specific, They may include weight loss, anemia, vomiting, headache [3,4] nephropathy, infertility, liver (severe protein cast with dilatation in portal vein with toxic material as a black spots in liver cells, testis (testicular necrosis)heart changes (necrosis of muscle fibers) [5].

Zingiber officinale R., family: Zingiberaceae. (Ginger), and its constituents are stated to have anti-emetic,antithrombotic[6],antihepatotoxic[7],anti-inflammatory[8]stimulant of one unpaired electron such as a superoxide ion (O^{2-}), nitrogen oxide (NO) and hydroxyl radical (OH^{-})[9]. Even though naturally present in the organism, they are mainly confined to cell compartments and counterbalanced by natural antioxidant molecules, such as glutathione,glutathione peroxidase, superoxide dismutase[10], vitamin E and vitamin C, acting as free radical scavengers [11]. Ginger extracts have been extensively studied for a broad range of biological activities, especially antioxidant activities [12,13] found that ginger significantly lowered lipid per oxidation by maintaining the activities of the antioxidant enzymes such as super oxide dismutase, catalase and glutathione peroxides in rabbits. This research focuses on whether oral administration of ginger prevents cadmium induced liver oxidative stress.

Materials and Methods:

Twenty four male rabbits (900-1kg) were used for this study. They were obtained from animal market of diwaniya were housed in temperature controlled rooms (27°C) with constant humidity (50%) and12/12 h light/ dark cycle prior to use in experimental protocols.

All animals were treated in accordance to the principles of laboratory animal care. All rabbits were fed a standard diet and water. The daily intake of animal water was monitored at least 3 days prior to start of treatments in order to determine the amount of water needed per experimental animal.

Grouping of animals:

The rabbits were grouped into 3 groups (groups 1, 2, and 3, n = 8). Animals in group 1 served as the control group and were drinking

distilled water. Animals in groups 2and 3 were drinking 2% cadmium chloride ,Group 3 animals were, in addition to drinking cadmium chloride treated with 250 mg/kg of ginger. All treatments were for 12 weeks.

Blood sample obtained from each rabbit was divided into 2: One half in a plain bottle and The other half in an ethylenediamminetetraacetic acid(EDTA) bottle Liver was excised from Each rabbit and fixed in % 10 formalin buffer and prepared for histological sections. The Samples were prepared for measurements of plasma super oxide dismutase (SOD), catalase (CAT) and malondialdehyde(MDA) were determined using the method described by [16].

Collection of samples:

Twelve weeks after the last treatment, each animal was sacrificed and blood samples were Collected via heart puncture.

Statistical analysis:

Livers from each rabbit were homogenized for tissue superoxide dismutase (SOD), Catalase (CAT) and malondialdehyde (MDA) were determined using the method described By [11]compared using ANOVA test. $P < 0.05$ was considered as statistically significant.

Results:

Table 1. Showed result of plasma SOD, CAT, MDA, hepatocytes in whole Control and experimental groups.

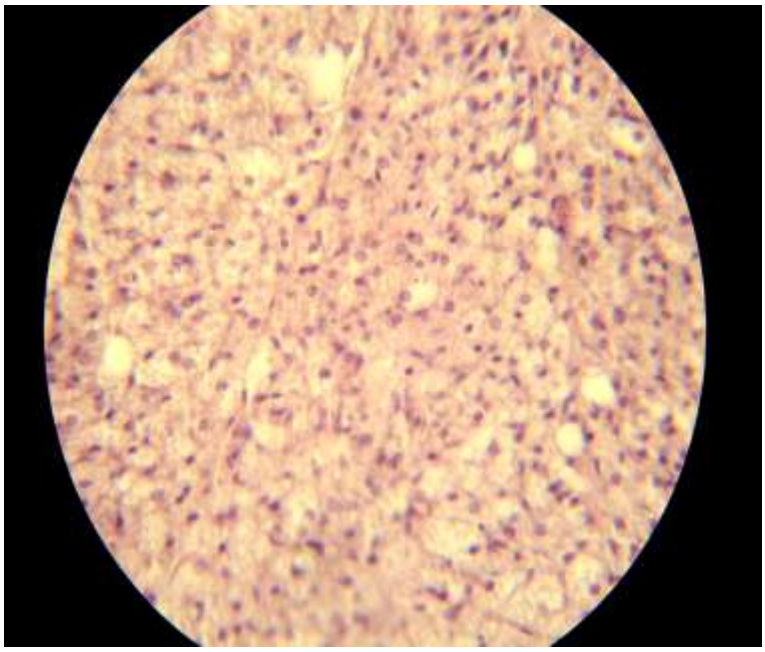
Data were presented as mean ± S E. *Significant different at $p< 0.05$ level

Groups n=8	Control	Cadmium chloride 0.02mg/kg	Cadmium chloride + ginger(250mg/kg)
Plasma SOD mmol/l	1.623±0.06	0.454±0.03	0.29 ±0.02
Plasma mmol/l CAT	1.233±0.05*	0.500±0.03*	2.4±0.07*
Plasma MDA	$1.576_{\pm}0.02$*	$1.992_{\pm}$ 0.05	2.332±0.04*

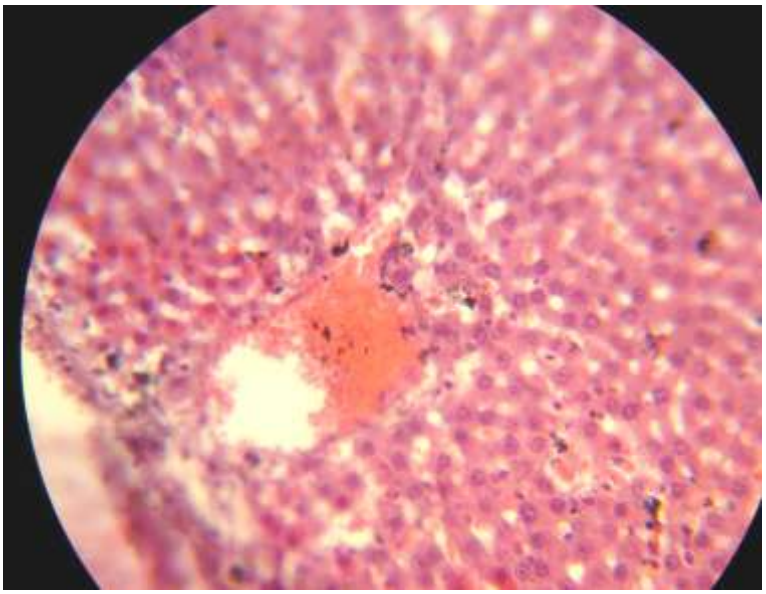
Group 2 showed a significant decrease in plasma SOD activity. Group 3 was, however, not significantly ($P> 0.05$) different from the control in terms of the plasma SOD activity (Table

1),Plasma CAT Group 2 showed a significant decrease in the plasma CAT activity, whereas group 3,showed no significant difference in the CAT activity from the control(p< 0.05) (Table 1) ,Plasma MDA concentration Group 2 showed a significant increase in the plasma MDA concentration, while group 3 showed no significant difference in the MDA activity from the control (P> 0.05), the plasma MDA Group 3 showed no significant (P > 0.05) difference from the control (Table 1).

Histological changes :



figure(1)control group normal liver



Figure(2) group (2) show severe protein cast with dilatation in portal vein with toxic material as a black spots in liver cells. (A)H&E,(40×)

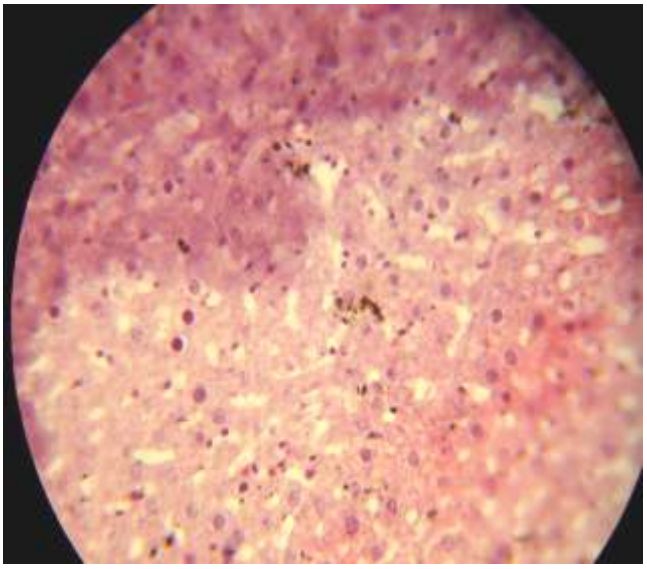
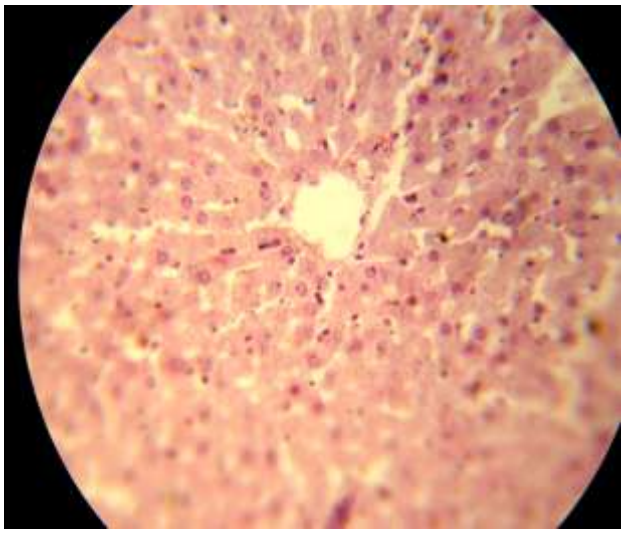


Figure (3) group(2)show toxically black spots distribution in liver tissue(A)H&E, (10×).



Figure(5)group(2) show distention in the portal vein with some hemorrhage near that.(A&E) (10×).

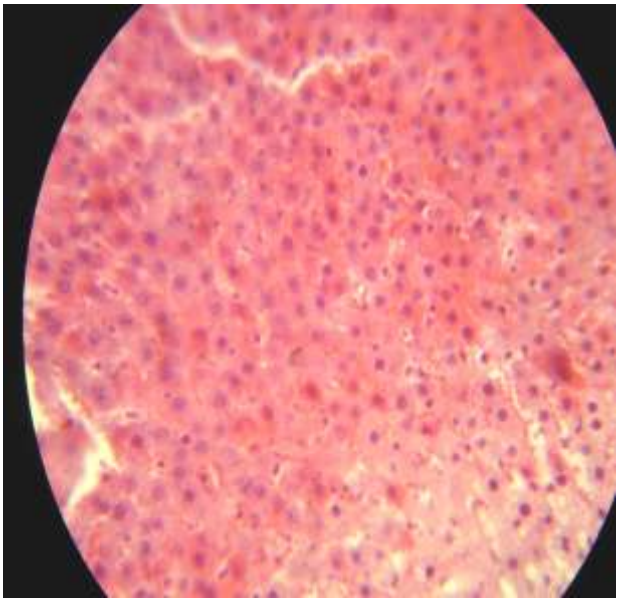


Figure (4)group (3)show no changes can be detection in structural of liver tissue in rabbits(A&H) (10×).

Discussion:

Cadmium turn prevent or reduced lipid peroxidation & tissue injury or damaged that may be induced by oxidative trauma/stress. the oxidative effects of cadmium are mediated through the activation of proteinkinase C(pkc) during single transduction, PKC activity is interns dependent on cytosolic calcium ion concentration induced oxidative stress[12.13,14), in blood and other soft tissues has been postulated to be one of the possible mechanisms of cd[15.16.)Disruption of pro-oxidant/anti oxidant balance might lead to the tissue injury. It was reported that (cd) increased the level of lipid peroxidation [17.18) and brain thiobarbituric acid-reactive substances and altered the antioxidant defense system [19]. Similar effects were also reported in the hepatic tissues [20.21].

A number of recent studies confirmed the possible involvement of reactive oxygen species (ROS) in cd-induced toxicity [22] Several antioxidant enzymes and molecules have been used to evaluate cd-induced oxidative damage in animal and human studies. Reduced glutathione concentrations, as well as modifications in superoxide dismutase (SOD) activity are the most frequently used markers in(GSH) and glutathione disulfide (GSSG) tissues or in blood [23]. Based on the observation that free radical was generated during the pathogenesis processes induced by cd exposure, it was similar some time to lead presumed that supplementation of antioxidants could be an alternative method for chelation therapy [24]. Specifically, ascorbic acid, the known chelating agent with antioxidant features, was widely reported with the capability of protecting cells from oxidative stress [25]. More importantly, due to the presence of health-protective antioxidants such as lycopene, vitamin C, and vitamin A in TP [26] despite its relatively low caloric value (21 kcal/100 g) and low protein content (0.85% by weight) [27]. There was no significant ($P > 0.05$) difference in the SOD activity of *the plasma of the control and that of the animals treated with tomato along with cd. But, there was a significant ($P < 0.05$) decrease in the plasma SOD activity in animals treated with cd only compared with the control. This finding is in agreement with [28]. There was a significant ($P <0.05$) decrease in plasma CAT activity of animals treated with cd only relative to the control. There was, however no significant difference ($P > 0.05$) between the control and the animals treated with ginger along with cd in this respect.

This further establishes that ginger must have reduced the oxidative stress that cd could cause. Finally, there was no significant ($P > 0.05$) difference in both the plasma and the tissue MDA concentration of the control and those of the animals

treated with ginger along with cd, whereas animals treated with cd only showed a significant ($P < 0.05$) increase in plasma MDA concentration. This confirms that it was ginger, the source of antioxidants, [29] that reduced the oxidative stress that cd exposure could have caused in the ginger - treated animals. Free radical-induced oxidative damage has been implicated in the pathogenesis of a number of injury and disease states. The, necrosis or injury of cells led to the free radical attack of membrane phospholipids and handrail membrane potential, which caused the inter membrane proteins, such as cytochrome c, to be released out of the mitochondria and ultimately triggered caspase-3 activation. Caspase-3 activation led to DNA breakage, nuclear chromatin condensation and cell apoptosis [30].

The histological changes in liver cells occurs due to powerful harm oxidative stress effect of cadmium chloride. [31,32].

In summary, ginger can decreased the damage to liver cells from oxidative damage induces by cadmium, and it is dependent on their antioxidant effects.

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