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ORIGINAL ARTICLE

Role of +(–)catechin against cadmium toxicity in the rat testes

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Abstract

Objective. Cadmium (Cd) is one of the most toxic and carcinogenic heavy metals to organisms. Exposure to the metal occurs mainly through environmental pollution and its wide range of uses in industrial fields. Cadmium performs its effect on living organisms by accumulating in various tissues and affecting tissue antioxidant enzyme systems. The testes are critical target organs following cadmium exposure. This study aimed to determine the possible effects of cadmium on zinc concentration and the role of +(–)catechin against the toxic effects of cadmium in rat testis tissue. *Material and methods.* Wistar albino rats were divided into three groups: control, cadmium and cadmium + catechin-receiving groups. The experimental groups received cadmium chloride and +(–)catechin via their drinking water for 30 days. Cadmium and zinc concentrations were measured in testis tissue of rats. Lipid peroxidation measurements were also taken in the tissue. *Results.* Accumulation of cadmium was observed in testis tissue during the experimental period. Increased lipid peroxidation was observed in the tissues of the cadmium and cadmium + catechin groups. The cadmium and zinc concentrations in the +(–)catechin group were not found significant differences with controls. *Conclusion.* The data suggest that lipid peroxidation was associated with cadmium toxicity in testes and +(–)catechin does not seem to be helpful against cadmium toxicity.

Key Words: *Cadmium, catechin, rat, testis, zinc.*

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 [1,2]. Cadmium can cause a number of lesions in many organs, such as the liver, kidney and testis [3–5].

The reproductive toxicity of cadmium as an industrial pollutant, a food contaminant and in its contribution from cigarette smoke is well established. The testis is known to be one the important targets of cadmium. Many studies indicate that cadmium induces testicular damage in many species of animals. It has been suggested that reactive oxygen species (ROS) are involved in cadmium-induced testicular damage [4,6–8]. Certain ions such as cadmium, cobalt and lead are powerful promoters of free radicals. Free radical damage to phospholipids is an important factor in the development of toxic conditions. Lipid peroxidation, which is an exceedingly damaging process, has been known to occur via peroxidation of unsaturated fatty acids in all aerobic biological systems. Lipid peroxidation has been considered a primary initiating mechanism during cadmium injury [3,9,10]. Recently, increasing consideration has been given to interactions occurring in the organism between toxic metals and bioelements essential for life. These interactions are complex and involve biometals such as zinc (Zn), copper (Cu), selenium (Se) and toxic elements, including cadmium [1]. Zinc is a trace element essential for living organisms and an essential component of the oxidant defence system and functions at many levels. Zinc is relatively non-toxic and plays a very important role in human metabolism. Several study has shown that zinc deficiency in the diet paves the way for cell damage in the rat testis [2,6,11–13].

Various natural and synthetic substances possessing antioxidant properties should be investigated as to their possible protective effects on cadmium-induced tissue damage [3]. Antioxidant therapy

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could be important in the treatment of cadmium poisoning. Concomitantly, the interrelationships between cadmium and essential nutrients have been investigated [14]. Toxic effects of cadmium exposure, such as testicular damage, can be prevented by the administration of green tea catechin [15]. The catechin in green tea is a polyphenol-type chemical that is highly available in this tea. Green tea catechin, among other natural substances, is known for its various pharmacological actions, such as decreasing blood cholesterol, antioxidation, metal chelation, enzyme inhibition and the possibility of inhibiting platelet coagulation. The green tea beverage promotes detoxification activity by inhibiting the body's absorption of heavy metals and promoting their excretion. This substance binds with the metal ions to form an insoluble complex with ionic salts to remove the heavy metals [15–17].

This study examined the levels of cadmium, zinc and lipid peroxidation that are considered to be involved in testicular tissue damage caused by cadmium exposure. The expression of +(–)catechin in testicular tissues induced by cadmium exposure was also examined.

Material and methods

Adult Wistar albino male rats, weighing 200–250 g (purchased from the Cerrahpasa Medical Faculty, Istanbul University), were randomly divided into the following groups: control ($n=8$), cadmium-exposed rats ($n=8$) and coexposed rats (cadmium + catechin) ($n=8$). The animals were kept in stainless-steel mesh cages, housed under controlled conditions (22 ± 2°C, 12:12 h light:dark cycle) with a rat diet ad libitum.

The control group was administered drinking water. The cadmium group received cadmium chloride solution in drinking water (120 mg/l). The cadmium + catechin group also received +(–) catechin solution in drinking water (0.02 g/100 ml).

The control and treated groups were euthanized, all of the testis tissues were washed with cold saline solution and the tissue weights were obtained. The tissues were cut into small pieces and placed into glass bottles. They were then homogenized in ice-cold Tris–HCl buffer solution in a homogenizer.

Tissue cadmium and zinc levels were measured by a hollow cathode lamp, which emits light at a special wavelength for cadmium and zinc in the atomic absorption spectrophotometer (Shimadzu AA-680, Kyoto, Japan) [18]. Testicular tissue malondialdehyde (MDA) levels were analysed by a method based on the reaction with thiobarbituric acid. In the thiobarbituric acid test reaction, MDA or MDA-like substances and thiobarbituric acid react together to produce a pink pigment with an absorption maximum of 532 nm [19].

The experimental design was approved by the committee for the care and use of laboratory animals of the Cerrahpasa Medical Faculty, Istanbul University.

Statistical analysis

The Mann–Whitney U test was used to compare the groups, and $p<0.05$ was accepted as statistically significant. The values were presented as means ± standard deviation (SD).

Results

The zinc level decreased in the testis tissue of the cadmium group (19.65 ± 1.80 μg/g) and the cadmium + catechin group (21.10 ± 1.77 μg/g) compared with values obtained in the control group (28.09 ± 1.14 μg/g) (both $p<0.05$) (Table I). In the cadmium (0.58 ± 0.08 μg/g) and cadmium + catechin (0.60 ± 0.12 μg/g) groups tissue cadmium levels were significantly increased compared with the control group (0.22 ± 0.10 μg/g) (both $p<0.01$) (Table I). No significant differences were observed in the testis weight among any of the studied groups. A significant increase in lipid peroxidation level was observed in the cadmium group ($p<0.01$) and cadmium + catechin group ($p<0.01$) compared with values obtained in controls (Table II).

Discussion

Cadmium is a toxic metal, which promotes oxidative stress and contributes to the development of serious degenerative changing in several tissues. The effects of cadmium have been shown to be due to oxidative damage by enhancing the peroxidation of membrane lipids in different tissues. It has been suggested that cadmium has pro-oxidant catalytic activity and can initiate membrane peroxidation by generating free radicals and thereby interfering with the antioxidant system in tissues [10]. It is well known that the testis is very sensitive to cadmium toxicity. Cadmium is known to influence the oxidative status by depleting

Table I. Levels of cadmium (Cd) and zinc in the testis tissue of control and experimental groups of rats.

Groups	Cadmium (μg/g)	Zinc (μg/g)
Control	0.22 ± 0.10	28.09 ± 1.14
Cd	0.58 ± 0.08**	19.65 ± 1.80*
Cd + catechin	0.60 ± 0.12**	21.10 ± 1.77*

Significantly different from control group: **$p<0.01$, *$p<0.05$.

Table II. Levels of malondialdehyde (MDA) in the testis tissue of control and experimental groups of rats.

Groups	MDA (nmol/g)	Testis weight (g)
Control	21.80±0.40	0.61±0.10
Cd	29.6±0.58*	0.53±0.14
Cd+catechin	31.0±1.05*	0.56±0.04

Cd = cadmium.
Significantly different from control group: $^{**}p<0.01$, $^{*}p<0.05$.

protein-bound sulfhydryl groups, resulting in increased lipid peroxidation [7,20]. In the present study, cadmium-exposed testes tissues showed a significant increase in lipid peroxidation levels. This result is agreement with various reports demonstrating that cadmium induces oxidative stress by increasing lipid peroxidation [9].

The basis of cadmium toxicity is its negative influence on the enzymic systems of cells, resulting from substitution of other metal ions (mainly Zn^{2+}, Cu^{2+} and Ca^{2+}) in metalloenzymes and its very strong affinity to biological structures containing sulfhydryl (-SH) groups, such as proteins, enzymes and nucleic acids [1,21]. Many of the effects of cadmium action result from interactions with necessary microelements and macroelements, especially calcium, zinc, copper, iron and selenium. These interactions can take place at different stages of the absorption, distribution and excretion of the bioelements and cadmium, as well as at the stage of biological functions of essential elements [1,22]. Cadmium acts as a competitive inhibitor of zinc and produces malignant tumours in animals. Thus, partial or total inhibition of regulatory zinc-dependent enzymes is one possible mechanism for the carcinogenicity of cadmium [5]. In this study, cadmium exposure and concurrent treatment with cadmium and +(–)catechin decreased the testes zinc concentration. Zinc is relatively non-toxic and plays a very important role in human metabolism. Studies on the reciprocal effects of cadmium and zinc suggest that zinc prevents the degenerative effect of cadmium and that this process is a complex one [2,23]. It was reported that the testis could be protected from the toxic effects of cadmium, mainly by antioxidant treatment [3].

It is very difficult to find any in vivo studies on pure catechin extracts and their detoxification effects or mechanisms regarding metabolic disorders caused by cadmium. In addition, both cadmium detoxification using physiologically active natural materials, such as green tea catechin, and the clinical symptoms of circulation disorders due to cadmium intoxication have been insufficiently researched [15]. Green tea catechins have been found to be efficient scavengers of free radicals in a number of in vitro system, but the exact mechanisms for this radical scavenging activity are not known. The ability of a compound to act as a free radical scavenger is partly related to its one-electron reduction potential, a measure of the reactivity of antioxidants as hydrogen or electron donors. The ability of flavonoids in general, and catechins in particular, to chelate metal ions, such as iron and copper, may contribute to their antioxidant activity by inhibiting transition metal-catalysed free radical formation. However, it is not clear whether metal chelation is a physiologically relevant antioxidant activity, because most metal ions are bound to proteins in vivo where they cannot participate in metal-catalysed free radical formation [15,16]. The present findings indicate that administration of combined cadmium and +(–)catechin is ineffective on lipid peroxidation in cadmium-exposed rats. The interaction between cadmium and essential trace elements could be one of the reasons for increased free radicals in the rat testes.

In conclusion, the results showed that the administration of cadmium increased the products of lipid peroxidation in testes. +(–)Catechin may not be very useful in protecting against cadmium-induced lipid peroxidation.

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