Saudi Journal of Biological Sciences (2016) 23, 667–673

King Saud University

Saudi Journal of Biological Sciences

www.ksu.edu.sa
www.sciencedirect.com

ORIGINAL ARTICLE

Antioxidant effects of captopril against lead acetate-induced hepatic and splenic tissue toxicity in Swiss albino mice

Badr A. Aldahmash [a,*], **Doaa M. El-Nagar** [b]

[a] *Zoology Department, College of Science, King Saud University, Riyadh, Saudi Arabia*
[b] *Zoology Department, College of Girls for Science, Arts and Education, Ain Shams University, Cairo, Egypt*

Received 24 August 2015; revised 2 May 2016; accepted 3 May 2016
Available online 11 May 2016

KEYWORDS

Captopril;
Mice;
Liver;
Spleen

Abstract Considering that lead caused a lot of health problems in the world, the present study was carried out to investigate the protective effect of captopril as antioxidants to reduce liver and spleen toxicity induced by lead. Animals were divided into 3 groups, the 1st group served as control group, the 2nd group received 20 mg/kg of lead acetate and the 3rd group received 50 mg/kg of captopril one hour prior to lead administration for 5 days. Results showed that lead intake caused severe alterations in the liver and spleen manifested by hepatocytes degeneration, leukocytic infiltration, fibrosis in liver and moderate to severe liver pathological score. Spleen showed ill-defined architecture, presence of large macrophages and lymphoid necrosis. Administration of captopril reduced hepatotoxicity, liver fibrosis and decrease in pathological scoring system. Moreover, reduced toxicity in spleen is represented by reduction in necrotic areas, more or less healthy lymphoid follicles and decreasing in pathological scoring system.

1. Introduction

Lead is a naturally occurring bluish-gray metal found in small amounts in the Earth's crust and can be found in all parts of our environment (Gupta, 2007). Lead is found in our food, water, air and soil. Lead emitted by smelters and boilers that burn used motor oil is frequently deposited in the soil, where it is taken up by crops (Chiras, 2009). Lead is known as an enzymatic toxicant, is neurotoxic, hemato and cardiovascular toxic, nephrotoxic, immunotoxic, carcinogenic, teratogenic and mutagenic (Kiran et al., 2009; Moreira and Moreira, 2004). Lead damages cellular materials, alters cellular genetics and produces oxidative damage. It causes hyperproduction of free radicals and decreased availability of anti oxidant reserves to respond to the resultant damage. It also interrupts enzyme activation and competitively inhibits trace mineral absorption. Lead binds to sulfhydryl proteins (interrupting structural protein synthesis), alters calcium homeostasis and lowers the levels

* Corresponding author at: Zoology Department, College of Science, King Saud University, P.O. Box: 2455, Riyadh 11451, Saudi Arabia.
E-mail address: dr_badr211@hotmail.com (B.A. Aldahmash).
Peer review under responsibility of King Saud University.

Production and hosting by Elsevier

http://dx.doi.org/10.1016/j.sjbs.2016.05.005
1319-562X

of available sulfhydryl antioxidant reserves in the body (Lynpatrick, 2006). The toxicity of lead is closely related to age, sex, route of exposure level of intake, solubility, metal oxidation state, retention percentage, duration of exposure, frequency of intake, absorption rate, mechanisms and efficiency of excretion. Lead has been associated with various forms of cancer, nephrotoxicity, central nervous system effects and cardiovascular diseases in humans (Pitot and Dragan, 1996).

Captopril (D-3-mercapto-2-methyl-propanoyl-L-proline) is an angiotension-converting enzyme (ACE) inhibitor. Besides, its role as a treatment for hypertension (Sultana et al., 2007), it is commonly used as a cardioprotective drug (Khattab et al., 2005). Like other ACE inhibitors, captopril inhibits the conversion of angiotensin I, a relatively inactive molecule, to angiotensin II which is the major mediator of vasoconstriction and volume expansion induced by the renin–angiotensin system. Captopril, an inhibitor of angiotensin converting enzyme (ACE), has also been postulated as a free radical scavenger because of its terminal sulfhydryl group (Bagchi et al., 1989; Andreoli, 1993). Some *in vitro* studies indicate that captopril functions as an antioxidant both by scavenging ROS and by increasing the activities of antioxidant enzymes such as superoxide dismutase and glutathione peroxidase (Westlin and Mullane, 1988; Kojsova et al., 2006). Captopril has been shown to decrease serum lipid peroxide concentrations in diabetic patients (Ha and Kim, 1992).

Therefore, the aim of the present work is to evaluate the possibility of reducing toxic effects induced by lead in the liver and spleen by captopril and investigate its antifibrotic effects.

2. Material and methods

2.1. Design of experiment

Thirty male Swiss albino mice (25 ± 3 g) Mice were housed in polypropylene cages inside a well-ventilated room at 22 ± 1 C and 12-h periods of light and dark, with free access to clean water and commercial mice food The experiments were approved by state authorities and followed Saudi Arabian rules for animal protection.

Mice were randomly divided into three groups, ten mice per each group. First group served as control group received saline, second group received oral administration of 20 mg/kg of lead acetate by gavage, and third received oral administration of 50 mg/kg of captopril one hour prior to administration of 20 mg/kg of lead acetate for five days, All animals were sacrificed one day-post to the end of experiment.

2.2. Liver and spleen index

At the end of the experimental period, each mouse was weighed, liver and spleen were then removed and weighed. Finally, the liver and spleen indices were calculated by dividing the weight of liver or spleen by the body weight and then multiplying by 100 and the results were statistically analyzed by SPSS 16.

2.3. Histopathological analysis

2.3.1. Histological preparation

Livers and spleens were collected and cut into small pieces, fixed in 10% neutral buffered formalin. Following fixation, specimens were dehydrated, embedded in wax, and then sectioned to 5 μm thickness. Sections were stained with hematoxylin and eosin. Also, other sections were stained with Masson trichrome stain according to Drury and Wallington (1980).

2.3.2. Pathological scoring system for changes in liver and spleen architecture

Liver sections stained with HE were examined for pathological score of the following criteria: ballooning, inflammation, apoptotic cells and fibrosis. Scoring values were registered according to Table 2. Spleen sections were examined for pathological score of the following criteria: lymphoid necrosis and red pulp expansion and scoring values registered according to Table 2 (Klopfleisch, 2013).

2.3.3. Spleen lymphoid follicle analysis

Lymphoid follicles areas were measured by microscope measurement system (Motic-2000) in 20 different fields per section, the number of macrophages in peri-outer zone of follicles was counted 200xfield and areas of macrophages were measured by microscope system.

2.4. Statistical analysis

A one-way ANOVA was carried out, and the statistical comparisons among the groups were performed with Duncan's test using a statistical package program (SPSS version 16.0). All P values are two-tailed and $P < 0.05$ was considered as significant for all statistical analyses in this study.

3. Results

3.1. Liver and spleen index

Liver index of mice group receiving lead acetate showed an insignificant increase compared to the control group, whereas the mice group receiving lead acetate and captopril showed insignificant differences compared to the control group (Table 1) and insignificant decrease compared to the group receiving lead acetate only. Spleen index of mice group received lead acetate and the other one received lead acetate and captopril showed insignificant increase compared to control group (Table 1).

3.2. Histopathological analysis

3.2.1. Histological examination

3.2.1.1. Liver. Non-treated mice liver served as control investigated for the purpose of comparison showed the normal struc-

Table 1 Liver and spleen index in control, lead and lead treated with captopril groups.

Index	Control	Lead	Lead and captopril
Liver index	6.4 ± 0.2	8.04 ± 0.8	5.9 ± 0.6
Spleen index	0.65 ± 0.09	0.8 ± 0.1	0.72 ± 0.08

Data = Mean ± SEM (standard error of means).