ELSEVIER

Pathophysiology 20 (2013) 269–274

ISP PATHOPHYSIOLOGY

www.elsevier.com/locate/pathophys

Common onion (*Allium cepa*) extract reverses cadmium-induced organ toxicity and dyslipidaemia via redox alteration in rats

S.F. Ige, R.E. Akhigbe *

Department of Physiology, College of Health Sciences, Ladoke Akintola University of Technology, Ogbomoso, Oyo State, Nigeria

Received 14 February 2013; received in revised form 7 April 2013; accepted 14 April 2013

Abstract

Background: Cadmium (Cd) remains an important environmental pollutant of public health concern as it causes organ toxicity, and cardiovascular diseases (CVD), but the roles of common foods such as onion (*Allium cepa*) need further clarification. The aims of this study were to clarify whether or not Cd-induced organ dysfunction was associated with blood protein, lipid and lipid peroxidation and the effects of onion extract AcE in a rat model. **Methods**: Control and Cd-treated rats were maintained on control diet, while AcE+Cd-treated rats were also orally administered AcE (1 ml/100 g body weight). Cd-treated and AcE+Cd-treated rats also received cadmium as $CdSO_4$ (1.5 ml/kg body weight of 0.3 mg/L of $CdSO_4$) via drinking water. **Results**: It was found that Cd significantly increased total cholesterol, triglycerides, LDL-cholesterol, serum albumin, and reduced HDL-cholesterol, total plasma protein, and plasma testosterone. Administration of AcE restored the liver and kidney toxicities and blood protein and lipid profiles. Moreover, AcE improved Cd-induced decrease in urinary volume and renal clearance, and also protected against Cd-induced oxidative stress by normalizing redox status. However, AcE did not affect Cd-induced altered plasma testosterone. **Conclusion**: Our study suggests that Cd-induced CVD was associated with altered blood dysproteinemia, dyslipidaemia, and oxidative stress. It also provided the first evidence of the therapeutic efficacy of AcE against atherosclerotic conditions and organ toxicity in Cd-intoxicated rats via a mechanism independent of the circulating testosterone level.

Keywords: Cadmium; *Allium cepa*; Hemorheology; Dyslipidaemia; Oxidative stress; Testosterone

1. Introduction

Cadmium (Cd) is a ubiquitously present xenobiotic heavy metal. It is a long-lived toxic metal commonly used in industries for pigments, batteries, plastics and metal coatings. Pan et al. [1] documented its common sources of exposure to be food, water and cigarettes. Depending on the dose, route, and duration of exposure, it can cause damages to various organ-systems [2], especially the respiratory, renal, hepatic, musculoskeletal, haematopoietic, endocrine, and cardiovascular systems [3–6]. Cd has been implicated in several pathologic conditions that include, but not limited, to chronic kidney disease [7], bone dysplasia [8,9], gastrointestinal tract damage [10,11], and vascular endothelial dysfunction and hypertension [12–16].

Several mechanisms have been suggested to be responsible for Cd-induced vascular endothelial dysfunction and hypertension. Fowler [3] associated cardiovascular dysfunction seen in Cd toxicity with the deregulation of cellular signaling caused by oxidative stress. Cd could induce production of free radicals, reactive oxygen species (ROS) and reactive nitrogen species, by displacing iron and copper from cytoplasmic and membrane proteins which eventually releases and increases the concentration of free iron and/or copper ions [15,17]. Furthermore, Cd depletes glutathione and oxidation of protein bound sulfhydryl groups resulting in increased ROS production [18,19] which in turn leads to DNA damage, protein modification, and lipid peroxidation and consequent cellular dysfunction and necrotic cell death [20].

There has been a surge in demand for the use of plants and their products in the management of a large range of pathologies which has led to interest in studies with the desire to evaluate the therapeutic potentials of botanicals

* Corresponding author.
E-mail addresses: akhigberoland@gmail.com, funkeige2006@yahoo.com (R.E. Akhigbe).

0928-4680/$ – see front matter © 2013 Elsevier Ireland Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.pathophys.2013.04.002

[21–26]. Though, various antioxidants have been formulated to protect against oxidative damage, there is still a great need to determine the antioxidant potentials of plant species in different disease conditions as formulated antioxidants are often too expensive and most has been shown to cause radio-sensitization, mutagenic activity, and tumor growth [27]. Common onion (*Allium cepa*), a traditional medicinal plant, has been reported to possess antioxidant property, and it is also widely used as food. Its phytochemical constituents include flavonoids, carbohydrates, glycosides, proteins, alkaloids, saponins, acid compounds, reducing sugars and oils [28]. It has been documented to protect against hepatotoxicity [29] and nephrotoxicity [30,31], however, there seems to be no study of its potential use in Cd-induced atherosclerotic conditions. The present study was designed to investigate whether or not Cd-induced cardiovascular hypertension is due to hemorheological alteration, dyslipidaemia, and lipid peroxidation and the possible influence of *Allium cepa*.

2. Materials and methods

2.1. Animals

The experiments were performed in male Wistar rats weighing 175 ± 2.6 g. Animals were obtained from the Animal Holdings of the Department of Physiology, Ladoke Akintola University of Technology, Nigeria. Experimental protocols were in accordance with the NIH guidelines for the care and use of laboratory animals and was handled under standard laboratory conditions of a 12:12 h light/cycle in a temperature and humidity controlled room [32]. Rats were allowed free access to standard rat chow and water. Rats were randomly allocated to one of the three experimental groups of 10 animals each. Control rats were given deionized water. Cd-treated and AcE+Cd-treated rats received 1.5 ml/kg body weight of 0.3 mg/L of $CdSO_4$ via drinking for 4 weeks. In addition to daily Cd administration, AcE+Cd-treated rats also received orally 1 ml/100 g body weight of AcE concomitantly for 8 weeks. Doses of Cd and AcE were based on our previous studies [29–31] similar to other studies [15,33]. Body weights of rats were recorded throughout the experiment.

2.2. Extract preparation

AcE was prepared following procedures from previous study studies [29–31]. Briefly, fresh common onion (*Allium cepa*) bulbs were rinsed thoroughly in distilled water, air dried, and 200 g was then blended. The resulting paste was allowed to stand for 24 h. Juice was then filtrated and squeezed out of it using a tight sieve. The filtrate/juice was prepared on weekly basis following the same procedure and kept at 4 °C. This is to prevent it from losing its potency.

2.3. Sample collection

On the last day of experiment, rats were housed in metabolic cages for 24 h urine collection for the measurements of urinary volume, urea and creatinine. At the end of the experiment, blood samples were collected via cardiac puncture. Liver and kidney of rats were harvested, weighed and homogenized in phosphate buffer for determination of oxidative stress.

2.4. Biochemical assays

2.4.1. Renal clearance

Plasma and urinary urea and creatinine were determined, and renal clearance of urea and creatinine were calculated [30,34].

2.4.2. Blood proteins, especially lipid profiles variables and plasma testosterone

Fasting plasma levels of total cholesterol (TC), triglyceride (TG), and HDL-cholesterol (HDL-C) were assayed by standard enzymatic method coupled with spectrophotometry using assay kit (Randox Lab Ltd., UK). LDL-cholesterol (LDL-C) was calculated using Friedewald's formula [35]. Total plasma protein, serum albumin, and plasma testosterone were also determined using standard laboratory kit (Randox Lab Ltd., UK) [36].

2.4.3. Oxidative stress markers

Lipid peroxidation index, malondialdehyde (MDA) and super oxide dismutase (SOD) were used to assess redox status. Plasma and tissue MDA and SOD were evaluated as previously documented [37,38].

2.5. Statistical analyses

Data are expressed as mean ± S.E.M. (of 10 replicates). One-way analysis of variance (ANOVA) was used to analyze for the significance of differences between means followed by post hoc Duncan's multiple range test. Statistical significance was assigned at a p-value of less than 0.05.

3. Results

3.1. Effect of Cd and AcE on body and organ weights

The overall toxic effect of Cd was observed by the reduction in weight gain and reduced relative liver weight seen in Cd treated rats when compared with other groups (Table 1). The body weight gain observed in rats of the control group was about 20% from the initial values compared to the 6% weight gain seen in Cd-treated rats. Co-administration of AcE enhanced the body weight gain. Similarly, Cd led to reduced liver weight as compared to the control. This