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Yucca schidigera extract modulates the lead-induced oxidative damage, nephropathy and altered inflammatory response and glucose homeostasis in Japanese quails

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ABSTRACT

The present study was conducted to explore the toxic effects of lead (Pb) on the physiological responses of Japanese quails and to investigate the potential modulatory role of *Yucca schidigera* extract (YSE) against these effects. 360 mature Japanese quails (at 2 months of age) were used and the experiment was lasted for 8 weeks. The birds were divided into six equal groups as follow: control (basal diet, BD), BD + Pb (100 mg/kg diet), BD + YSE (100 mg/kg diet), BD + YSE (200 mg/kg diet), BD + Pb (100 mg/kg diet) + YSE (100 mg/kg diet) and BD + Pb (100 mg/kg diet) + YSE (200 mg/kg diet). Pb induced a significant reduction in superoxide dismutase (SOD) and catalase (CAT) activities and reduced glutathione (GSH) level. While, increased protein carbonyl (PC) and malondialdehyde (MDA) content in tissues of exposed birds. Pb increased level of 8-hydroxy-2-deoxyguanosine (8-OHdG) and lactate dehydrogenase (LDH) activity in serum. YSE significantly reduced the Pb -induced oxidative stress in co-treated groups especially at 200 mg/kg diet. YSE could modulate the Pb –induced decreased urea, creatinine and beta-2 microglobulin (B2M) levels. YSE200 was found to be better than the YSE100 in decreasing levels of inflammatory markers including tumor necrosis factor (TNF-α), nitric oxide (NO), transforming growth factor-β1 (TGF-β1) and vascular endothelial growth factor (VEGF). Furthermore, YSE significantly regulates glucose homeostasis in co-exposed quails. Pb residues were found to be significantly higher in kidney and pancreas tissues of Pb group compared to other groups. YES decreased the expression of metallothionein-1 in the renal and pancreatic tissues, while elevated insulin expression in the pancreatic cells by immunostaining in co-exposed groups. In conclusion, the present results conclusively demonstrate the potential modulatory effect of YSE against the Pb-induced toxic effects in different organs of Japanese quails.

1. Introduction

The increased environmental pollution makes animals and birds more sensitive to the external stressors from their surroundings (Liu and Zhao, 2014). Most of the environmental pollutants could result in acute stress response, altered physiology, and poor performance and further reduce the production yield of animals and birds. Lead (Pb) is one of the most common and persistent environmental pollutants that are widely distributed in industrial areas with increased human activities such as smelting and mining (Sidhu et al., 2016, 2017; Havens et al., 2018). The residence period of Pb in soil is too long so it its threat to the environment remains for decades after its release, and results in a toxic cumulative impacts that can affect all biological systems exposed to it through different sources like, water, food and air (Berglund et al., 2010).

Birds are exposed to Pb from the general environment. Additionally, contamination of soil and feed by food and agricultural processing as well as industrial pollution represent the main sources of exposure (Haig et al., 2014). Lead affect birds either indirectly through reduction of food supply or directly through affecting the different body organs inducing abroad range of biochemical, physiological, behavioral and morphological dysfunctions in many parts of the body, including the

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central and peripheral nervous systems, hematopoietic system, cardiovascular system, liver and reproductive systems and also resulted in poor performance and death in animals (Suradkar et al., 2009; Elayat and Bakheetf, 2010). Exposure to Pb has a strong association with kidney function impairments and the untreated chronic exposure could lead to chronic or even irreversible nephropathy (Phetsombat and Kruat, 2006). Moreover, the kidneys are considered as one of the most important organs that keep the glucose homeostasis in birds (Lies Franssens et al., 2016). Glucose acts as metabolic substrate and represents the fuel of the body and Pb has been reported to induce abnormality in its metabolism (Yokoyam et al., 2000).

Oxidative stress also has been suggested to have a role in Pb pathophysiology. Where, Pb has been reported to generate ROS (reactive oxygen species) which could disturb the function of the body antioxidant defense system and damage the cell structure through lipid peroxidation and oxidation of nucleic acids and amino acids (Orun and Talas, 2008; Pandya et al., 2012; Winiarska-Mieczan, 2013).

Heavy metals including Pb have been reported to induce lipid peroxidation, reduce the activity of antioxidant defense system and result in altered biochemical functions in in various organs rainbow trout (Talas et al., 2008; Ates et al., 2008).

Increased oxidative stress could be implicated in disturbed insulin responsiveness, impaired glucose tolerance, dyslipidemia, β-cell dysfunction leading to type 2 diabetes mellitus (T2DM) (Tangvarasittichai, 2015). Lipid peroxidation by-products such as malondialdehyde (MDA) and conjugated dienes are increased in obesity, metabolic syndrome and T2DM (Slater, 1984). Additionally, peroxidative damage, increased production of ROS and inflammatory reactions has been reported to be associated with hyperglycemia (Talior et al., 2003).

Yucca schidigera, known as yucca, is a plant from the family "Agavaceae", native to the South-Western United States and Mexico. Yucca is recognized by Indians as one of the nicest desert herbs with multiple health promoting activities and they called it ‘a tree of life (Tenon et al., 2017). It has many beneficial effects like antioxidant, growth promoter, hypoglycemic, hypocholesterolemic, anti-inflammatory, immunostimulatory, and anticarcinogenic (Alagawany et al., 2016). Yucca is a commercial source of saponins, antioxidants, resveratrol (RES) and various enzymes (Chrenková et al., 2012). Yucca extract in animals feed has a positive effect on their growth and feed intake. Environmentally, yucca plays crucial functions because its extract affects the nitrogen metabolism in the body and reduces urea concentration in the blood (Piacente et al., 2005).

On the bases of previous studies, yucca extract has been used only as a nontoxic feed additive to animal and poultry feed. However its role in modulating the different types of stress applied on the birds upon exposure to various environmental pollutants and its chelating effect against heavy metals which could be accumulated in tissues of birds from different environmental sources still need more investigations. So the main objectives of the present study are to investigate the lead-induced oxidative deteriorations of biological macromolecules, nephropathy and their relation to the disruption of glucose homeostasis in Japanese quails and the possible beneficial role of *Yucca schidigera* extract in modulating these effects. Japanese quail could be used as a model in the studies related to effects of environmental contamination on ecosystem health as they are ready available, similar to wild birds and there are solid information concerning their normal physiology as reported by (Franson and Pain, 2011).

2. Material and methods

2.1. Birds and diets

The present study was carried out at Poultry Research Farm, Faculty of Agriculture, Zagazig University, Egypt. All experimental procedures were carried out according to the Local Experimental Animal Care Committee and approved by the ethics of the institutional committee of Zagazig University, and Zagazig, Egypt.

A total number of 360 mature Japanese quails (*Coturnix coturnix japonica*) at two months of age with initial body weight 240.50 ± 2.00 g were used in a complete randomized design experiment with six treatments of 60 birds each. Each group was subdivided into four replicates with 15 birds. The experiment lasted for eight weeks. Birds were fed the basal diet with or without supplemental lead (Pb) or *Yucca schidigera* extract (YSE) which formulated to meet laying quail. The treatments were as follows: (1) control basal diet (BD), (2) BD + 100 mg lead (Pb) /kg diet, (3) BD + YSE (100 mg/kg diet), (4), BD + YSE (200 mg/kg diet), (5) BD + Pb (100 mg/kg diet) YSE (100 mg/kg diet) and (6) BD + Pb (100 mg/kg diet) + YSE (200 mg/kg diet). The basal diet contained 20% CP and 2900 kcal/kg ME. Quails were reared in conventional cage (50 × 30 × 50 cm^3; 1500 cm^2 of floor space) with feed and drinking water provided *ad-libitum*. Quails also were maintained on a 24 h light throughout the trial and all quails were reared under the same managerial conditions.

2.2. Tested chemicals

Lead in the form of lead acetate (99.6% purity) was purchased from El-Gomhoria Chemical Co., Egypt. Yucca schidigera extract (YSE) was purchased from Free Trade Egypt Company (El-Behera, Egypt). All other chemicals were purchased from Sigma (St. Louis, MO, USA). All other reagents used were of analytical grade

2.3. Blood collection and tissue sampling

At the end of the experiment, 2 samples of blood were collected from each sacrificed bird. One sample was collected in heparinized tube for separation of plasma. While, the other sample was collected in a dry test tube and allowed to coagulate for 30 at ambient temperature min for serum separation by centrifugation (3000 rpm for 15 min) and stored at − 20 °C till assayed. Specimens from kidneys and pancreas were dissected and immediately rinsed with physiological saline (0.9% NaCl). Samples were divided in to two parts. The first part was used for histological studies, whereas the second part was stored frozen at −80 °C for further biochemical analyses.

2.4. Antioxidant assay markers

For antioxidant assays, kidney and pancreas samples were homogenized (10% w/v) in potassium phosphate buffer solution (pH 7.4) and then centrifuged at 3000 rpm for 15 min. The resulting supernatant was used to determine catalase (CAT) and superoxide dismutase (SOD) activity and contents of reduced glutathione (GSH) using commercial biodiagnostic kits provided from (BioMérieux, Marcy l’etoile, France) according to the manufacturer instructions.

2.5. Biomarkers of lipid peroxidation and protein and DNA oxidation

Lipid peroxidation (malondialdehyde; MDA) and Protein carbonyls (PC; the marker of oxidative damage of protein) were measured in kidney and pancreas tissues using commercial Biodiagnostic kits from abcam Co, UK (Cat No. ab118970, ab126287 respectively). While DNA oxidative damage was determined by measuring the 8-hydroxy-2-deoxyguanosine (8-OHdG) level in serum using chicken ELISA kits from MyBiosource.com, San Diego, California (Cat No. MBS261211) following the manufacturer's instructions. While, lactate dehydrogenase (LDH) was used as a marker of Pb -induced tissue injury. LDH was estimated using commercial biodiagnostic kits from abcam Co, UK (Cat No. ab102526) according to the manufacturer's instructions

2.6. Kidney function and glomerular filtration markers

Urea was estimated as specific markers of renal function in serum,