Journal of Trace Elements in Medicine and Biology 36 (2016) 27–37

Contents lists available at ScienceDirect

Journal of Trace Elements in Medicine and Biology

journal homepage: www.elsevier.com/locate/jtemb

Alterations in blood pressure, antioxidant status and caspase 8 expression in cobalt chloride-induced cardio-renal dysfunction are reversed by *Ocimum gratissimum* and gallic acid in Wistar rats

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ARTICLE INFO

Article history:
Received 23 January 2016
Received in revised form 28 February 2016
Accepted 29 March 2016

Keywords:
Cobalt
Gallic acid
Ocimum gratissimum
Oxidative stress
Heart
Kidneys
Apoptosis
Blood pressure

ABSTRACT

The protective abilities of the chloroform extract of *Ocimum gratissimum* (COG) and gallic acid against cobalt chloride ($CoCl_2$) – induced cardiac and renal toxicity were evaluated. Rats were exposed to $CoCl_2$ (350 ppm) for 7 days, either alone, or in combination with COG (100 and 200 mg/kg) or gallic acid (120 mg/kg). $CoCl_2$ given alone, caused significant increases ($p < 0.05$) in oxidative stress parameters (hydrogen peroxide, H_2O_2 and malondialdehyde, MDA) and increased expression of the apoptotic initiator caspase 8 in the heart and kidneys. There was significant reduction ($p < 0.05$) in reduced glutathione (GSH) in cardiac and renal tissues; reduction in superoxide dismutase (SOD) activity in the kidneys and adaptive increases in Glutathione S-transferase (GST) and catalase (CAT). $CoCl_2$ also produced significant reduction ($p < 0.05$) in systolic (SBP), diastolic (DBP) and mean arterial (MAP) blood pressures. Oral COG and gallic acid treatment significantly reduced ($p < 0.05$) the levels of H_2O_2 and MDA; with reduced expression of caspase 8 and restoration of GSH levels, GPx, SOD and CAT activities, howbeit, to varying degrees in the heart and kidneys. COG (200 mg/kg) was most effective in restoring the blood pressures in the rats to near control levels. $CoCl_2$-induced histopathological lesions including myocardial infarction and inflammation and renal tubular necrosis and inflammation were effectively ameliorated by the treatments administered. This study provides evidence for the protective roles of *O. gratissimum* and gallic acid by modulation of $CoCl_2$-induced alterations in blood pressure, antioxidant status and pro-apoptotic caspase 8 in Wistar rats.

1. Introduction

Cobalt is a trace element present in the diet as a component of Vitamin B12. It is biologically functional as a co-factor in many enzyme-catalyzed reactions [1] and also enhances the production of erythropoietin [2]. Exposure to large quantities of cobalt produces toxicity to biological tissues and usually occurs by other means in the environment. The metal has found wide applications in industrial, agricultural, medical and domestic settings and this has led to emerging concerns about the possibility of widespread exposures to toxic levels of the metal [3–5]. Several reports of acute and chronic exposures abound in scientific literature [1,6,7].

The mechanisms of toxicity of cobalt involve the production of reactive oxygen species (ROS); induction of apoptosis and the activation of the hypoxia-inducible factor (HIF) [8,9]. Cobalt induces hypoxic conditions by increasing the levels of HIF. This is achieved by interfering with prolyl hydroxylation of this protein, a process that otherwise targets HIF for degradation. Compounds that stabilize HIF have been linked to an over-stimulation of the 'pro-death' response, leading to cell injury and apoptosis [2,10]. Cobalt-induced hypoxia can also lead to an over-production of ROS and oxidative stress, as well as the activation of transcription factors involved in oxidative injury and inflammation [11]. Several in vitro studies have employed different antioxidants to counteract cobalt-induced apoptosis [5,12,13,14]. Positive results obtained in these studies suggest that ROS are involved in cobalt apoptosis, which is known to involve both the intrinsic and extrinsic apoptotic pathways [13,15,16].

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http://dx.doi.org/10.1016/j.jtemb.2016.03.015
0946-672X/