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ORIGINAL ARTICLE

Effects of curcumin on the social behavior, blood composition, reproductive hormones in plasma and brain acetylcholinesterase in cadmium intoxicated mice

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Abstract Cadmium (Cd) exposure can induce acute lethal health-related threats in humans since it has an exceptional ability to accumulate in living organism tissues and cause toxicological effects. Curcumin (Cur) on the other hand has a wide variety of biological activities and several studies have suggested its potential therapeutic or protective effects against several ailments and infections.

To study the effect of Cur on the toxicity of Cd, Swiss–Webster strain male and female mice (sixty each) were divided into 6 groups of ten each at random. Group-1 served as the naïve control and received no treatment. Group-2, 3 and 4 were the experimental controls and were administered once a day with a single oral dose of 50% dimethyl sulfoxide (DMSO), Cur (300 mg/kg) or Cd (100 mg/kg) respectively, for 2 weeks. Group-5 and 6 received Cur and Cd in combination once a day orally for 2 weeks except that Cur in a dose of 150 and 300 mg/kg to group 5 and 6 respectively, was administered one hour before Cd administration to both groups.

After treatment period, the male animals were subjected to social standard opponent test and females were subjected to the tube restraint tests and thereafter, their blood was collected to measure the blood composition indices and level of reproductive hormones. The animals were sacrificed to collect their brain for the estimation of acetylcholinesterase (AChE).

Results indicated that Cd significantly increased nonsocial activities in males and latency to first bite in females, whereas the social activities in males and the number of bites in females were significantly decreased. All measured indices of blood composition and levels of progesterone (female) and testosterone (male) in blood and AChE in their brain tissues were significantly decreased due to Cd treatment.

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However, administration of Cur along with Cd had an ameliorating effect on all the behavioral and biochemical parameters studied herein and reduced the toxicity of Cd significantly and dose-dependently. Thus, Cur may be beneficial for general health and for protection from Cd intoxication.

1. Introduction

Cadmium (Cd) represents one of the most toxic and carcinogenic heavy metal (IARC, 1993). Cd is an important industrial and environmental pollutant that currently ranks seventh in the Agency for Toxic Substances and Disease Registry (ATSDR)/EPA list of hazardous substances (Attia et al., 2014). It has been shown to be an environmental toxic pollutant metal from health-related threat point of view to humans as well as to other living organisms (Antonio et al., 1999; Singh et al., 2007; Tarasub et al., 2011). It is invariably present in our society, either as useful products in the form of nickel–cadmium batteries, dyes, plastics, electrochemicals, and paint pigments or in controlled wastes as a major source of pollution in water and as a constituent of food material (Jarup et al., 1998; Ikeda et al., 2000). The main source of Cd is through the diet and smoking (Barregard et al., 2014).

Women often have a higher Cd uptake compared to men due to iron deficiency (causing increased intestinal Cd uptake), which is more common in women. In humans it has been found to produce a wide range of biochemical and physiological dysfunctions as manifested in the forms of various diseases viz. Itai-itai, kidney malfunction, inflammation, Parkinson's disorder, liver malfunction (Singh et al., 2011; NTP, 1993).

Curcumin (Cur) is a well-known biologically active natural phytochemical phenolic compound (diferuloylmethane) found as a major component in turmeric, a yellow curry spice, extracted from the rhizome of *Curcuma longa* L. (family Zingiberaceae). Cur is well absorbed in the body system and has exceedingly low toxicity (Rahman et al., 2006). It possesses many beneficial activities in the body and is effective in several disorders including anorexia, coryza, cough, hepatic diseases, and sinusitis (Khanna, 1999; Tirkey et al., 2005). Recent studies provide scientific evidence regarding the potential pharmacological, prophylactic or therapeutic use of Cur, as anti-inflammatory, anticarcinogenic, antiviral, antifungal, antiparasitic, antimutagenic, antiinfectious and antioxidant compound (Chen et al., 2006; Perez-Arriaga et al., 2006). Multiple beneficial effects of Cur have also been elaborated in neurogenesis process which in turn have been reported for their neuroprotective effects in age-related neurodegenerative diseases (Ramsewak et al., 2000). Several studies have shown that Cur exhibits protective effects against oxidative damage and has antioxidant properties exerting powerful oxygen free radical scavenging effects and increased intracellular glutathione concentration, thereby protecting lipid peroxidation (Aggarwal et al., 2007; Cole et al., 2007; Kuhad et al., 2007; Ciftci et al., 2010, 2011). Commercial Cur contains 77% curcumin, 17% de-methoxycurcumin and 3% bisdemethoxycurcumin and virtually all these three components in Cur are biologically active and possess protective properties (Ahsan et al., 1999; Jayaprakasha et al., 2006). Numerous reports indicate that the effects of Cd in laboratory animals can be prevented or markedly reduced by the administration of excess Cur (Cole et al., 2007; Jayaprakasha et al., 2006).

In the light of the above information it appears that Cur may prove beneficial in several ways for Cd toxicity and this aspect needs more and more research work. Thus, the present study was undertaken to explore the effects of Cur against the Cd induced social behavioral deficits and biochemical toxicity in male and female mice.

2. Materials and methods

2.1. Experimental animals

Sixty male and sixty female Swiss–Webster strain mice (8–10 weeks old) were housed in opaque plastic cages under hygienic conditions in the animal facility of the Zoology Department, King Saud University, Riyadh, Saudi Arabia. All animals were maintained under reversed lighting conditions with white lights on from 22.00 to 10.00 h local time. The ambient temperature was regulated between 20 °C and 22 °C. Food (Pilsbury's Diet) and water were available *ad libitum*, unless otherwise indicated. All procedures were carried out in accordance with the ethical guidelines for care and use of laboratory animals, and all protocols were approved by the local Ethics and Care of Experimental Animals Committee.

All animals were divided into six different groups with ten animals in each. Group I consisted of untreated mice and served as naïve controls. Group II was treated with 50% DMSO (solvent of Cur). Group III was treated with 300 mg/kg Cur dissolved in 50% DMSO. Group IV was treated with Cd (100 mg/kg). Groups V and VI consisted of mice administered with Cur + Cd in combination in doses of 150 + 100 and 300 + 100 mg/kg respectively. All exposures were through oral administration, once a day, for two weeks, except that in groups V and VI, Cur was administered one hour before Cd exposure.

2.2. Cur and Cd administration

Cur of analytical grade, Sigma Chemical Company, USA, was dissolved in 50% DMSO to give a dose of 150 and 300 mg/kg body weight and diluted further with drinking water in 1.0 ml volume and was administered orally once a day. Cd was also administered orally once a day in the form of cadmium chloride (analytical grade, Riedel de Haen, Germany) dissolved in drinking tap water at a dose of 100 mg/kg body weight in 1.0 ml volume. In the fifth and sixth groups of animals where Cur and Cd were administered together orally once a day, Cur was administered one hour before Cd administration. The naïve control group received 1.0 ml plain tap water only. The doses of Cur and Cd used in this study are at par with