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Chemoprotective role of quercetin in manganese-induced toxicity along the brain-pituitary-testicular axis in rats

Isaac A. Adedara*, Temitayo I. Subair, Valerie C. Ego, Oluwasetemi Oyediran, Ebenezer O. Farombi

Drug Metabolism and Toxicology Research Laboratories, Department of Biochemistry, College of Medicine, University of Ibadan, Ibadan, Nigeria

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ABSTRACT

Reproductive dysfunction in response to manganese exposure has been reported in humans and animals. Quercetin, a bioflavonoid widely distributed in fruits, vegetables and beverages has been shown to possess antioxidant, anti-inflammatory and anti-apoptotic activities in different experimental model systems. However, there is dearth of scientific information on the influence of quercetin on manganese-induced reproductive toxicity. This study was designed to evaluate the influence of quercetin on manganese-induced functional alterations along the brain-pituitary- testicular axis in rats. Manganese was administered alone at 15 mg/kg body weight or orally co-treated with quercetin at 10 and 20 mg/kg body weight for 45 consecutive days. Results indicated that quercetin co-treatment significantly ($p < 0.05$) inhibited manganese-induced elevation in biomarkers of oxidative stress whereas it increased antioxidant enzymes activities and glutathione level in the brain, testes and epididymis of the treated rats. Furthermore, quercetin mediated suppression of inflammatory indices and caspase-3 activity was accompanied by preservation of histo-architectures of the brain, testes and epididymis in manganese-treated rats. The significant reversal of manganese-induced decreases in reproductive hormones (i.e. luteinizing hormone, follicle-stimulating hormone and testosterone) and testicular activities of acid phosphatase, alkaline phosphatase and lactate dehydrogenase by quercetin was complemented by an increase in sperm quality and quantity in the treated rats. Collectively, quercetin modulated manganese-induced toxicity along the brain-pituitary-testicular axis in rats via its intrinsic antioxidant, anti-inflammatory and anti-apoptotic activities, and may thus represent a potential pharmacological agent against manganese-induced male reproductive deficits in humans.

1. Introduction

Manganese is a trace element and nutrient essential for biological processes involved in the regulation of reproduction, brain function, formation of connective tissue and metabolism of lipid and carbohydrate [1,2]. The diet remains one of the major routes of manganese exposure for humans whereas inhalation of fumes and dusts is associated with occupations such mining, welding, dry cell battery manufacturing, automotive mechanics and agricultural application of manganese containing pesticides [3]. Although low concentrations of manganese are essential to the body, excessive manganese exposure is well reported to be associated with several cellular dysfunctions. Chronic manganese exposure is associated with neurobehavioral effects [4]. Besides the neurotoxic effects of manganese, reproductive dysfunction in response to manganese toxicity has been reported in humans. For instance, epidemiological studies indicated that men who were exposed to manganese dust in workplace had decreased libido, sperm motility, sperm concentration and impotency [5,6]. Moreover, clinical observations of impotence and reduced excretion of 17 β-ketosteroids in humans chronically exposed to manganese dust have been reported [7,8].

Several studies using different experimental animals demonstrated that excessive exposure to manganese significantly reduced sperm counts and sperm motility in spite of normal testicular histology of CD-1 mice [9] whereas severe degeneration of the seminiferous epithelium, depletion in the number of spermatids with absence of spermatocytes in the seminiferous tubules were

* Corresponding author. Drug Metabolism and Toxicology Research Laboratories, Department of Biochemistry, College of Medicine, University of Ibadan, 20005 Nigeria.
E-mail address: dedac2001@yahoo.co.uk (I.A. Adedara).

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