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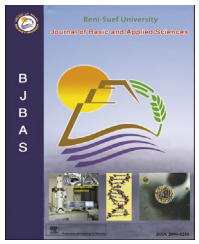

Full Length Article

The effect of high dietary fructose on the kidney of adult albino rats and the role of curcumin supplementation: A biochemical and histological study

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Background: Consumption of fructose, in the form of added sugars such as high fructose corn syrup (HFCS) or sucrose, has increased markedly in the last few years, which is strongly correlated with the prevalence of metabolic syndrome. It is widely used as a food ingredient and has potential to increase oxidative stress. Curcumin is a phenolic compound, and it exhibits protective effects against oxidative damage.

Objective: The aim of the study was to investigate the effects of curcumin on renal injury in fructose-fed rats and the possible underlying mechanism.

Methods: Eighty male rats were randomly divided into control group, fructose group, 200 mg/kg curcumin group and curcumin-fructose group. The histopathological changes in the kidney of rats were observed using hematoxylin and eosin and Masson's trichrome stains. The expressions of renal reduced glutathione (GSH) concentration, glutathione reductase (GR), super oxide dismutase (SOD), catalase activities, lipid peroxidation (LPO), DNA fragmentation %, inducible nitrous oxide (INOS) and homooxygenase 1 (HO-1) mRNA in renal tissue homogenates were assessed. Immunohistochemical detection of alpha-smooth muscle actin (α-SMA) and tumor necrosis factor alpha (TMF-α) were also investigated.

Results: Compared to the control group, GSH, GR, SOD and catalase activities were significantly decreased in the fructose group, while there was a significant increase in LPO, DNA fragmentation %, INOS and HO-1. These changes were accompanied by renal tubular injury, increased collagen deposition and lipid accumulation. Immunohistochemical results revealed increased expression of both α-SMA and TNF-α. Curcumin at 200 mg/kg evidently improved renal tubular injury, suppressed the expressions of renal LPO, DNA fragmentation %, INOS and HO-1, and decreased the expression of both α-SMA and TNF-α in kidney tissue.

Conclusion: Curcumin administration protected the kidney cells from fructose induced oxidative stress by increasing the antioxidant defence mechanism of the kidney cells and its ability to act as a free radical scavenger.

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1. Introduction

Fructose is a highly lipogenic sugar that has intense metabolic effects. Fructose becomes a major constituent of our modern diet. Fructose consumption has steadily increased over the past 30 years in parallel to the growth of the obesity/metabolic syndrome epidemic. Fructose and high-fructose corn syrup are ingredients in many commercially produced food products (Chen et al., 2004). Excess consumption of fructose is an important contributor to the metabolic syndrome (Ahangarpour et al., 2012). Metabolic syndrome is a well-established risk factor for diabetes, cardiovascular disease and mortality. Recently, studies have suggested that the metabolic syndrome may also contribute to the development of chronic kidney disease (Chen et al., 2004; Kurella et al., 2005). It has been hypothesized that fructose consumption in our diet may be among the factors that contribute to the epidemic of the metabolic syndrome and, consequently, to the epidemic of chronic renal disease (Chen et al., 2004; Elliott et al., 2002; Nakagawa et al., 2006). This hypothesis is supported by the preliminary evidence demonstrating that high fructose consumption induces kidney damages in both rats (Kizhner and Werman, 2002; Oudot et al., 2013) and mice (Aoyama et al., 2012).

Increase catabolism of fructose is associated with the cellular energy depletion that can increase the susceptibility of cells to lipid peroxidation (Punitha et al., 2005) Furthermore, it has been postulated that increased catabolism of fructose can accelerate free radical production similar to glucose and impairs the free radical defense system leading to oxidative stress (HS Kumar and Anandan, 2007; Reddy et al., 2009).

Curcumin is a phenolic compound extracted from *Curcuma longa* rhizome commonly used in Asia as a spice, pigment and additive. In traditional medicine of India and China, curcumin is considered as a therapeutic agent used in several foods. Numerous studies have shown that curcumin has broad biological functions particularly antioxidant and anti-inflammatory. In fact, it has been established that curcumin is a bifunctional antioxidant; it exerts antioxidant activity in a direct and an indirect way by scavenging reactive oxygen species and inducing an antioxidant response, respectively (Trujillo et al., 2013).

Curcumin is considered to be a potent cancer chemopreventive agent plus it has a protective effect against oxidative damage (Aggarwal et al., 2005; Duvoix et al., 2005). A protective effect of curcumin has been previously shown on hepatic lipid peroxidation in mice and rats (Eybl et al., 2006).

2. Materials and methods

2.1. Chemicals

Fructose was obtained from Sigma Aldrich, Egypt.

Curcumin was obtained from Sigma Chemical Company, USA.

2.2. Experimental animals

Eighty male albino rats, 16 weeks of age weighing average 150–200 grams were gathered for this experiment and housed in the laboratory of Biochemistry department, Faculty of Veterinary, Beni-Suef University. All rats were placed in a stable environment maintained at 22 ± 1 °C with 12-h light/day cycle. After an acclimatization period of 1 week, the rats were randomly assigned to 4 groups with twenty rats (n = 20) in each group:

Group I: control group was received 0.5 ml of corn oil via gavage for 5 weeks
Group II: fructose group was received 10% fructose in drinking water for 5 weeks (Gao et al., 2012; Wang et al., 2013) daily.
Group III: curcumin group was received curcumin at a dose of 200 mg/kg/day (Buyuklu et al., 2014) as a suspension in corn oil via gavage for 5 weeks.
Group IV: fructose and curcumin group was received both curcumin at a dose of 200 mg/kg/day as a suspension in corn oil via gavage and fructose 10% in drinking water daily for 5 weeks.

2.3. Sampling

Sampling was performed 24 h after the last dose of fructose and curcumin.

2.4. Blood sampling

Blood was collected from the medial canthus blood capillaries of the eye in dry centrifuge tubes. The tubes were placed in an inclined position for 5 min, allowing the blood to coagulate, and then placed in an incubator at 37 °C for 10 min. Centrifugation at 1000 × *g* for 20 min was performed and clear sera were separated and kept in the deep freezer (–80 °C) till use according to the instruction of assay kits of each measured parameter.

2.5. Specimen collection

At the time of sacrifice, all animals were killed under light anesthesia. Kidneys were dissected out and divided into 3 pieces (0.5 g each): the first part was kept in the deep freezer for oxidative, antioxidant parameters evaluation, the second part was kept for molecular parameters, and the third part was immediately fixed in 10% formol saline for 24 h for histological study.

2.6. Tissue homogenates

After scarification of rats, kidneys were collected and rinsed with physiological saline for removing any clotted blood or blood cells. 0.5 g of kidney was homogenized in 5 ml of physiological saline by using homogenizer (Ortoalresa, Spain). The homogenates were centrifuged at 1000 × *g* for 15 min. The supernatant was collected in Eppendorf tubes that were kept in the deep freezer (at –80 °C) for further biochemical investigations or according to the instructions of the biochemical assay kits.

2.7. Measured parameters

2.7.1. Serum biochemical parameters

Creatinine and urea concentrations in serum were determined colorimetrically as described by Bartles et al. (1972) and

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