JOURNAL OF FUNCTIONAL FOODS 10 (2014) 397–406

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Improved islet function is associated with anti-inflammatory, antioxidant and hypoglycemic potential of cinnamaldehyde on metabolic syndrome induced by high tail fat in rats

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ARTICLE INFO

Article history:
Received 29 May 2014
Received in revised form 8 July 2014
Accepted 9 July 2014
Available online

Keywords:
High fat diet
Cinnamaldehyde
Metabolic syndrome
Oxidative stress
Rat

ABSTRACT

Cinnamon is used in traditional medicine and foods. In this study the protective effects of cinnamaldehyde, one of the most abundant compound of cinnamon against metabolic syndrome induced by high fat diet, were investigated. To induce metabolic syndrome, male Wistar rats were given high fat diet for 16 weeks. Cinnamaldehyde was administrated orally (143.8 μmol/kg body weight) concomitant with high fat feed. Changes in islet morphology, lipid profile, TNF-α, TBARS, insulin resistance were analyzed. Metabolic syndrome was induced by high fat diet. Cinnamaldehyde reversed this process and significantly reduced insulin secretion and content in isolated islets of high fat diet. Beta cell enlargement, TNF-α and TBARS significantly increased with high fat diet, cinnamaldehyde restored both to the control level. Cinnamaldehyde prevented all symptoms of metabolic syndrome by improving oxidative and inflammatory conditions in pancreatic islets with no effect on insulin secretion but by enhancing insulin reserve and preventing beta cell damage.

1. Introduction

Metabolic syndrome (MetS) is a multifactorial disease, including a complex of metabolic risk factors for cardiovascular disease and diabetes. The criteria consist of obesity, dyslipidaemia [elevated triacylglycerol (TAG), low high density lipoprotein-cholesterol (HDL)], and hypertension and insulin resistance (hyperglycaemia/hyperinsulinaemia). Studies show that in most countries in the world, 30% of adult populations are suffering from MetS and its prevalence considerably increases with obesity and age (Ervin, 2009). The prevalence of

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http://dx.doi.org/10.1016/j.jff.2014.07.014
1756-4646/

obesity is increasing, such that about 500 million adults worldwide are obese. Epidemiological studies have shown that high fat containing diets lead to weight gain and the similar calorie intake from fat compared with protein or carbohydrates is associated with the higher increase in the body weight (Buettner, Scholmerich, & Bollheimer, 2007). Similar to humans, fat rich diets induce obesity and metabolic disorders in experimental animal models. To induce obesity in animal models, numerous high fat diets with different types of fat (plant or animal; with different degrees of unsaturation) with various percent of fat have been used (Lia et al., 2014; Mashmoul et al., 2014). It is estimated that each year about 50,000 tonnes of tail tissue (Alipanah & Emamjomeh Kashan, 2011) are used as a source of fat production. It is therefore important to investigate the suitability of this fat for human consumption. The underlying mechanisms of the condition are various and complicated; MetS and obesity are associated with low grade inflammatory condition (Cano et al., 2009) and oxidative stress also is involved in the pathogenesis of metabolic syndrome (Roberts & Sindhu, 2009). There are various anti-obesity drugs in the market, but most of them affect physiological function by mechanisms regulating body weight and display several side effects. This highlights the importance of functional food for management of metabolic syndrome and associated disorders (Ritesh et al., 2013). Cinnamon in most societies, especially those in Asia is widely used as a spice. Cinnamon essential oil, the main constituent of the plant which makes up 1% of the bark, is widely used in medicine, cooking and cosmetics. Cinnamaldehyde (CNMA) is an oily and yellowish liquid with a warm, sweet odour and pungent taste which is composed of 90% of the oil (Wijesekera, 1978). In traditional medicine, cinnamon is also used for therapeutic purposes. It especially lowers blood sugar without any side effects for years, although some clinical studies have reported conflicting results (Plaisier et al., 2011; Rafehi, Ververis, & Karagiannis, 2012). Prospective randomized controlled trials have shown that consumption of cinnamon did not significantly alter haemoglobin A_{1C} level, fasting plasma glucose, or plasma lipid profiles in type 1 and type 2 diabetes (Baker, Gutierrez-Williams, White, Kluger, & Coleman, 2008). It does not improve whole-body insulin sensitivity or oral glucose tolerance and does not modulate blood lipid profile in postmenopausal patients with type 2 diabetes (Vanschoonbeek, Thomassen, Senden, Wodzig, & van Loon, 2006). To our knowledge so far the effects of CNMA on the islets of pancreas histology and their insulin release and depot have not been reported. In this study we induced metabolic syndrome using high fat diet in rat and have looked for possible protective effects of CNMA against induced MetS.

2. Methods

2.1. Animals and diets

A total of 40 male Wistar rats (12 weeks old, 220–250 g,) were supplied from Pasteur Institute, Tehran, Iran. All experiments were conducted in accordance with standard ethical guidelines and the study was approved by the local ethics committee of the Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences (No: 91/08/168). The animals were housed individually per cage (dimensions 45, 25, 15 cm) under standard conditions (12 h light–12 h dark cycle starting at 0700, at 24 °C in a controlled humidity) throughout the experimental period with free access to food and water. After 1 week period of adaptation to laboratory situation, rats were randomly assigned to four different experimental groups (n = 10 per group): Group A; as a control was fed control chow diet, Group B; was fed a semi-purified high fat diet (HFD) consisting of the 25% (w/w) of fat (1% soya bean oil and 24% fat), Group C; was fed a regular chow diet with CNMA and Group D; was fed a HFD with CNMA supplement. Animals were orally given CNMA (W228613, Sigma-Aldrich, Shanghai, China, purity ≥ 95%) 143.8 μmol/kg body weight in corn oil daily, through gavages for the duration of experiment (16 weeks) as reported previously (Gowder & Devaraj, 2006). The control chow diet and HFD were supplied from Javaneh, Khorasan animal food company, Mashhad, Iran. High fat food was prepared freshly and stored at 4 °C during the duration of the experiment (16 weeks). The composition of the control regular chow diet was 20% protein, 1% soybean oil and 14% fibre by weight, while HFD group received high fat food consisting 18% protein, 1% soybean oil, 24% tail fat and 10% fibre by weight. The amount of energy (per 100 g diet), in regular chow and HFD was 1172.3 kJ (280 kcal) and 1716.58 kJ (410 kcal), respectively. The main fatty acid composition of soybean oil was saturated fatty acids (SFA; C16:0, 11.65%; C18:0, 4.45%), 16·1%, monounsaturated fatty acid (MUFA; C18:1, 20.02%; C20:1, 98%) 22.0% and polyunsaturated fatty acid (PUFA; C18:2 n-6, 47.57%; C18:3 n-3, 12.11%) 61.5%. The fatty acid composition of tail fat was analyzed by gas chromatography and included SFA (C14:0, 3.64; C16:0, 22.55; C17:0, 4.10; C18:0, 12.54%) 44.9%; MUFA (C14:1, 1.44; C16:1, 4.18; C17:1, 2.18; C18:1, 41.15%) 51.64%; PUFA (C18:2 n-6, 3.11%; C18:3 n-3, 0.34%) 3.45% and the cis form of fatty acids was 93.82%. A curved stainless steel gavage needle with ball tip was used for gavaged rats and was washed thoroughly and wiped between animals. Oral gavages were performed by skilled personnel so daily CNMA gavages were not stressful in rats that have been acclimated to handling.

2.2. Experimental procedures

2.2.1. Anthropometrical parameters

Body weight and food intake were recorded between 0900 and 1200 during 16 weeks of experiments. Corrections were made for the small quantities (g) of food spilled per cage. Naso-anal length was measured in anaesthetized rats at the end of the study in a ventral position; one observer stretched the animals until snout, spinal column, and middle of the pelvis were in a straight line, while the other observer measured nose-to-anal length by use of a caliper (mm) and then the Lee index was calculated: $\text{Lee Index} = \frac{\sqrt[3]{\text{Weight (g)}}}{\text{Length (cm)}} \times 1000$. The values of Lee Index greater than 310 were considered as obesity.

2.2.2. Measurement of blood pressure (BP)

Blood pressure was determined using a non-invasive tail-cuff method (Narco Bio-Systems, Inc., Houston, TX, USA) in conscious animals at the beginning and at the end of the study. To acclimate, the animals were placed in a constant-temperature (29 ± 2 °C) chamber for at least 15 min on 2–3