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Helianthus tuberosus (Jerusalem artichoke) tubers improve glucose tolerance and hepatic lipid profile in rats fed a high-fat diet

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ABSTRACT

Objectives: To analyze the effects of feeding *Helianthus tuberosus* (HT) tubers on glucose tolerance and lipid profile in rats fed a high-fat diet (HFD).

Methods: A normal HFD or HFD including 10 w/w% HT tubers (HFD + HT) was fed to F334/Jcl rats. After 10 weeks, organ weights, glucose tolerance, and lipid profile were analyzed.

Results: The body weight, liver weight, and epidermal fat content in the HFD group were higher than those of the normal group, and similar to those of the HFD + HT group. The oral glucose tolerance test at 10 weeks revealed that the blood glucose level 30 min after beginning the test in the HFD + HT group was significantly lower than that in the HFD group. Liver triglyceride and total cholesterol levels in the HFD + HT group were significantly lower than those in the HFD group. Fecal triglyceride and total cholesterol levels in the HFD + HT group were higher than those in the HFD group. Histological analyses revealed that fat and glycogen accumulation increased in the HFD group, but decreased in the HFD + HT group.

Conclusions: These results indicate that HT tubers have anti-fatty liver effects based on improvements in glucose tolerance and the hepatic lipid profile.

1. Introduction

Non-alcoholic fatty liver disease (NAFLD) is a recognized condition that may progress to end-stage liver disease [1]. Previous studies have shown that 10%–40% of patients with NAFLD develop non-alcoholic steatohepatitis (NASH) [2]. Because NAFLD and NASH are risk factors for liver cancer, preventing their progression is important [3]. The progression of NAFLD and NASH is associated with type 2 diabetes mellitus and hyperlipidemia [4,5]. Therefore, preventing hyperlipidemia and changes in glucose tolerance is necessary to limit the progression of NAFLD and NASH.

Hyperlipidemia and type 2 diabetes mellitus are induced by excess intake of high-calorie and high-fat diets [6,7]. One way to prevent the progression of hyperlipidemia and type 2 diabetes mellitus is to refrain from ingesting such diets. However, maintaining a restricted diet is difficult for many people, and compliance with this restriction is poor. Alternatively, hyperlipidemia and type 2 diabetes mellitus can be prevented or treated with drugs or by consuming functional foods that have anti-hyperlipidemia or anti-type 2 diabetes mellitus effects. Of these options, functional foods have high safety and can be used as part of a normal diet. Therefore, functional foods that improve hyperlipidemia and glucose tolerance may be useful candidates for preventing the progression of NAFLD and NASH. However, such functional foods have not been reported.

Helianthus tuberosus (HT, Jerusalem artichoke) is a perennial plant whose tubers are used as a food worldwide; it grows well in the semi-arid tropics. HT tubers contain inulin, a non-degradable oligosaccharide polymer comprising 30–35 fructose units that are linearly arranged in β-1,2 linkages with an α-1,2-linked D-

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glucose at the non-reducing end [8–10]. Previous reports indicated that inulin improved glucose tolerance and liver lipid profile in rats fed a high-fat diet (HFD) [11,12]. Based on this background information, we hypothesized that feeding HT tubers might improve the hyperglycemia or hyperlipidemia induced by an HFD, suggesting their potential as a useful functional food for preventing the progression of NAFLD and NASH. In the current study, rats fed an HFD were used to assess the effect of feeding HT tubers on glucose tolerance and the hepatic lipid profile.

2. Materials and methods

2.1. Animals and diets

Four-week-old F344/Jcl rats were purchased from CLEA (Tokyo, Japan). The rats were acclimated for one week before use. The animals were cared for according to approved procedures, and the experiments received institutional animal approval (approval number: 13137). Normal diets and HFDs were purchased from the Oriental Yeast Company (Tokyo, Japan). Components of the HFD were milk casein (256 g/kg), L-cystine (3.6 g/kg), maltodextrin (60 g/kg), α-cornstarch (160 g/kg), sucrose (55 g/kg), soybean oil (20 g/kg), lard (330 g/kg), cellulose (66.1 g/kg), calcium carbonate (1.8 g/kg), and choline bitartrate (2.5 g/kg). HT tuber powder was provided by the Tokushima Prefectural Government. HT tuber components were carbohydrates (325 g/kg), inulin (452 g/kg), protein (92 g/kg), ash (68 g/kg), water (54 g/kg), and fat (9 g/kg). The HFD + HT diet was prepared by mixing the HFD diet with HT tuber powder. The final concentration of HT powder was 10% (w/w). The basic composition of each diet is as follows, normal diet; carbohydrate: 553 g/kg, protein: 231 g/kg, fat: 51 g/kg, HFD diet; carbohydrate: 248 g/kg, protein: 230 g/kg, fat: 350 g/kg, HFD + HT diet; carbohydrate: 256 g/kg, protein: 216 g/kg, fat: 316 g/kg, inulin: 45 g/kg. Rats ingested each diet and water freely. Eight rats were included in each group.

2.2. Measurements of body and organ tissue weights

Body weight in each group was measured weekly for 10 weeks. After 10 weeks, urethane (2.5 g/kg) was administered intraperitoneally and liver and epididymal fat were sampled and weighed. These samples were stored at −80 °C before use. Slices of the liver were preserved in formalin for histological analyses. Caloric intake was calculated by measuring the total feed consumed by each group.

2.3. Plasma glucose level measurements and oral glucose tolerance test (OGTT)

After 10 weeks, blood glucose was measured in each group of rats using blood drawn from the tail vein after 16 h of fasting. The OGTT was performed by administering 1 g/kg glucose to each rat and harvesting blood samples from the tail vein intermittently. After centrifugation (2000 ×*g*, 10 min), blood glucose was measured in the serum. The blood glucose measurement kit was purchased from Sanwa Kagaku (Aichi, Japan). The measurements were performed according to the manual provided by the manufacturer.

2.4. Plasma aspartate aminotransferase (AST) and alanine aminotransferase (ALT) measurement

Blood samples used for fasting glucose measurements were also used for measurement of serum AST and ALT levels. AST color endpoint assay kit and ALT color endpoint assay kit were purchased from Empire Genomics (Buffalo, NY, USA). Measurements were performed according to the manual provided by the manufacturer.

2.5. Lipid profile analyses

Blood samples used for fasting glucose measurements were also used for measurement of serum triglyceride (TG) and total cholesterol (TC) levels. Total lipids of liver tissue and feces between 8 and 9 weeks of feeding were extracted by the Folch method [13]. Briefly, liver tissue and feces were homogenized in phosphate buffer. Folch solution (chloroform/methanol: 2/1) was added to this lysate and vortexed. These samples were centrifuged at 1500 ×*g*, for 15 min and the lower layer was collected. Sodium chloride solution (0.5%) was added and centrifuged at 1500 ×*g* for 15 min. The lower layer was collected and concentrated using a rotation evaporator. The obtained lipids were dissolved in 2-propanol and used for measurement of TC and TG. TC and TG measurement kits were purchased from Wako (Osaka, Japan). Measurements were performed according to the manual provided by the manufacturer.

2.6. Histological analyses

Liver tissues were embedded in paraffin and cut into sections (4 μm thick). Sections were stained with hematoxylin and eosin (H&E) or 1% periodic acid-Schiff's (PAS) solution as described previously [14].

2.7. Statistical analyses

Results are shown as the mean ± SD. Data were subjected to a one-way analysis of variance and differences between groups were determined using the Holm's sequential Bonferroni procedure. All analyses were performed using Microsoft Excel (Redford, WA, USA). All *P*-values were two-sided. Differences with $P < 0.05$ were considered significant.

3. Results

3.1. Changes in body and organ tissue weights

The average body weight of rats in the HFD group was significantly higher than that in the normal diet group from 3 to 10 weeks, but the same as that in the HFD + HT group throughout the experiment (Figure 1). Caloric intake was identical between the HFD and HFD + HT groups (Table 1). The liver and epididymal fat weights of rats in the HFD group were higher than those of the normal group rats, but identical to those of the HFD + HT group rats (Table 1). These data indicated that intake of HT tubers did not affect the changes in body and organ tissue weights induced by the HFD.