Short Communication

Anti-obesity effects of *Schisandra chinensis* fruit water extract in rats fed a high-fat diet

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Abstract

Obesity has become a major public health problem worldwide. To date, many studies on obesity prevention have been performed. In this study, we examined the anti-obesity effects of *Schisandra chinensis* (Turcz.) Baill. fruit (SC) water extract in rats fed a high-fat diet. We gave the rats high-fat chow including SC water extract for 10 weeks. Although these rats ate the same amount of chow as the high-fat diet group, their weight gain was significantly inhibited compared to that in the high-fat diet group. Moreover, the SC group showed significantly decreased epididymal fat weight and levels of plasma triglycerides, total cholesterol, and leptin compared to the high-fat diet group. In the oral glucose tolerance test (OGTT), the SC group showed lower blood glucose levels than the high-fat diet group 90 min after eating. This is the first study to show that SC water extract has anti-obesity effects. It may be beneficial to drink SC water extract or tea after eating to prevent obesity.

Key words traditional medicine, anti-obesity effect, schisandra fruit, epididymal fat, high-calorie diet.

Introduction

*Schisandra chinensis* (Turcz.) Baill. fruit (gomishi in Japanese, SC) is widely used as a tonic and restorative adaptogen with liver-protecting effects in traditional Chinese medicine.1) It has also been used to abrogate asthmatic cough, to treat spermatorrhea, to improve the efficiency of brain activities, and so on.2,4) In Korea, people drink schisandra fruit tea (omija-cha in Korean) to enhance their health, and it has been reported that a Korean traditional medicine including SC inhibits obesity in OLETF rats.5) Therefore, we hypothesized that SC extract would have anti-obesity effects.

Obesity has become a major public health problem worldwide and is associated with many chronic diseases and adverse health consequences, including diabetes mellitus type 2,4) dyslipidemia,5) hypertension,6) and coronary artery disease.7) Obesity develops from an imbalance between caloric intake and energy expenditure, as well as from behavioral (e.g., physical inactivity) and inherited factors.8) Recently, several studies have reported natural products that might be useful as anti-obesity treatments. Miyakita et al. reported that a water extract of *Houttuynia cordata* Thunb. leaves exerts anti-obesity effects.9) It was also reported that some beverages and teas, such as garcinia extract, hibiscus tea, marine algae, and green tea, have potential as anti-obesity agents.10–12) However, the anti-obesity effects of SC have not been examined. In this study, we analyzed the anti-obesity effects of SC water extract in rats fed a high-fat diet.

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Materials and Methods

Animals: Five-week-old male BrlHan:WIST@Jcl (GALAS) rats were purchased from CLEA Japan (Tokyo, Japan). All rats were housed in an air-conditioned room at 23 ± 2 °C and 50% ± 10% humidity under controlled lighting conditions (12:12-h light-dark cycle). The rats were given free access to food and water and then acclimatized for 3 days on a standard diet (MF: Oriental Yeast, Tokyo, Japan) before being used in the experiment. All animal care procedures and treatments were conducted in accordance with the guidelines of the animal care and use committee of the University of Tokushima.

Experimental diets: The following cubed diets were used in this experiment: the normal diet (MF: 3.6 kcal/g; 13% fat, 60% carbohydrate, 26% protein), the high-fat (HF) diet (F2HFD2: 6.4 kcal/g; 82% fat, 3% carbohydrate, 15% protein), and the HF+SC diet. MF and F2HFD2 chow were purchased from Oriental Yeast. The HF+SC diet group was given the HF chow including SC water extract. Dried SC material, “gomishi” (Tsumura Inc., Tokyo, Japan), was extracted with 10 volumes of hot water (100 °C) for 1 hour, and the extract was evaporated using a rotary evaporator in vacuo and exsiccated. The extract was mixed in the HF diet with 10% (as raw material: 6.3 kcal/g).

Measurement of food intake: The food consumption of the animals was calculated by subtracting the weight of the leftover food. The food intake was described in terms of calories.

Experimental design: At 5 weeks of age, the rats were randomly divided into three groups: the normal diet, n=6; the HF diet, n=6; and the HF+SC diet, n=6. The rats in each group were allowed to eat freely for 10 weeks. After 10 weeks, the right kidney, liver, and epididymal fat were immediately collected and weighed after the rats had been killed under anesthesia with urethane (5 g/kg intraperitoneally; Sigma, St. Louis, MO, USA).

Measurement of blood biochemical parameters: Blood samples were obtained from the tail veins of the rats. The collected blood samples were immediately centrifuged in order to separate out the plasma. The sera were stored at -80 °C until being thawed for analyses. The levels of triglycerides (TG) and total cholesterol (T-Chol) were measured using commercial reagents according to the manufacturer’s recommendations (Wako Pure Chemical Industries, Osaka, Japan). Plasma leptin concentrations were determined by an enzyme-linked immunosorbent assay using the Rat Leptin Kit (Morinaga Institute of Biological Science, Yokohama, Japan).

Oral glucose tolerance test (OGTT): An OGTT was performed 10 weeks after the start of the experiment. After the rats had fasted for 18 h, glucose was administered orally (1g/kg). Blood samples were obtained before and at 30, 60, 90, and 120 min after glucose loading. After blood samples were obtained from the tail veins, blood glucose concentrations were immediately measured using a glucose analyzer (Glucose Pilot; Aventir Biotech, Carlsbad, CA, USA).

Histological analysis: The epididymal fat was dissected, fixed overnight in 10% (v/v) formaldehyde, embedded in paraffin, and stained with hematoxylin-eosin.

Statistical analysis: All values are expressed as the mean ± SD. One-way ANOVA followed by Bonferroni’s multiple comparison test was performed to evaluate the differences among the three groups. Differences were considered significant at P<0.05.

Results

Body weight, caloric intake, and tissue weight: Body weight and caloric intake were significantly higher in the HF diet group than in the normal diet group (P<0.001, P<0.01, respectively) (Fig. 1). In the HF+SC diet group, there were no significant differences in caloric intake compared to the HF diet group (Fig. 1b); however, body weight was significantly lower than in the HF diet group (P<0.05). In the HF diet group, epididymal fat and liver weights were significantly higher than in the MF diet group at 10 weeks. And the weight of epididymal fat was significantly lower in the HF+SC diet group than in the HF diet group in the same period.
(P < 0.01), although there were no differences in liver weight. There were no differences in kidney weight throughout this period within each group (Fig. 2). In the morphological examination, cell diameters were measured and averaged. This indicated that epididymal fat cells in the HF+SC diet group became significantly smaller than those in the HF diet group (Fig. 3).

**Biochemical analyses of plasma TG, T-CHO, and leptin**: The plasma TG level was significantly higher in the HF diet group than in the normal diet group (P < 0.01) (Fig. 4a), but the level of T-CHO did not differ between the normal and HF diet groups (Fig. 4b). In the HF+SC diet group, the levels of plasma TG (Fig. 4a) and T-CHO (Fig. 4b) were significantly lower than in the HF diet group (P < 0.05, P < 0.01, respectively). Furthermore, the level of plasma leptin was significantly higher in the HF diet group than in the normal diet group (P < 0.001) and significantly lower in the HF+SC diet group than in the HF diet group (P < 0.01) (Fig. 4c).

**OGTT**: The HF diet group showed significantly greater increases in blood glucose than the normal diet group at 30 and 120 min after glucose loading (Fig. 5). Blood glucose was significantly higher in the HF+SC diet group than in the normal diet group at 30 and 60 min, but was significantly lower than that in the HF diet group at 90 min.

![Graphs showing changes in body weight and food intake](image)

**Figure 1** Changes in body weight (a) and food intake (b) in rats fed the normal, HF, or HF+SC diet. Data are shown as the mean ± SD. *P < 0.05 vs. the HF diet; **P < 0.01 and ***P < 0.001 vs. the normal diet (one-way ANOVA followed by post hoc comparisons using Bonferroni’s multiple comparison test).

![Graphs showing tissue weights](image)

**Figure 2** Tissue weights of liver (a), kidney (b), and epididymal fat (c) in rats fed the normal, HF, or HF+SC diet for 10 weeks. Data are shown as the mean ± SD. **P < 0.01 vs. the HF diet; ***P < 0.01 and ****P < 0.0001 vs. the normal diet (one-way ANOVA followed by post hoc comparisons using Bonferroni’s multiple comparison test).
Figure 3 (a) Ematoxylin-cosin staining of epididymal fat in rats fed the normal, HF, or HF+SC diet for 10 weeks. Scale bar: 100 µm. (b) Calculated average size of cell. Data are shown as the mean ± SD. ***p<0.001 vs. the HF diet (one-way ANOVA followed by post hoc comparisons using Bonferroni’s multiple comparison test).

Figure 4 Level of plasma triglycerides (a), total cholesterol (b), and leptin (c) in rats fed the normal, HF, or HF+SC diet for 10 weeks. Data are shown as the mean ± SD. *p<0.05 and **p<0.01 vs. the HF diet; †p<0.05, ‡p<0.01, and ##p<0.001 vs. the normal diet (one-way ANOVA followed by post hoc comparisons using Bonferroni’s multiple comparison test).

Figure 5 OGTT in rats fed the normal, HF, or HF+SC diet. Blood glucose levels. Data are shown as the mean ± SD. *p<0.05 vs. the HF diet; †p<0.05, ‡p<0.01, and ##p<0.001 vs. the normal diet (one-way ANOVA followed by post hoc comparisons using Bonferroni’s multiple comparison test).
Discussion

In the present study, we demonstrated that SC water extract prevented weight gain and decreased both epididymal fat weight and the levels of plasma TG, T-CHO, and leptin. The average one-day intake of SC per rat was 1.5g, the maximum dose before a rat rejects food in the portions used in this experiment. Morphologic observation demonstrated that SC water extract inhibited the enlargement of epididymal fat cells. Furthermore, SC water extract slightly improved impaired glucose tolerance. Although there have been many reports on the pharmacological effects of SC ligands, including anti-inflammatory, anti-oxidative, anti-hepatotoxic, anticancer, and anti-HIV effects, this is the first report that SC has an anti-obesity effect. Although obesity is associated with environmental and genetic factors, it develops from adipocyte differentiation and subsequent fat accumulation. The primary functions of adipose tissue are to store energy in the form of triglycerides during periods of energy excess and to secrete adipokines including leptin and adiponectin. These findings suggested that the SC water extract inhibits adipocyte differentiation or lipid accumulation via an unknown mechanism, reduces epididymal fat weight, and subsequently decreases the levels of plasma triglycerides and leptin. The inhibition of hepatic weight gain in the SC group supports this. The improvement of impaired glucose tolerance may have been caused by the prevention of weight gain. However, further studies are required to confirm the relationship between SC water extract intake and adipocyte differentiation or lipid accumulation.

In conclusion, SC water extract displayed anti-obesity effects. It may be beneficial to drink SC water extract (tea) after eating in order to prevent obesity.

Acknowledgments

We are grateful to Dr. Ashraf A. Ewis and Dr. Masako Sei of The University of Tokushima for their helpful discussions.

References


