Eur J Nutr (2004) 43 : 116–124
DOI 10.1007/s00394-004-0450-x

ORIGINAL CONTRIBUTION

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Green tea supplementation ameliorates insulin resistance and increases glucose transporter IV content in a fructose-fed rat model

Summary *Background* Sprague-Dawley rats fed a fructose-rich diet exhibit insulin resistance and hypertension, a pathologic status resembling human type II diabetes mellitus, and are an excellent laboratory animal model for research on insulin action and the development of hypertension. Since green tea has numerous beneficial effects, we tested its effect on fructose-fed rats. *Aim of the study* The present study was therefore designed to further evaluate the effects of green tea supplementation on insulin resistance, hypertension, and the glucose transporters I and IV contents in adipose tissue in the fructose-fed rat model. *Methods* The animals were divided into three groups and fed for 12 weeks with standard chow and water (control group), a high fructose diet and water (fructose group), or the same high fructose diet, but with green tea (0.5 g of lyophilized green tea powder dissolved in 100 mL of deionized distilled water) instead of water (fructose/green tea group). During the 12 weeks study period, fresh water or green tea was provided daily at 6:00 PM. Blood pressure was measured twice a week, and an oral glucose tolerance test performed after 12 weeks of diet supplementation. At the end of the experiment, plasma triglyceride (TG), free fatty acid (FFA), glucose, and insulin were assayed. The epididymal fat pads from all rats in the same group were pooled and adipocytes isolated and tested for insulin binding, glucose uptake, and their content of glucose transporters I (GLUT I) and IV (GLUT IV). *Result* Compared to the control group, the fructose group developed fasting hyperglycemia, hyperinsulinemia, and elevated blood pressure. Insulin-stimulated glucose uptake and insulin binding of adipocytes were significantly reduced, and the glucose transporter IV content of adipocytes also decreased. The fructose/green tea group showed improvement in all of these metabolic defects and in insulin resistance and blood pressure. *Conclusion* Based on these results, we suggest that the amelioration of insulin resistance by green tea is associated with the increased expression of GLUT IV.

Key words green tea – insulin resistance – hypertension – fructose – glucose transporter

Received: 16 June 2003
Accepted: 26 August 2003
Published online: 6 January 2004

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Introduction

Visceral obesity, hyperlipidemia, hyperinsulinemia, hypertension, increased levels of very low-density lipoprotein, and decreased levels of high-density lipoprotein, collectively called "Syndrome X" [1, 2], are associated with a high incidence of cardiovascular diseases. A similar cluster of metabolic abnormalities is frequently diagnosed as type II diabetes mellitus [3]. However, no definitive biochemical or metabolic mechanism has been proposed to explain the etiology of this syndrome. Several animal models are available for studying these metabolic disorders. For example, rats fed a high fruc-

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tose diet develop insulin resistance, hypertriglyceridemia, and hypertension, a pathologic status resembling type II diabetes mellitus [4, 5].

Current management of type II diabetes mellitus involves a combination of a dietary plan, an exercise program, and the use of drugs, such as sulfonylureas and biguanide. There is growing interest in the use of medical plants and health foods for the treatment and prevention of disease. For example, fish oil has been shown to ameliorate insulin resistance and hypertension in fructose-fed rats [6].

Tea is one of the most commonly consumed beverages worldwide. Among its commercial varieties, green tea is an unfermented product containing a relatively larger amount of polyphenol compared to other teas. In addition to its use as a beverage, it is suggested to have several biological properties, including antioxidant [7], antifungal [8], and antitumor [9] activity. For example, oral administration of green tea reduces aortic lesion formation and prolongs the lag phase of LDL oxidation, suggesting it has antiatherosclerotic activity [10]. Furthermore, there is strong evidence from in vitro studies [10, 11], animal studies [10, 12], and human investigations [11, 13] that green tea and its main constituents can prevent cardiovascular disease. We were therefore interested in determining whether green tea also has significant hypoglycemic effects.

Little research has been carried out on the relationship between tea drinking and plasma glucose homeostasis. Gomes et al. [14] found that aqueous extracts of green or black tea have hypoglycemic effects in streptozotocin-induced diabetic rats. Some studies have shown that plasma glucose levels in diabetic rats are lowered when the rats are given (-)-epicatechin [15, 16], a substance also found in teas. Green tea has also been shown to enhance in vitro insulin activity, and the primary active component in green tea was shown to be epigallocatechin gallate [17]. Previous studies have focused mostly on changes in blood glucose [14–16], and there was no report on the effect of green tea on insulin sensitivity. The present study was therefore designed to further evaluate the effects of green tea supplementation on insulin resistance, hypertension, and the glucose transporters I & IV contents in adipose tissue in the fructose-fed rat model.

Materials and methods

Preparation of green tea

Green tea, which was manufactured from the same batch of summer tea leaves of TTES No. 12 variety, was provided by the Taiwan Tea Experiment Station. It was ground to a powder and passed through a 30 mesh sieve. Tea infusion was prepared according to the standard method of Taiwan Tea Experiment Station. Ten grams of tea powder was soaked for 5 min in 500 mL of water at 100 °C, then filtered, and the filtrate was freeze-dried and the lyophilized powder was stored in a desiccator. The freeze-dried green tea extract contained Epicatechin 18.53 mg/g extract, Epicatechin gallate 21.51 mg/g extract, Epigallocatechin 57.87 mg/g extract, and Epigallocatechin gallate 199.49 mg/g extract. For use, 0.5 g of the lyophilized powder was dissolved in 100 mL of deionized distilled water.

Animals and diets

Male Sprague-Dawley rats weighing 200 to 250 g were housed three to a cage in an air-conditioned room (22 °C ± 2 °C) on a 12-hour light cycle (6:00 AM to 6:00 PM). These animals were maintained according to the guidelines established in "Taiwan Government Guide for the Care and Use of Laboratory Animals." The rats were divided into three groups of 8 animals: a control group that was given deionized distilled water to drink and fed standard rat chow (Purina, St Louis, MO) composed of 60 % vegetable starch, 12 % fat, and 28 % protein; a fructose group that was given deionized distilled water and fed a diet of 66 % fructose, 12 % fat, and 22 % protein (Teklad, Madison, WI) as a percentage of total calories; and a fructose/green tea group fed the same fructose-rich diet, but given green tea instead of water. During the 12 weeks study period, fresh water or green tea was provided daily at 6:00 PM. Blood pressure was measured twice a week, and an oral glucose tolerance test performed after 12 weeks of diet supplementation. At the end of the experiment, the rats were decapitated after overnight fasting, blood samples collected in heparinized tubes, and the plasma separated by centrifugation and stored at – 20 °C until assayed for triglyceride (TG), free fatty acid (FFA), glucose, and insulin. The epididymal fat pads from all rats in the same group were pooled and adipocytes isolated and tested for insulin binding, glucose uptake, and their content of glucose transporters I (GLUT I) and IV (GLUT IV), as described below.

Analytical methods

Blood pressure (BP) was measured using a tail-cuff method and a Narco Bio-System Physiograph (Houston, TX) [18]. The rats were transported to a quiet environment and kept in cages with free access to water/green tea. The small animal unit of the equipment has a rat holder base with a built-in warming element which allows the ambient temperature to be increased to 37 °C, thus maintaining adequate circulation in the rat's tail to allow reliable measurement of the systolic BP. The mean

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of five consecutive readings was calculated for each BP measurement.

After 12 weeks on their diets, the rats were subjected to an oral glucose tolerance test (OGTT) as described by Whittington et al. [19]. After overnight fasting, a 0-hour blood sample (0.5 mL) was taken by cutting the tail tip, then a glucose solution (2 g/mL/kg body weight) was immediately administered by gavage. Four more blood samples were taken from the tail vein at 30, 60, 90, and 120 minutes after glucose administration. All blood samples were collected in Eppendorf tubes pre-rinsed with heparin solution (10 IU/mL), and were kept on ice until centrifuged (3,500 × g at 4 °C for 30 minutes) to separate the plasma. The plasma specimens were frozen at – 20 °C until assayed for glucose and insulin.

The concentration of plasma glucose was measured using a glucose analyzer (Model 2300; Yellow Springs Instruments, Yellow Springs, OH). Plasma insulin was measured using a radioimmunoassay developed in our laboratory [20]. Plasma level of TG was measured using a commercial kit (Merck, Germany) and FFA levels were measured by colorimetry [21].

Insulin binding and glucose uptake of adipocytes

The epididymal fat pads from all rats in each group were pooled and adipocytes isolated using the method of Rodbell [22] with minor modifications. Fat pads from 2–3 rats were pooled for each sample of test. Briefly, the fat tissue was minced and incubated for 1 hour at 37 °C in Krebs-Ringer bicarbonate (KRB) buffer solution containing 1 % bovine serum albumin (KRBB) and 0.1 % collagenase in an oxygen-rich shaking chamber (CO_2:O_2, 5:95; 75 strokes/min). The suspension was then filtered through nylon mesh (400 µm) and centrifuged at 100 rpm for 1 minute. The supernatant containing the adipocytes was harvested and the cells washed twice with, and resuspended, in KRBB. The number of adipocytes was determined after fixation with 2 % osmium tetraoxide. The lipocrit was measured and used for normalization of the fat cell number before, during, and after each experiment.

Binding of insulin to adipocytes was measured as described previously [23]. Briefly, a 400 µL aliquot of adipocytes (2×10^5 cells) was mixed with 50 µL of [^{125}I]insulin (final concentration 0.25 nM; ~5×10^5 cpm) and 50 µl of unlabeled insulin (none, or final concentration 1 pM to 1 µM), then the mixture was incubated for 30 minutes at 37 °C in a 95 % oxygen chamber with gentle shaking (75 strokes/min). Three hundred microliters of the cell suspension was transferred to a new centrifuge tube containing 200 µL of silicon oil and the mixture centrifuged at 1,000 × g for 90 s, then the cellular layer was transferred to a vial containing a 4 mL of cocktail for the counting of radioactivity using a liquid scintillation counter.

Insulin-stimulated glucose uptake by adipocytes was determined by measuring the transport of 2-deoxyglucose (2-DG) into the cells as described by Garvey et al. [24] with some modifications. Briefly, 400 µL of adipocyte suspension was mixed with 50 µl of insulin (none, or final concentration 1 pM to 100 nM) and incubated for 30 minutes as described above. Then 50 µL [^{3}H]-labeled 2-DG was added (final concentration 50 µM), and incubation continued for 3 minutes. The reaction was terminated by addition of 200 µL of unlabelled 2-DG (final concentration 0.14 M), then 300 µL was transferred to a new vial containing 200 µL silicon oil and processed as described for the insulin binding assay.

Glucose transporter content

A crude membrane fraction was prepared using the method of Leu et al. [25] with modifications. The adipocytes were washed with KRB buffer and homogenized in 8 mL of ice-cold buffer A containing 250 mM sucrose, 20 mM HEPES, 1 mM EDTA, and 1 % protease inhibitor cocktail (Merck), pH 7.4. To remove the fat cake, the homogenate was centrifuged at 6,000 × g for 10 min at 4 °C, then the supernatant was aspirated and centrifuged at 250,000 × g for 1.5 hours at 4 °C. The pellet (total cellular membranes) was resuspended in buffer B (20 mM HEPES, 1 mM EDTA, pH 7.4).

The adipocyte crude membrane fraction was subjected to electrophoresis on 10 % sodium dodecyl sulfate (SDS) polyacrylamide gels and electrophoretically transferred to a PVDF membrane [26]. The membrane was then blocked for 1 hour at room temperature with PBS buffer containing 5 % skimmed milk and 0.5 % Tween-20 (v/v), and incubated for 1 hour at room temperature with polyclonal rabbit anti-Glut1 (Biologicals, Southbridge, MA) or anti-Glut4 (Biologicals, Southbridge, MA) antibody. The blots were then developed using the enhanced chemiluminescence method (ECL, Amersham), using horseradish peroxidase-conjugated goat anti-rabbit IgG (1 hour at room temperature) (ORGANON TEKNIKA, Belgium). Quantification of the relative band intensity was performed by laser scanning densitometry.

Statistical analysis

The individual data for plasma glucose, insulin, TG, FFA, and the total area under the curve (AUC) for glucose and insulin were expressed as the mean ± SD (n = 8) and compared using Student's *t* test. The adipocytes were isolated from the pooled fat pads of all the rats in each group and assays were performed in triplicate. The insulin binding and glucose uptake data were expressed as the mean ± SD (n = 3). Statistical analyses were per-

formed using a program provided in the Microsoft Excel Kit (GreyMatter International, Cambridge, MA). The difference between any two groups was considered statistically significant when the *P* value was less than 0.05.

Results

No weight difference was found between the groups at any time-point over the 12-week period, showing that the dietary supplement did not affect growth (data not shown). The systolic BP in the fructose group began to increase after two weeks, and significant differences were found between the fructose and control groups from week 3 to the end of the experiment, showing that high fructose supplementation resulted in elevated blood pressure. The fructose/green tea group also showed an increase in BP compared to the control group, but this was significantly lower than that seen in the fructose group (Fig. 1).

After 12 weeks of diet supplementation, the basal fasting plasma glucose and insulin levels in the fructose group were significantly higher than those in the control group, while no differences were found between the fructose/green tea and control groups (Fig. 2). During the 2 hours following glucose ingestion, plasma glucose levels in the fructose group were significantly higher than those in the control group at 60, 90, and 120 minutes, indicating that the rats in the fructose group had developed hyperglycemia (Fig. 2A). There were no differences at any time-point in plasma glucose levels between the fructose/green tea group and the control group. Plasma insulin levels (Fig. 2B) were significantly higher in the fructose group than in the control group over the entire 2 hour period. Plasma insulin levels in the fructose/green tea group were significantly lower at 90 and 120 minutes than in the fructose group, but there was no difference at any time-point between the fructose/green tea group and the control group. The total area under the curve (AUC) for glucose was 293 ± 10, 322 ± 17, and 306±25 mg·h/dL, and that for insulin 40 ± 3, 52 ± 9, and 44 ± 4 μU·h/mL in the control, fruc-

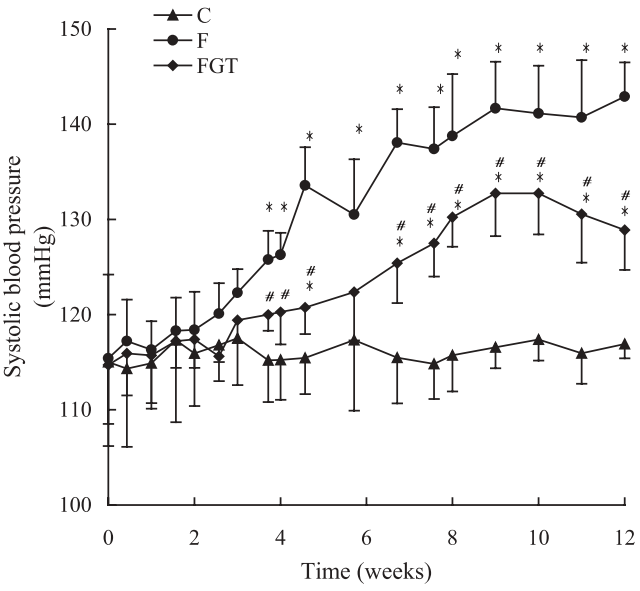

Fig. 1 Blood pressure changes in rats during 12 weeks on the different diets. Group C (▲) was fed standard chow with plain water, group F (●) a high fructose diet with plain water, and group FGT (◆) the same high fructose diet with green tea.Values are shown as the mean ± SD. *p < 0.05 compared to group C. #p < 0.05 compared to group F

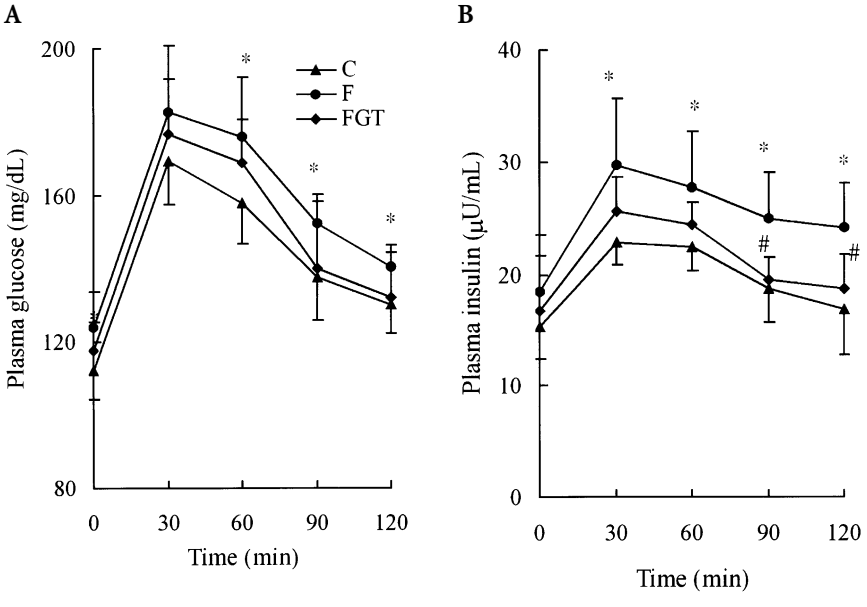

Fig. 2 Changes in plasma glucose (**A**) and insulin (**B**) in rats in an oral glucose tolerance test (2 g glucose/kg BW) performed after 12 weeks on the different diets. Values are shown as the mean ± SD. *p < 0.05 compared to group C. #p < 0.05 compared to group F

tose, and fructose/green tea group, respectively. The glucose and insulin responses of the fructose group were significantly higher than those of the control group ($p = 0.006$ and 0.016 for glucose and insulin, respectively). Green tea supplementation led to a decrease in responses, and no differences were found between the fructose/green tea and control groups ($p = 0.30$ and 0.14 for glucose and insulin, respectively).

At sacrifice, there were no significant differences between the groups in body weight or epididymal fat pad weight, but the relative epididymal fat pad weight was significantly higher in the fructose group (Table 1). The concentrations of fasting plasma glucose, insulin, TG, and FFA in the three groups are also analyzed (Table 1). Fasting hyperinsulinemia and fasting hyperglycemia were observed in the fructose group, confirming the OGTT finding. Plasma TG levels in the fructose group were significantly higher than in the control or fructose/green tea group. There was no significant difference in plasma FFA levels between the three groups.

Insulin stimulated glucose uptake by adipocytes in a dose-dependent manner (Fig. 3). Insulin-stimulated adipocyte glucose uptake was significantly lower in the fructose group than in the control group, but there was no difference between the fructose/green tea and control groups. Adipocyte insulin binding tests provided further evidence for the detrimental effect of the fructose diet (Fig. 4), since the maximum insulin binding in the fructose group was significantly lower than that in the control and fructose/green tea groups. There was no significant difference between the results for the control and fructose/green tea groups, showing that green tea supplementation prevented the decrease in the maximum binding of insulin caused by the fructose diet.

To further evaluate the possible mechanism by which green tea improved insulin resistance, we measured the glucose transporter content of adipocytes. When the amounts of Glut I and Glut IV protein in a crude membrane preparation of isolated adipocytes were quantified by Western blotting, no significant difference was seen between the three groups in terms of Glut I

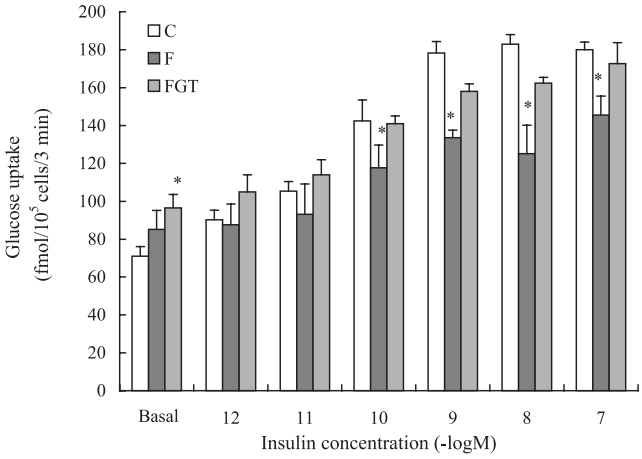

Fig. 3 Glucose transport by adipocytes isolated from rats after 12 weeks on the different diets. Values are shown as the mean ± SD. *p < 0.05 compared to group C

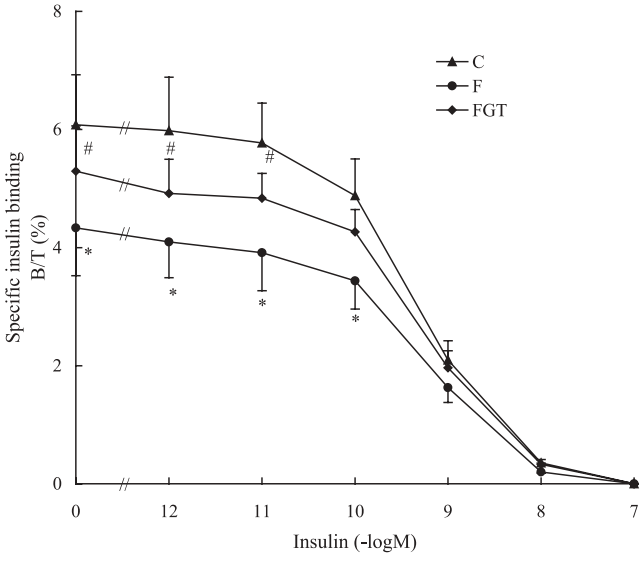

Fig. 4 Insulin binding of adipocytes isolated from rats after 12 weeks on the different diets. Values are shown as the mean ± SD. *p < 0.05 compared to group C. #p < 0.05 compared to group F

Table 1 Body weight, epididymal fat pad weight, relative epididymal fat pad weight, and fasting plasma levels of glucose, insulin, triglyceride, and free fatty acid at the end of the various 12-week diets

Group	Control	Fructose	Green tea
Body weight (g)	493±57	484±52	499±32
Epididymal fat pad weight (g)	5.4±1.88	6.81±1.32	5.77±1.05
Relative epididymal fat pad weight (g/100 g BW)	1.05±0.29	1.34±0.15*	1.13±0.22
Fasting plasma glucose (mg/dL)	96.8±5.5	107.4±9.7*	104.0±8.4
Fasting plasma insulin (μU/mL)	9.9±4.8	18.5±6.1*	13.4±6.4
Fasting plasma triglyceride (mg/dL)	56.1±10.1	86.2±12.9*	54.6±8.5#
Fasting plasma free fatty acid (μM)	293.6±19.8	289.5±34.4	262.1±29.7

[a] Values are shown as the mean ± SD; * $p < 0.05$ compared to group C; # $p < 0.05$ compared to group F

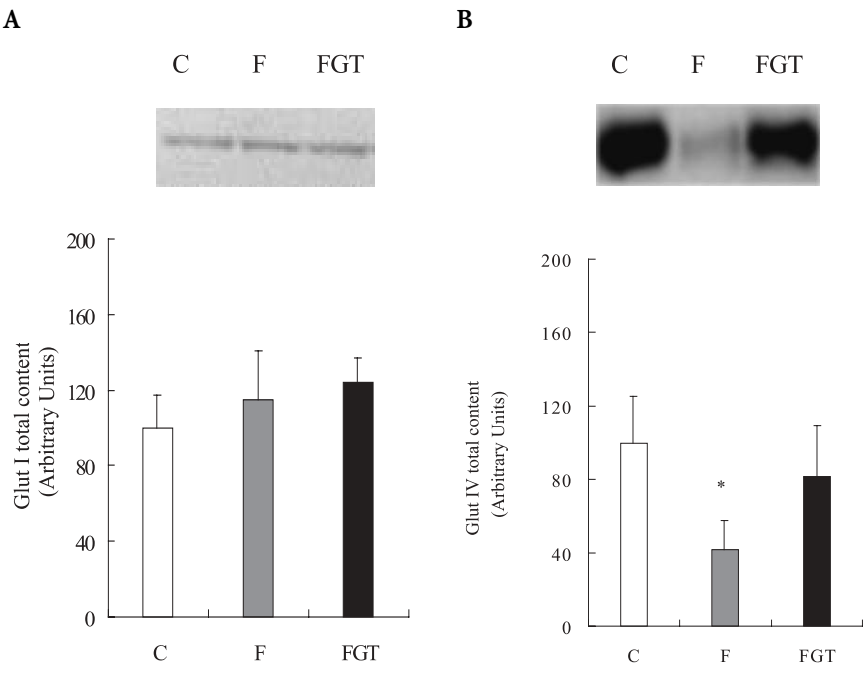

Fig. 5 Glucose transporter I (**A**) and glucose transporter IV (**B**) contents in adipocytes isolated from rats after 12 weeks on the different diets. *$p < 0.05$ compared to group C

(Fig. 5A*)*. In contrast, as compared with the control group, reduction in Glut IV protein levels in the fructose and fructose/green tea groups were 58% and 19%, respectively (Fig. 5B*)*. The data indicate that high fructose ingestion resulted in a decreased Glut IV content, and this effect could be overcome by green tea supplementation.

Discussion

Most previous studies on animal models of diabetes have involved the use of drugs to destroy β cells, resulting in a lack of insulin secretion, leading to diabetes. This type of diabetic model is very similar to type I diabetes mellitus, but not type II, the form from which most diabetic patients suffer. Compared to the general population, patients with type II diabetes have a much higher cardiovascular morbidity and mortality, as they present many contributory risk factors, such as hyperlipidemia, hyperinsulinemia, and hypertension [27]. Although the evidence for interrelationships between these risk factors is so strong that they are now collectively called "syndrome X," the underlying biochemical mechanism for these associations is not clear [1]. The fructose rat model provides an ideal means of investigating the causes of a simulated syndrome X in animals. In addition, this model provides convincing evidence that dietary imbalance can initiate the development of syndrome X. Previous research has shown that high fructose supplementation can induce hyperinsulinemia, hypertension, hypertriglyceridemia, and insulin resistance in rats [28]. Our study in Sprague-Dawley rats fed a diet in which fructose replaced carbohydrates produced similar results, as the animals developed elevated blood pressure, hyperinsulinemia, and hyperlipidemia.

The cause of the elevated blood pressure induced by a high fructose diet is unknown. It has been suggested to be secondary to hyperinsulinemia, which leads to increased sympathetic activity and decreased adrenal medullary activity [29]. In addition, it has been assumed to be related to levels of endothelin-1 [30], nitric oxide [31], and angiotensin II [32]. The effect of green tea in counteracting the fructose effect on the BP was expected, as a study on a large human population showed that the systolic BP is inversely related to tea consumption [33]. It has also been shown that epicatechin derivatives from green tea leaves can relax rat mesenteric arteries, probably by inhibiting Ca^{2+} influx [34] and increasing nitric oxide release [35].

In the OGTT, the significantly higher basal fasting plasma glucose and insulin levels in the fructose group indicated insulin resistance. Our findings of reduced adipocyte insulin binding and insulin-stimulated glucose uptake in the fructose group were consistent with the OGTT results. These results confirm those of a previous study demonstrating that fructose feeding leads to glucose intolerance and decreased insulin sensitivity in intact animals [36]. The mechanism of fructose-induced insulin resistance is not clear. Several hypotheses have been advanced to explain insulin resistance in fructose-fed rats. Fructose feeding can, for example, alter signal transduction in insulin target cells [37], the activity of several enzymes regulating hepatic carbohydrate me-

tabolism [38], and the plasma magnesium concentration [39]. In this study, green tea supplementation had a beneficial effect on the insulin sensitivity of fructose-fed rats. Numerous studies have suggested a beneficial effect of green tea on glucose homeostasis. For example, Gomes et al. [14] found that aqueous extracts of green tea or black tea significantly reduce blood glucose levels and have an antidiabetic effect in rats, while Chakavarthy et al. [16] showed that (-)-epicatechin, a naturally occurring flavonoid in tea, reverses the diabetogenic action of alloxan in rats. Nevertheless, until the present study, no mechanism had been proposed to explain the effect of green tea.

Tissue-specific regulation of the expression of the glucose transporter IV in adipose tissue appears to play a pivotal role in the development of insulin resistance [40], and high-fat feed is associated with profound impairment of GLUT IV expression and insulin-stimulated glucose uptake in rat adipocytes [41], suggesting that dietary imbalance can cause abnormality of GLUT IV gene expression. In the present study, we found that adipocytes in the fructose group had the lower GLUT IV content than in the control group. This demonstrates, for the first time, that a fructose diet can decrease the GLUT IV content of rat adipocytes, and that this decrease may lead to insulin resistance. In addition, our results showed that green tea supplementation reversed the effect of fructose of GLUT IV content, and increased insulin sensitivity.

Our results demonstrated that dietary fructose resulted in an increase in plasma TG levels and confirmed the hypertriglyceridemic reaction to fructose or sucrose reported by many investigators. Sebokova et al. [42] reported that the underlying molecular mechanism involves an increase in gene expression of several enzymes, including acetyl-coenzyme A carboxylase and fatty acid synthase, which are involved in TG synthesis in the liver and adipose tissue, and malic enzyme, which supplies NADPH for the synthesis of long-chain fatty acids. The epidemiological study has also shown an inverse association between tea consumption and coronary heart disease [33]. Increased consumption of green tea has been associated with decreased serum levels of TG and cholesterol [43]. Some studies have indicated that green tea has a hypolipidemic activity in animal models which is due to its effect on the absorption of dietary fat [44] and the inhibition of acetyl-co A carboxylase activity [45].

Previous studies have shown that enhanced lipid peroxidation is a consequence of experimentally induced diabetes mellitus, and have indicated that oxidative stress may be involved in the genesis of diabetic complications [46]. Faure et al. [47] found that a fructose diet had a deleterious effect on the antioxidant defense system in rats, and that supplementation with the antioxidant, vitamin E, could improve the oxidative stress and have a beneficial effect on insulin sensitivity. These observations suggest that enhanced oxidative stress could also be associated with insulin resistance or its metabolic consequences, and that antioxidant supplementation could reverse these metabolic defects. Since green tea has free radical scavenging activity [7] and an oxidative stress lowering effect [48], we suggest that this antioxidant activity might be another explanation for the antidiabetic effect of green tea in a fructose-fed rat model.

Broadhurst et al. [49], who treated rat epididymal fat pad adipocytes with aqueous extracts of medicinal plants, found that green or black tea stimulated adipocyte glucose uptake and concluded that they have an insulin-like effect. They also added polyvinyl pyrrolidone, which absorbs polyphenols, to the insulin-like medicinal plant aqueous extracts and found that the activity was lost, and therefore suggested that the insulin-like effect might be due to polyphenols. Anderson and Polansky [17] also have proved that green tea can potentiate in vitro insulin activity, and the primary active component in green tea was shown to be epigallocatechin gallate. Kao et al. [50] repeatedly injected SD rats i. p. with epigallocatechin gallate (EGCG) and found that levels of endocrine factors, such as insulin, glucose, TG, and cholesterol, were lowered. EGCG is therefore regarded as having a modulating effect on the endocrine system and might have improving effects on obesity, diabetes, and cardiovascular disease. Therefore, we suggested that green tea increases insulin sensitivity might be the consequence of polyphenols that enhance insulin activity. Further studies are needed to verify the mechanism of green tea action on insulin activity.

We used adipocytes as a model to investigate insulin resistance in this study. Although this is an accepted model, the effect of green tea on other insulin target organs, such as liver and muscle, should be further evaluated to confirm the overall effect of green tea in fructose-fed rat. In the present study, green tea was supplied in the form of regular drink to fructose-fed rats. We were not able to attribute our findings solely to polyphenol intake nor to predict the impact of green tea supplementation on diabetes mellitus. Nevertheless, we have demonstrated that green tea supplementation can improve insulin sensitivity in an insulin-resistance animal model. In conclusion, in this study, we found that Sprague-Dawley rats fed a high fructose diet develop elevated blood pressure, fasting hyperinsulinemia, and hyper-triglyceridemia, and have a reduced GLUT IV content, and that green tea supplementation improves these metabolic defects.

Acknowledgments We thank the Taiwan Tea Experiment Station for providing the green tea. The financial support from the Department of Health is also acknowledged.

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