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Effect of Compositae Plants on Protein Levels in Streptozotocin-induced Diabetic Rats

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ABSTRACT The investigation assessed the influence of Compositae plants consumption on the protein profile in streptozotocin (STZ)-induced diabetic rats. Diabetes was induced in Sprague-Dawley rats by injection of STZ (45 mg/kg body weight) into tail vein. The rats were randomly assigned to five groups: normal and STZ-control fed an AIN-93 diet, and groups whose diets were supplemented with 10% Compositae powder containing *Artemisia iwayomogi* (*A. iwayomogi*), *Atractylodes lancea* (*A. lancea*) or *Taraxacum mongolicum* (*T. mongolicum*). To observe the effects of Compositae plants in the animal model, the levels of protein in liver, kidney, lung, pancreas, and brain were determined after 4 weeks. The level of protein in kidney increased significantly in rats receiving the *A. iwayomogi*- and *T. mongolicum*-supplemented diet compared to the STZ-control group. The level of protein in lung was increased significantly in the *A. iwayomogi*-supplemented group. Blood glucose level correlated well with brain protein level but did not correlate with other protein levels. Also, blood glucose correlated inversely with kidney, lung and brain protein levels. It is suggested that supplementation with *A. iwayomogi* in diabetic rats leads elevates protein in kidney and lung.

KEYWORDS: *Artemisia iwayomogi, Atractylodes lancea, Taraxacum mongolicum,* protein level

INTRODUCTION

Diabetes is the most common metabolic disorder and its prevalence is increasing in developing countries in most of the world (Zimmet 1992; King et al 1993). Regions with greatest potential are Asia and Africa, where diabetes mellitus rates could rise 2~3 fold from the present rates (American Diabetes Association 1997).

The search for more effective and safe hypoglycemic agents from natural sources has been continuing because synthetic hypoglycemic agents for diabetes treatment may cause potent side effects including hematological coma and disturbances of the liver and kidney (Larner 1985). Plant-derived drugs are considered to be less toxic and less prone to side effects than synthetically-derived drugs. For this reason, interest in hypoglycemic agents from natural sources has been increasing.

Many traditional plant treatments for diabetes mellitus are used throughout the world. Medicinal plants continue to provide valuable therapeutic agents, both in modern medicine and in ancient traditional systems. More than 1,200 plant species have been used empirically for their alleged hypoglycemic activity (Marles and Farnsworth 1995). Despite this, few traditional antidiabetic plants have received proper scientific screening. More recently, there has been renewed interest in plants as pharmaceuticals because they synthesize a variety of secondary metabolites with antioxidant potential, which can play a major role in protection against molecular damage induced by reactive oxygen species (Cao et al 1997; Vaya et al 1997).

Artemisia iwayomogi (*A. iwayomogi*), a member of the Compositae, is a perennial herb ubiquitously found in Korea (Park 1999). It is the source of important medicinal materials that are utilized in traditional Asian medicines, refereed to in Korea as 'Iinjin', which have been utilized traditionally in Korea, China and Japan for the treatment of diuresis and as anti-inflammatory agents (The Korean Herbal Pharmacopoeia 2002). *A. iwayomogi* has been traditionally used for treatment of various liver diseases including hepatitis and has been shown to have various biological functions. The aerial part of *A. iwayomogi* has traditionally been used for antitumor, immunomodulating, antimutagenic, antioxidant, antibacterial, antifungal, liver protective effect, and choleretic purposes in Korea (Bae et al 1992; Kim et al 1997; Lee et al 1998; Song et al 2001a; Yu

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et al 2003). The rhizomes of *Atractylodes lancea* (*A. lancea*) have been used as an important crude drug since antiquity. It has traditionally been used as a stomach ailment remedy in China and Japan, and also as an important crude drug against rheumatic diseases, digestive disorders, night blindness and influenza (Xio 2002). In the Korea and Japanese pharmacopoeias, *A. lancea* was prescribed in traditional medicine as a diuretic and gastric drug (Kitajima et al 2003). It has been reported that *A. lancea* improves stomach damage through antiulcer effects (Kubo et al 1983) and inhibition of gastric secretion (Nogami et al 1986), and inhibits angiogenesis in adjuvant-induced granuloma in mice (Kimura et al 1991).

Fresh leaves of *Taraxacum mongolicum* (*T. mongolicum*) have long been used by local people as a vegetable food in northern China. It is most commonly used by Chinese local herbal physicians. Traditionally, dried whole plants of *T. mongolicum* are used for the treatment of boils, sores, mastitis, lymphadenitis, eye inflammation, sore throat, lung and breast abscesses, acute appendictis, jaundice, and urinary tract infections (Li 1992; Ou and Li 1994). In addition, in vitro antifungal, antileptospiral, and antiviral effects of the herb have also been documented (Li 1992). *T. mongolicum* has received wide attention due to its remarkable curative effect especially for mastopathy, faucitis, furuncles, and nephritis (Song et al 2001b). It is a representative anticancer medicinal herb that has been traditionally used for cancer treatments in China, Japan and Korea.

We have previously reported that supplementation of Compositae plants produces hypoglycemic and hypolipidemic activities in streptozotocin (STZ)-induced diabetic rats that are absent in the STZ-control group (Han et al 2009). The present study extended these observations by examining the influence of the oral intake of Compositae plants on the levels of protein in different tissues of STZ-induced diabetic rats.

MATERIALS AND METHODS

Plant material

A. iwayomogi was purchased from Chungsoo Pharmaceutical Co. (Incheon, Korea) and *A. lancea* and *T. mongolicum* were purchased from Human Herb (Gyeongsanshi, Korea). The dried plants were powdered with an electric grinder.

Animals and induction of diabetes

Male Sprague-Dawley rats (230 g, 7 weeks old) were bred in the Samtako (Osanshi, Kyunggido, Korea) and fed a standard pellet laboratory diet and provided with distilled water ad libitum. Diabetes was induced by a single intravenous injection of STZ (Sigma-Aldrich, St. Louis, MO, USA; 45 mg/kg body weight, prepared in 10 mM citrate buffer, pH 4.5) into the tail vein of rats after fasting for 16 h. Normal rats were injected with equal volume of citrate buffer. After 24 h, rats having blood glucose levels >300 mg/dL were considered diabetic.

Experimental design and treatment

Rats were divided into five groups; normal, STZ-control, *A. iwayomogi* -supplemented group, *A. lancea*-supplemented group and *T. mongolicum*-supplemented group. Normal and STZ-control groups received AIN-93 diet (Reeves 1997) and the experimental groups received powdered form the particular plant, incorporated at a 10% level at the expense of an equivalent amount of corn starch, casein and soybean oil in the AIN-93 diet. Diets were supplied ad libitum to the rats for 4 weeks after the confirmation of diabetes.

Collection of samples

At the end of the experimental period, the rats were anesthetized by ethyl ether and killed by decapitation. Liver, kidney, lung, pancreas and brain were immediately removed, weighed and washed using cold phosphate buffered saline, pH 7.4. Tissues were minced and homogenized (10% w/v), separately, in 1.15% KCl buffer in a homogenizer.

Determination of tissue protein

Tissue proteins from liver, kidney, lung, pancreas and brain were determined using bovine serum albumin as a standard, and the optical density was measured at 750 nm (Lowry et al 1951).

Statistical analysis

Statistical evaluation was done using one way analysis of variance (ANOVA) followed by Duncan's multiple range test by using SPSS ver. 17.0 for windows. The significance level was set at $p<0.05$ between treatment. The correlation coefficients were calculated.

RESULTS AND DISCUSSION

Preliminary studies in our laboratory had demonstrated the capacity of the powder of Compositae plants to decrease blood glucose when used to supplement the diet of STZ diabetic rats. The present study investigated the protein levels in different tissue of the Compositae plants in STZ-induced diabetic rats.

Protein levels

The levels of protein in liver, kidney, lung, pancreas and brain in the experimental groups are shown in Figs. 1~5. The level of protein in kidney (10.1%) and lung (17.8%) were significantly decreased in STZ-control rats when compared to those of normal rats. On the other hand, no change was observed in the level of liver, pancreas and brain in STZ-control rats when compared to that of normal rats. The protein levels in kidney (20.1%) and lung (14.9%) were

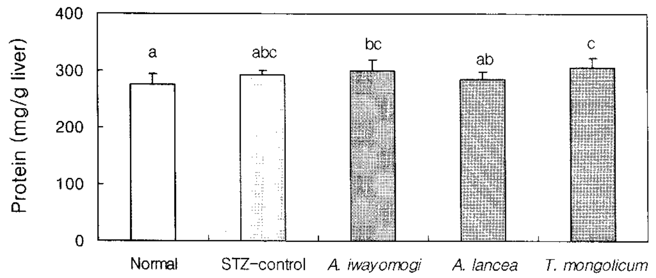

Fig. 1. Protein levels in liver of normal and diabetic rats fed Compositae plants. Values are expressed as mean±SD of seven rats from each group and represent mg/g tissue. Values with the different letters on a bar are significantly different at $p<0.05$ by Duncan's multiple range test.

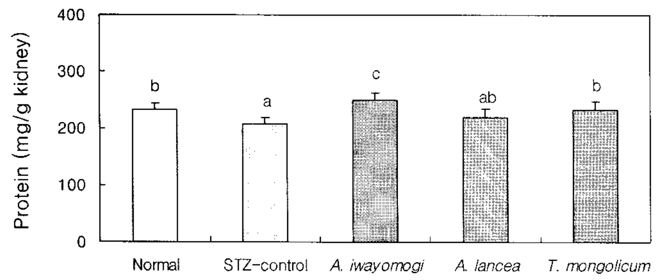

Fig. 2. Protein levels in kidney of normal and diabetic rats fed Compositae plants. Values are expressed as mean±SD of seven rats from each group and represent mg/g tissue. Values with the different letters on a bar are significantly different at $p<0.05$ by Duncan's multiple range test.

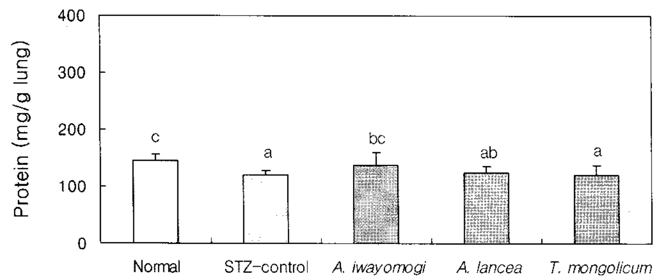

Fig. 3. Protein levels in lung of normal and diabetic rats fed Compositae plants. Values are expressed as mean±SD of seven rats from each group and represent mg/g tissue. Values with the different letters on a bar are significantly different at $p<0.05$ by Duncan's multiple range test.

significantly increased in diabetic rats whose diets were supplemented with *A. iwayomogi* when compared to those of STZ-control rats. The protein levels in kidney (11.6%) were significantly increased in the diet of diabetic rats supplemented with *T. mongolicum* when compared to those of STZ-control rats. Diabetes mellitus is characterized by derangement in metabolism not only of glucose and fat but also of protein (Gougeon et al 1995). However, protein has received less attention that fat and glucose, in terms of both metabolic alterations and nutritional implications. The present results revealed reduction in protein levels in kidney.

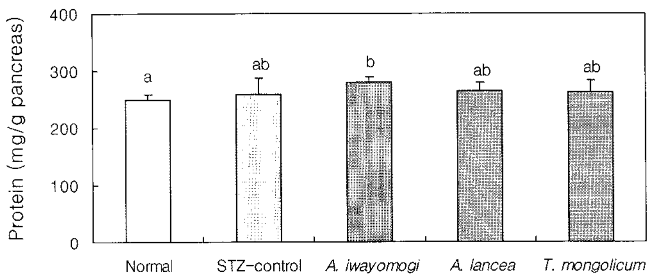

Fig. 4. Protein levels in pancreas of normal and diabetic rats fed Compositae plants. Values are expressed as mean±SD of seven rats from each group and represent mg/g tissue. Values with the different letters on a bar are significantly different at $p<0.05$ by Duncan's multiple range test.

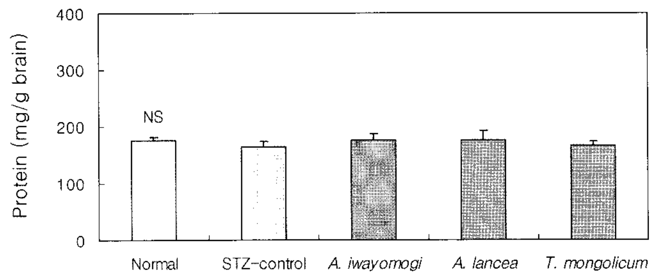

Fig. 5. Protein levels in brain of normal and diabetic rats fed Compositae plants. Values are expressed as mean±SD of seven rats from each group and represent mg/g tissue. Values with the different letters on a bar are significantly different at $p<0.05$ by Duncan's multiple range test.

Table 1. Pearson correlation analysis between blood glucose level and protein level

Variable	Correlation coefficient	p value
Liver protein	0.311	0.069
Kidney protein	-0.086	0.623
Lung protein	-0.215	0.215
Pancreas protein	0.096	0.584
Brain protein	-0.385	0.022

STZ injection incrementally increased the protein level in liver, which was accompanied by corresponding incremental increase in the DNA content (Calle et al 2008). Treatment of STZ-induced diabetic rats with Compositae plants only marginally altered the elevated values of protein induced in the diabetic rats. Rats fed a diet supplemented with *A. iwayomogi* had significantly higher protein levels in the kidney compared with normal rats. *T. mongolicum* consumption also significantly increased protein levels in lung in diabetic rats compared with the STZ-control group. Distinct metabolic renal alterations lead to a negative nitrogen balance, enhanced proteolysis and lowered protein synthesis in experimental diabetes (Pathak and Dhawan 1998). The results indicate the therapeutic potential of *A. iwayomogi* and *T. mongolicum* in remediating insulin deficiency.

Correlation between blood glucose and protein level

The correlation coefficient of blood glucose level was 0.331 in the liver, -0.086 in the kidney, -0.215 in the lung, 0.096 in the pancreas and -0.385 in the brain. There was a significant correlation between the level of blood glucose and level of brain protein (p<0.05). There were no significant correlations with changes in blood glucose and other protein levels.

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