6-Methylsulfinylhexyl Isothiocyanate, an Antioxidant Derived from *Wasabia japonica* MATUM, Ameliorates Diabetic Nephropathy in Type 2 Diabetic Mice

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Many studies have examined the protective effects of antioxidative agents against diabetic nephropathy, using various models. 6-Methylsulfinylhexyl isothiocyanate (6-MSITC) isolated from wasabi (*Wasabia japonica* MATUM) induces glutathione S-transferase in vitro, thus 6-MSITC may act as an antioxidant in vivo. The aim of this study was to examine whether wasabi powder (WP) and 6-MSITC suppress oxidative stress in vivo and inhibit the impairment of renal function and diabetic nephropathy, using type 2 diabetic mice. KK-A' type 2 diabetic mice were assigned to three groups (n = 10 each); control mice were fed normal chow (CRF-1) and two experimental groups were fed CRF-1 containing 0.5% WP or 0.03% 6-MSITC for 4 wk. Urine volume, urinary albumin excretion, and creatinine clearance were significantly lower in the 6-MSITC group than in the control group. There was statistically no difference in TBARS or other biomarkers of oxidative stress among the three groups. However, urinary 8-hydroxy-2'-deoxyguanosine (8-0HdG), one of the markers of oxidative stress tended to be lower in the 6-MSITC group than in the control group. In conclusion, the present results show that a sufficient supply of dietary 6-MSITC may prevent or delay renal dysfunction in diabetes by protecting against oxidative stress, and that dietary 6-MSITC may have beneficial effects on diabetic complications in type 2 diabetic mice.

Keywords: wasabi, antioxidant, diabetic nephropathy, 6-methylsulfinylhexyl isothiocyanate (6-MSITC).

Introduction

Diabetic nephropathy is a major complication of long-term diabetes mellitus (Selby et al., 1990). Many pathogenetic mechanisms contribute to the development of diabetic nephropathy including oxidative stress (Brownlee, 1994). Hyperglycemia causes the auto-oxidation of glucose (Wolff & Dean, 1987), the glycation of proteins and the activation of polyol metabolism (Lee & Chung, 1999). These changes accelerate generation of reactive oxygen species (ROS), and result in an increase in the lipid peroxidation of erythrocytes, endothelial cells and glomerular mesangial cells (Jain, 1989; Lorenzi, 1992). In addition, free radicals promote the glycosylation of proteins and may initiate a series of autoxidative reactions that cause the accumulation of advanced glycosylation end products (AGEs) in tissues (Brownlee, 1994). These compounds interfere with proliferation and perturb production of the extracellular matrix by glomerular cells. Oxidative stress contributes to the development of diabetic microangiopathic and macroangiopathic complications. Therefore, treatment with antioxidants may prevent or reverse abnormalities associated with diabetic nephropathy.

Wasabi is a very popular pungent spice in Japanese meals. A major wasabi flavor compound, 6-methylsulfinylhexyl isothiocyanate (6-MSITC), has been shown to have antimicrobial (Ono et al., 1998; Kiba et al., 2003), anticancer, and antiplatelet activities (Morimitsu et al., 2000). Recently, it has been reported that 6-MSITC also expresses an antioxidative activity. Kinae et al. (2000) reported the antioxidative activity of wasabi samples determined by Fenton reaction-lipid peroxidation system in vitro. Morimitsu et al. (2002) have reported that 6-MSITC activated the antioxidant response element (ARE), induced nuclear localization of the transcription factor NrF2 that binds to ARE, and induced phase II enzymes such as the glutathione S-transferase (GST). Thus, 6-MSITC may act as an antioxidant agent in vivo. However, there have been no prior studies demonstrating a protective effect of dietary 6-MSITC against the diabetic nephropathy caused by oxidative stress.

In the present study, we demonstrated that 6-MSITC suppresses oxidative stress in vivo, and inhibits the impairment of renal function and diabetic nephropathy, using type 2 diabetic mice.
Materials and Methods

Materials  Authentic 6-MSITC was synthesized by the oxidation of 6-methylthiohexyl isothiocyanate provided by Kinjirushi (Nagoya, Japan). Rhizomes of wasabi were used for the preparation of wasabi powder (WP) by Kinjirushi. They were washed with water, frozen in liquid nitrogen, and then crushed. The frozen and crushed material (4.0 kg) was incubated at 37°C for 3 h to form maximum amounts of isothiocyanates, and then evaporated twice to remove volatile materials, which contain highly cytotoxic allyl isothiocyanate. Then it was heated at 80°C for 10 min in order to inactivate enzymes and sterilize microbes, air-dried at 50°C, crushed, and sifted. Contents of representative isothiocyanates contained in WP were determined by gas chromatography (Table 1). All other chemicals were purchased from Wako Pure Chemical Industries (Osaka, Japan). Ultraviolet absorption spectra were measured using a UV 1600 spectrophotometer (Shimadzu, Japan), and the fluorescence spectra were recorded using a RF 5000 spectrofluorophotometer (Shimadzu). Absorbance in a micro-ELISA plate was read using a Corona Electra MTP-300 microplate reader (Corona, Japan).

<table>
<thead>
<tr>
<th>Sample</th>
<th>Allyl isothiocyanate (%)</th>
<th>6-Methylthiohexyl isothiocyanate (%)</th>
<th>6-MSITC isothiocyanate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Raw material</td>
<td>0.247</td>
<td>0.003</td>
<td>0.038</td>
</tr>
<tr>
<td>WP</td>
<td>0.000</td>
<td>0.006</td>
<td>0.154</td>
</tr>
</tbody>
</table>

Experimental procedure  Male 6-wk old KK-A′/Ta Jcl (n = 30, Nihon Clea, Tokyo, Japan), hereditary type 2 diabetic mice were used (Iwatsuka et al., 1970). Mice were housed individually in plastic cages under controlled conditions (temperature 23 ± 1°C, humidity 55 ± 5%, light 08:00-20:00 h). All mice were treated in accordance with the NIH Guide for the Care and Use of Laboratory Animals. KK-A′ mice were allowed free access to water and a high fat diet containing 30% energy as fat, in order to induce obesity and diabetes for 2 wk before the experiment (Aoyama et al., 2000). After being fed the high fat diet, the mice were divided into three groups matched by body weight and fasting glucose level (n = 10 each). The control group was fed CRF-1 (Oriental Yeast, Tokyo), and the two experimental groups were fed CRF-1 containing 0.5% WP or 0.03% 6-MSITC for 4 wk They were allowed free access to water and a diet. The mice were then sacrificed by decapitation and blood was collected from the jugular vein. Gastrocnemius muscle, perirenal and epididymal white adipose tissue, the kidneys, and the livers were quickly removed and stored at −80°C.

Oral glucose tolerance test (OGTT)  OGTT was administered 3 wk after the mice had been fed the experimental diet. Mice were given a 1.0 mg/g body weight glucose solution by a stomach tube after fasting for 24 h. Blood samples to determine blood glucose were collected at 0, 30, 60, and 120 min after the administration of glucose from the tail vein. Concentrations of blood glucose were determined using an auto glucose analyzer (Glucocard, Kyoto Daiichi Kagaku, Japan) and plasma insulin concentrations were measured by enzyme-linked immunosorbent assay (ELISA) (Revis insulin kit, Shibayagi, Japan).

Measurement of urinary albumin excretion and renal function  The mice were detained in individual metabolic cages for 24 h for urine collection after being fed the experimental diet for 4 wk. Urine volume was measured, and urinary albumin excretion level was determined by means of ELISA, using a commercial kit (Levis Albumin, Shibayagi, Japan). Serum and urinary creatinine levels (SCr, UCr) were measured by an enzymatic method (Creatinine-Test Wako, Japan). Renal function was evaluated by calculating creatinine clearance [(UCr x urine volume/SCr)/g body weight]. O-HdG was determined by means of ELISA, using a commercial kit (8-OHdG Check, Japan Institute for the Control of Aging, Japan). The serum urea nitrogen was measured by means of a commercial kit (BUN B-Test Wako, Japan).

Other biochemical analyses  For measuring serum concentrations of total cholesterol (TC) and triglycerides (TG), commercial kits purchased from Wako (Osaka, Japan) were used. Fructosamine concentration was analyzed using a commercial kit (Liquittec Fructosamine, Roche, Basel, Switzerland). The extent of lipid peroxidation in serum, the liver, and the kidney was determined by TBARS as described (Kang et al., 1999).

ELISA  Microtiter plates (Nunc, Roskilde, Denmark) were coated overnight at 4°C with 50 µl of samples (10 µl protein/ml, diluted with PBS). The coating solution was discarded, and the wells were washed three times with PBS containing 0.05% Tween 20 (TPBS), followed by washing with distilled water. The wells were blocked with 200 µl of 4% skim milk for 1 h at 37°C with shaking. After being washed three times with TPBS and once with distilled water, each well was incubated with 100 µl goat monoclonal antibodies against N-(hexanoyl) lysine (HEL) (Kato et al., 1999), or dityrosine (Kato et al., 2000) for 2 h at 37°C with shaking. After being washed with TPBS and distilled water, the wells were incubated for 1 h at 37°C with 100 µl peroxidase-labeled goat anti-mouse IgG (American Qualex, La Mirada, CA) diluted to 1:5,000 in TPBS. After washing, 100 µl of o-phenylenediamine solution (5 mg o-phenylenediamine and 10 µl of 30% H2O2 in 10 ml of 0.1 M citrate phosphate buffer, pH5.5) was added to each well. The plate was sealed with aluminum foil and incubated for 15 min at room temperature. Adding 50 µl of 2 N sulfuric acid terminated the reaction. Absorbance at 492 nm was read using a micro-ELISA plate reader.

Enzyme assay  GST activity in the liver was measured using 1-chloro-2,4-dinitrobenzene as a substrate according to the method of Habig et al. (1974).

Statistical analyses  Data are presented as mean ± SD. The data were tested by ANOVA, followed by Fisher’s test to identify significant difference. All statistical analyses were performed using StatView version 5.0 (Abacus Concepts,
Berkeley, CA). A level of $p < 0.05$ was considered significant.

### Results

Energy intake and body weight  
Energy intake of the high fat diet was $134 \pm 13.8$ kJ/d. During the 2 wk of being fed a high fat diet, the blood glucose of the fasted mice increased from $125 \pm 45$ to $334 \pm 71$ mg/dl, and body weight increased from $27.1 \pm 1.23$ to $40.8 \pm 2.19$ g. During the 4 wk feeding of the control or experimental diet, there were no differences in food intake, final body weight, or organ weights among the three groups (Table 2).

TC, TG, and fructosamine also did not differ among the three groups (data not shown).

**Table 2.** Diet intake, final body weight, and organ weights.

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>WP</th>
<th>6-MSITC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diet intake (g/day)</td>
<td>3.83 ± 0.16</td>
<td>3.94 ± 0.25</td>
<td>4.01 ± 0.47</td>
</tr>
<tr>
<td>Final body weight (g)</td>
<td>47.7 ± 3.3</td>
<td>48.6 ± 1.8</td>
<td>48.3 ± 2.1</td>
</tr>
<tr>
<td>Organ weight (mg/g BW)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastrocnemius muscle</td>
<td>6.51 ± 0.42</td>
<td>6.59 ± 0.81</td>
<td>6.62 ± 0.60</td>
</tr>
<tr>
<td>Perirenal WAT</td>
<td>18.2 ± 1.21</td>
<td>20.9 ± 2.99</td>
<td>18.7 ± 1.17</td>
</tr>
<tr>
<td>Epididymal WAT</td>
<td>21.2 ± 3.79</td>
<td>25.9 ± 4.59</td>
<td>23.5 ± 3.4</td>
</tr>
<tr>
<td>Kidney</td>
<td>11.9 ± 0.55</td>
<td>11.6 ± 0.90</td>
<td>12.2 ± 0.79</td>
</tr>
<tr>
<td>Liver</td>
<td>52.2 ± 2.86</td>
<td>50.7 ± 4.52</td>
<td>52.2 ± 4.40</td>
</tr>
</tbody>
</table>

WAT: white adipose tissue, BW: body weight. Data are expressed as mean ± SD. $n = 10$.

OGTT  
OGTT was assessed after 3 wk of being fed the control or experimental diet. Mice were fasted 24 h before the test and were administered glucose solution of 1 mg/g body weight. There was no difference in fasting blood glucose among the three groups (Fig. 1). The highest glucose concentration was observed 30 min after the glucose administration in every group, and the glucose level decreased gently. There was no difference of blood glucose during the test. Plasma concentration of insulin was not significantly different during the OGTT among any of the dietary groups (data not shown).

**Fig. 1.** Blood glucose and insulin concentration during OGTT in KK-A$^y$ mice.

Urinary albumin excretion and creatinine clearance  
The urinary albumin excretion of each group after being fed the experimental diet for 4 wk is shown in Figure 2. Urinary albumin excretion, an accurate tool for monitoring early diabetic nephropathy, in the 6-MSITC group was significantly lower than that of the control group. Creatinine clearance, an index of renal function, decreased significantly in the WP and 6-MSITC groups compared with the control group (Fig. 3).

**Fig. 2.** Urinary albumin excretion in KK-A$^y$ mice after feeding of the control or experimental diets for 4 wk. Mice were detained in individual metabolic cages for 24 h for urine collection after being fed the control or experimental diet for 4 wk. Data are expressed as mean ± SD. $n = 10$. Values with different superscripts are significantly different, $p < 0.05$.

Serum and tissue levels of TBARS  
We examined the effect of WP and 6-MSITC administration on serum and tissue levels of TBARS. No significant difference in TBARS was seen in serum, liver, or kidney among the three groups during the study period (Table 4).

**Fig. 3.** Urinary albumin excretion in KK-A$^y$ mice after feeding of the control or experimental diets for 4 wk. Mice were detained in individual metabolic cages for 24 h for urine collection after feeding the control or experimental diets for 4 wk. Data are expressed as mean ± SD. $n = 10$. Values with different superscripts are significantly different, $p < 0.05$. 

**Table 3.** Effects of WP and 6-MSITC on water intake, urine volume, 8-OHdG, and BUN excreted in a 24 h period in urine of KK-A$^y$ mice.

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>WP</th>
<th>6-MSITC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water intake (ml/24 h)</td>
<td>12.5 ± 2.6</td>
<td>9.5 ± 2.5</td>
<td>11.4 ± 4.4</td>
</tr>
<tr>
<td>Urine volume (ml/24 h)</td>
<td>7.3 ± 2.4</td>
<td>4.9 ± 2.5$^b$</td>
<td>4.5 ± 2.7$^b$</td>
</tr>
<tr>
<td>8-OHdG (ng/24 h)</td>
<td>87.4 ± 44.6</td>
<td>65.4 ± 12.9</td>
<td>59.2 ± 29.7</td>
</tr>
<tr>
<td>BUN (mg/dL)</td>
<td>53.7 ± 3.67</td>
<td>38.3 ± 3.37</td>
<td>32.3 ± 3.90</td>
</tr>
</tbody>
</table>

Mice were detained in individual metabolic cages for 24 h for urine collection after being fed the control or experimental diet for 4 wk. Data are expressed as mean ± SD. $n = 10$. Values with different superscripts are significantly different, $p < 0.05$. 

Serum and tissue levels of TBARS  
We examined the effect of WP and 6-MSITC administration on serum and tissue levels of TBARS. No significant difference in TBARS was seen in serum, liver, or kidney among the three groups during the study period (Table 4).
Mice were detained in individual metabolic cages for 24 h for urine collection after feeding the experimental diet for 4 wk. Data are expressed as mean ± SD. n = 10. Values with different superscripts are significantly different, p < 0.05. Ucr: urine creatinine. Scr: serum creatinine. BW: body weight.

Table 4. Effect of WP and 6-MSITC on TBARS in liver, kidney, and serum of KK-Aº mice.

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>WP</th>
<th>6-MSITC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum (nmol MDA/ml)</td>
<td>5.22 ± 2.29</td>
<td>5.15 ± 1.40</td>
<td>6.62 ± 3.40</td>
</tr>
<tr>
<td>Liver (nmol MDA/mg tissue)</td>
<td>400 ± 165</td>
<td>405 ± 106</td>
<td>406 ± 189</td>
</tr>
<tr>
<td>Kidney (nmol MDA/mg tissue)</td>
<td>531 ± 63.8</td>
<td>501 ± 108</td>
<td>528 ± 43.9</td>
</tr>
</tbody>
</table>

Data are expressed as mean ± SD. n = 10.

The formation of HEL in serum, the liver and the kidney was not inhibited in the WP and 6-MSITC treated groups. We also measured dityrosine level, which is a fluorescent dimer of tyrosine and is formed by reactive oxygen species, in the organs. The formation of dityrosine was not affected in the experimental groups compared with the control group (Table 5).

Table 5. HEL and dityrosine in liver and kidney of KK-Aº mice.

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>WP</th>
<th>6-MSITC</th>
</tr>
</thead>
<tbody>
<tr>
<td>HEL</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liver</td>
<td>0.502 ± 0.061</td>
<td>0.495 ± 0.079</td>
<td>0.528 ± 0.129</td>
</tr>
<tr>
<td>Kidney</td>
<td>0.486 ± 0.073</td>
<td>0.455 ± 0.097</td>
<td>0.458 ± 0.127</td>
</tr>
<tr>
<td>Dityrosine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liver</td>
<td>0.357 ± 0.099</td>
<td>0.335 ± 0.076</td>
<td>0.372 ± 0.102</td>
</tr>
<tr>
<td>Kidney</td>
<td>0.414 ± 0.145</td>
<td>0.374 ± 0.101</td>
<td>0.397 ± 0.173</td>
</tr>
</tbody>
</table>

Data are expressed as mean ± SD. n = 10.

GST activity

GST activity in liver was determined. GST is a family of enzymes that catalyze the conjugation of reactive chemicals with glutathione (GSH) and plays an important role in protecting cells from oxidative stress. As shown in Figure 4, GST activity in liver was significantly higher in the WP group, but not in the 6-MSITC group, as compared with the control group.

Discussion

Many studies have been performed to examine the protective effects of antioxidative agents, such as vitamin E, vitamin C, and GSH, against diabetic nephropathy (Koya et al., 1998; Ueno et al., 2002). 6-MSITC isolated from wasabi induces GST in vitro (Morimitsu et al., 2002); thus, 6-MSITC may also act as an antioxidant in vivo. In the present study, we examined whether dietary WP and 6-MSITC could preserve renal function in type 2 diabetic mice. Urine volume, urinary albumin excretion, and creatinine clearance were significantly lower in the 6-MSITC group than in the control group. There was no difference in TBARS or other biomarkers of oxidative stress among the three groups; however, urinary 8-OHdG tended to be lower in the 6-MSITC group than in the control group. GST activity in the liver was significantly higher in the WP group than in the control group. These results suggest that 6-MSITC ameliorated diabetic nephropathy by reducing oxidative injury.

Wasabi contains the isothiocyanate components allyl isothiocyanate, 6-MSITC, 6-methylthiohexyl isothiocyanate, and 7-methylthioheptyl isothiocyanate, all of which have been suggested to have important medical benefits. Dietary administration of isothiocyanates to rats has been found to induce a range of detoxification enzymes, including QR, GST A5 submit, and aflatoxin aldehyde reductase (Kelly et al., 2000). Together, these data indicate that 6-MSITC may prevent diabetic nephropathy induced by oxidative stress through expression of detoxification and antioxidant enzymes such as QR and GST. However, it has been unclear whether dietary WP and 6-MSITC beneficially influence diabetic nephropathy. In this study, we showed that dietary 6-MSITC can ameliorate diabetic nephropathy.

Many studies have documented that diabetic patients, especially those with poor control of diabetes and hyperglycemia, show increased production of ROS and lipid peroxidation (Kitahara et al., 1980; Armstrong & Al-Awadi, 1991). Hyperglycemia leads to autoxidation of glucose (Wolf & Dean, 1987), lipid peroxidation, and as a consequence causes the glycoxidation of proteins (Fu et al., 1994). These changes accelerate the generation of ROS, and result in an increase in the oxidative modification of DNA. Urinary 8-OHdG is an index of oxidative DNA damage repair (Wiseman & Halliwell, 1996; Leinonen et al., 1997).
8-OHdG passes freely into the urine by glomerular filtration and has been used as an index of whole-body oxidative stress (Sigenaga et al., 1989). Oxidative DNA damage has been shown to be related to the peroxidation of membrane fatty acids and low antioxidant status (Haegeler et al., 1994), both present in diabetes. In the present study, the levels of TBARS and biomarkers of oxidative stress were unchanged by the administration of WP and 6-MSITC. However, the increased urinary 8-OHdG excretion in diabetic mice was ameliorated by dietary 6-MSITC, suggesting that this substance might improve diabetes-induced oxidative stress in vivo.

GST encompasses a family of enzymes that catalyze the conjugation of reactive chemicals with GSH and play an important role in protecting cells from oxidative stress. 6-MSITC is the major GST inducer of wasabi. It also potently induced both class α GSTA1 and class π GSTP1 isozymes in RL34 cells (Morimitsu et al., 2002). However, in this study, although the total intake of 6-MSITC was higher in the 6-MSITC group, GST activity in liver compared with the control was significantly higher in the WP group, but not in the 6-MSITC group. Kinae et al. (2000) reported on antioxidant activity of wasabi samples containing 6-MSITC, as determined by the Fenton reaction-lipid peroxidation system in vitro. Furthermore, Miyoshi et al. (2003) reported that benzyl isothiocyanate (BITC), an analog of 6-MSITC, indeed acts as an inhibitor of O$_2^-$ generation in mouse skin; they assumed that an intercellular target molecule with a reactive sulfhydryl moiety might be regulated by covalent attachment with BITC. Therefore, we speculate that the reduction of urinary 8-OHdG excretion in the 6-MSITC group may be due not to the activation of GST, but to the inhibition of the generation of ROS in vivo, as with BITC.

Early changes in the renal functions of diabetic patients and animals are characterized by glomerular hyperfiltration, cellular injury, glomerulosclerosis, mesangial cell proliferation, and urinary albumin excretion (Mogensen, 1971; Christiansen et al., 1981; Hostetter et al., 1981; Jensen et al., 1981). The urinary excretion of albumin is an important marker for detecting the early phase of diabetic nephropathy. Furthermore, urine volume is also an important tool for the estimation of diabetic nephropathy. Erman et al. (1998) previously reported that the urine volume in type 2 diabetic mice was 10-fold greater than in normal mice, and 3-fold greater than in insulin-treated diabetic mice. KK-A' mice were used in this study because they are considered to be a polygenic model for human type 2 diabetes mellitus (Suto et al., 1998), and have been used for studies on the development of a novel oral antiabetic agents (Matsuzaki et al., 1997). Okazaki et al. (2002) reported that blood hemoglobin A$_1c$ levels were significantly correlated with urinary albumin excretion in KK-A' mice. In this study, the mice excreted a significant amount of albumin in the urine; the amount was significantly smaller in the KK-A' mice fed the 6-MSITC diet than in the controls. This observation was supported by the findings that urine volume and creatinine clearance, an index of renal function, were improved by the 6-MSITC diet. These results suggest that supplementation of 6-MSITC to the diet prevented diabetic nephropathy, probably through its antioxidant function; the data regarding urinary 8-OHdG excretion support these results.

Hyperglycemia is responsible for the development and progression of diabetic nephropathy through metabolic derangement, including increased oxidative stress, renal polyp formation, activation of protein kinase C (PKC), mitogen-activated protein kinases (MAPKs), and accumulation of AGE (Kikkawa et al., 2003; Haneda et al., 1997; Kikkawa et al., 1987). Therefore, glycemic control can reduce both the onset and progression of diabetic nephropathy. In this study, blood glucose and plasma insulin concentrations in OGTT were unchanged by the administration of WP and 6-MSITC. These data indicate that WP and 6-MSITC do not improve glucose tolerance and insulin sensitivity, i.e., WP and 6-MSITC do not influence glucose absorption, metabolism or insulin secretion. Although the three groups were exposed to the same level of diabetes-inducing oxidative stress, diabetic nephropathy was ameliorated only in the 6-MSITC group. Specifically, we speculate that 6-MSITC improved diabetic nephropathy not by the improvement of hyperglycemia, but by its antioxidant function.

In conclusion, the present results show that a sufficient supply of dietary 6-MSITC may prevent or delay renal dysfunction in diabetes by protecting against oxidative stress, and that dietary 6-MSITC may have beneficial effects on diabetic complications in type 2 diabetic mice.

References


6-MethylsulfinylhexylIsothiocyanate, an Antioxidant


