Note

Welsh Onion Attenuates Hyperlipidemia in Rats Fed on High-Fat High-Sucrose Diet

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The effects of two types of Welsh onion, green-leafy and white-sheath types, on hyperlipidemia in rats fed on diets high in fat and sucrose were studied. A significant lowering effect on cholesterol in the plasma and on total lipids, triacylglycerol, and cholesterol in the liver was observed in rats fed on the green, but not white, Welsh onion. These Welsh onions had no significant effect on the hepatic enzyme activities responsible for fatty acid synthesis and degradation. The results suggest that the green Welsh onion might be effective in attenuating hyperlipidemia in a manner other than affecting fatty acid metabolism in the liver. Kaempferol seemed to be one of the components in green Welsh onion acting to lower lipid deposition.

Key words: Welsh onion; high-fat high-sucrose diet; hypolipidemic activity; flavonoid; kaempferol

An increasing interest in health foods is spurring many studies on dietary factors that may decrease plasma lipid levels. *Allium* vegetables have a beneficial medicinal effect on various aspects, including plasma lipid levels. The hypolipidemic effect of garlic and onion has been well studied.1-4) Welsh onion (*Allium fistulosum* L.) is one of the *Allium* families that is a popular vegetable in Asian countries and often used for flavoring. Like other *Allium* vegetables, Welsh onion can be expected as a good source of flavonoids and of many kinds of sulfur compounds. These components have recently been suggested as having beneficial medicinal effects, including those on arteriosclerosis. However, few reports on the hypolipidemic activity of Welsh onion have been reported. We studied in the present work the effects of Welsh onion on lipid levels in the plasma and liver. The effects of two types of Welsh onion, the green-leafy and white-sheath types, were compared because these vegetables are popular in many Asian countries.

Twenty-eight 7-week-old male Sprague-Dawley rats obtained from SLC Japan (Shizuoka, Japan) were randomly divided into four test groups of seven animals each to average the initial body weight. One group received a control diet (the control group), and the other three groups were fed on a high-fat high-sucrose (HFS) diet either containing or not containing 5.0% of the green or white type of Welsh onion (the HFS, GWO, and WWO groups). The composition of the control diet was as follows (wt%): soybean oil, 5.0; mineral mixture, 3.5; vitamin mixture, 1.0; choline bitartrate, 0.25; casein, 20.0; cellulose, 5.0; and α-cornstarch to make up 100. The composition of the HFS diet was similar to that of the control diet, except that 15.0% of lard, 0.5% of cholesterol, and 40.0% of sucrose replaced the starch. The composition of the diets containing Welsh onion was the same as that of the HFS diet, except that 5.0% of the powdered green or white Welsh onion was replaced with cellulose to minimize the difference in energy content of these three diets. The energy content of the diets containing Welsh onion was about 0.3% higher than the HFS diet, this being calculated by assuming that the energy contents of the green and white Welsh onions were 31 and 28 kcal/100 g.5) The two types of Welsh onion were purchased from a local market in Osaka prefecture, crushed, heated to 80 °C for about 5 min to denature the enzyme activity, freeze-dried, and milled to pass through a 60-mesh sieve. The composition of the mineral mixture was to AIN-93G-MX and that of the vitamin mixture was to AIN-93-3X-V.6) After a 4-week growth period, the rats were starved overnight, anesthetized, and their blood was collected in a heparinized syringe from the abdominal aorta. The concentrations of total cholesterol, HDL-cholesterol, and triacylglycerol in the plasma were determined with commercial kits (cholesterol E-test, HDL-cholesterol test, and triglyceride G-test, respectively) from Wako Pure Chemicals (Osaka, Japan). Total lipids extracted from the liver by the method of Folch et al.7) were measured by the gravimetric method. Liver lipids were dissolved in a mixture of tert-butylalcohol and Triton X-100 in methanol,8) and the total cholesterol and triacylglycerol contents in this solution were measured with the same diagnostic kits as those used for the plasma analysis. To measure the fatty acid metabolizing enzyme activity in the liver, a portion of liver was homogenized, and the cytosol and mitochondrial fractions were separated by centrifugation. The fatty acid synthase (EC 2.3.1.85) activity in the liver cytosol was measured by estimating the malonyl CoA-dependent oxidation of NADPH at 37 °C.9) The isolated mitochondrial fraction was used for assaying the carnitine palmitoyltransferase (EC 2.3.1.21) and acyl-CoA dehydrogenase (EC 1.3.99.3) activities. Carnitine palmitoyltransferase was spectrophotometrically assayed by following the release of CoA-SH from

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palmitoyl-CoA,\(^{10}\) and acyl-CoA dehydrogenase was assayed by measuring the reduced tetrazolium salt, with palmitoyl-CoA used as a substrate.\(^{11}\) Flavonoids in the green and white Welsh onion were assayed by HPLC with a Hitachi L-600 instrument, 655A detector and Shimadzu shimpack ODS column.\(^{12}\) All experiments were conducted in compliance with the Ethics Guideline for Animal Experiments of Osaka City University. Each data value for the animal experiments is expressed as the mean ± SEM of seven rats. The comparison between the control and HFS groups was analyzed by Student’s \(t\)-test. Differences between the HFS, GWO, and WWO groups were subjected to a one-way analysis of variance (ANOVA) and multiple-range comparison by Tukey’s honestly significant difference (HSD) test.

The body weight gain and liver and fat-tissue weights in the HFS group were higher than those in the control group, although there was no difference in the food intake among the groups (Table 1). The body weight gain and fat-tissue weight in the GWO group were slightly lower than those in the HFS group. Total cholesterol in the plasma was significantly higher in rats of the HFS group than in those of the control group, and these values for the rats in the WWO group, but not in the WWO group, were significantly lower than the values for the rats fed on the HFS diet. These results demonstrate the significant lowering effect of green, but not white, Welsh onion on plasma cholesterol and total lipids, triacylglycerol, and cholesterol in the liver of the rats fed with the diets high in fat and sucrose.

There have been many reports on the hypolipidemic effects of \textit{Allium} vegetables. Extracts of garlic have lowered plasma lipids in rats fed on a diet with or without cholesterol, suggesting that the effect was attributable in part to the depressed synthesis of cholesterol and fatty acid.\(^{1−3}\) The results concerning the hypolipidemic effects of onion on animal models have not been so consistent. A hypolipidemic effect of onion was both found\(^{4}\) and not found\(^{5}\) in animals fed with a cholesterol-added diet. The reason for such a difference in these results is not clear at the moment, but Gabler \textit{et al.} have suggested that the lipid-lowering effect of onion varies with the type and dose of the onion used.\(^{13}\) Few studies on the hypolipidemic activity of the Welsh onion have been reported, and this present study would be the first to propose the lipid-lowering effects of green Welsh onion in the plasma and liver of an animal model.

To make clear the effects of green Welsh onion in lowering triacylglycerol, the liver enzyme activities related to the degradation and synthesis of fatty acids were measured. There was no difference in the activities of fatty acid synthase and carnitine palmitoyltransferase among the rats from each of the four groups (Table 2). However, the activity of acyl-CoA dehydrogenase, which is the rate-limiting enzyme for fatty acid \(\beta\)-oxidation in liver mitochondria, was higher in the rats fed on the HFS diet than in those fed on the control diet. The activity in the rats of the GWO and WWO groups was not significantly different from that in the rats fed on

Table 1. Effects of Dietary Addition of Welsh Onion on Growth, Food Intake, and Liver and Fat-Tissue Weight in Rats Fed with a High-Fat High-Sucrose Diet for 4 Weeks

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>HFS</th>
<th>GWO</th>
<th>WWO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body weight gain (g/d)</td>
<td>4.9 ± 0.3</td>
<td>6.0 ± 0.1*</td>
<td>5.4 ± 0.3</td>
<td>5.8 ± 0.5</td>
</tr>
<tr>
<td>Food intake (g/d)</td>
<td>16.8 ± 0.7</td>
<td>16.2 ± 0.3</td>
<td>15.5 ± 0.4</td>
<td>15.8 ± 0.6</td>
</tr>
<tr>
<td>Liver (g)</td>
<td>8.67 ± 0.40</td>
<td>13.2 ± 0.7*</td>
<td>12.1 ± 0.4</td>
<td>12.3 ± 0.4</td>
</tr>
<tr>
<td>Epididymal fat (g)</td>
<td>5.35 ± 0.59</td>
<td>7.58 ± 0.68*</td>
<td>6.97 ± 0.43</td>
<td>7.50 ± 0.84</td>
</tr>
</tbody>
</table>

Each value represents the mean ± SEM of seven rats.

\(* p < 0.05\) compared with the control group by Student’s \(t\)-test.

![Fig. 1](Welsh Onion Attenuates Hyperlipidemia 403)

Fig. 1. Effects of the Dietary Addition of Welsh Onion on Triacylglycerol (A), Total Cholesterol (B) and HDL Cholesterol (C) in the Plasma, and on Total Lipids (D), Triacylglycerol (E), and Total Cholesterol (F) in the Liver of Rats Fed with a High-Fat, High-Sucrose Diet.

Each value represents the mean ± SEM of seven rats.\(\ast p < 0.05\) compared with the control group by Student’s \(t\)-test. Values with different letters in each assay are significantly different from each other between the HFS, GWO, and WWO groups by Tukey’s HDS test (\(p < 0.05\)).
the HFS diet. These results suggest that the two types of Welsh onion had no significant effect on the hepatic enzyme activities responsible for fatty acid synthesis and degradation. Previous studies of the effects on triacylglycerol level in the plasma have reported the suppressive effect of a garlic extract on the fatty acid synthase activity,\(^\text{14}\) but cycloalliin, a cyclic sulfur compound in onion, had no effect on triacylglycerol synthesis.\(^\text{15}\) We need further studies to examine the mechanism for the lipid-lowering effects of green Welsh onion.

Two kinds of flavonoid, kaempferol and quercetin, were detected in both types of Welsh onions. Kaempferol and quercetin in green Welsh onion respectively constituted 118 ± 12 and 7 ± 1 mg/kg of fresh weight, and those in white Welsh onion constituted 12 ± 10 and 4 ± 1 mg/kg of fresh weight. A much larger amount of kaempferol was therefore detected in green Welsh onion. Regarding cholesterol metabolism, kaempferol was stimulatory at a low concentration, and inhibitory at a high concentration toward hepatocellular cholesterol synthesis.\(^\text{16}\) We did not study the effects of flavonoids on cholesterol metabolism in this experiment, and the possibility of flavonoids, especially kaempferol, suppressing the biosynthesis or enhancing the degradation of cholesterol cannot be excluded. Many kinds of S-alk(en)yl cysteine sulfoxides in \textit{Allium} vegetables have been shown to inhibit cholesterol synthesis in rat hepatocytes.\(^\text{17}\) Further studies should therefore be conducted to elucidate whether or not the sulfur compounds and/or flavoloids in green Welsh onion are important to lowering cholesterol in the plasma and liver. Dietary fiber, as a component other than flavonoids and sulfur compounds, is a plausible cholesterol- and triacylglycerol-lowering agent in green Welsh onion. Although the fiber in onion was not effective in lowering plasma cholesterol,\(^\text{18}\) it remains to be studied whether or not the fiber in Welsh onion was one component for lowering plasma lipids. Assuming that the fiber contents of the green and white Welsh onions were 2.9 and 2.2 g/100 g,\(^\text{5}\) the dietary fiber contents of the HFS, GWO, and WWO diets in this experiment were 5.0, 1.5, and 1.3%, respectively. Experimental diets for further study should be formulated to contain the same amount of dietary fiber to evaluate the physiological effects of the dietary fiber in Welsh onions.

Hyperlipidemia is a serious etiological factor relating to atherosclerosis. We studied in the present experiment the effects of dietary Welsh onion on the lipid levels in the liver and plasma. Between the two types of Welsh onion, the green type beneficially alleviated hyperlipidemia and decreased the risk of cardiovascular disease in rats fed on a diet high in fat and sucrose. The detection of high levels of flavonoids, especially of kaempferol, suggests that kaempferol might be one of the lipid-lowering components in green Welsh onion.

### References


### Table 2

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>HFS</th>
<th>GWO</th>
<th>WWO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Activities of fatty acid degradation enzyme (nmol/min/mg protein)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carnitine palmitoyltransferase</td>
<td>3.01 ± 0.30</td>
<td>3.17 ± 0.33</td>
<td>3.60 ± 0.40</td>
<td>3.31 ± 0.42</td>
</tr>
<tr>
<td>Acyl-CoA dehydrogenase</td>
<td>11.5 ± 0.9</td>
<td>29.4 ± 1.9*</td>
<td>37.0 ± 3.7</td>
<td>25.3 ± 3.3</td>
</tr>
<tr>
<td>Activities of fatty acid synthesis enzyme (nmol/min/mg protein)</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Fatty acid synthase</td>
<td>8.97 ± 0.53</td>
<td>8.55 ± 0.90</td>
<td>8.76 ± 0.69</td>
<td>7.72 ± 0.44</td>
</tr>
</tbody>
</table>

Each value represents the mean ± SEM of seven rats.

* \(p < 0.05\) compared with the control group by Student’s \(t\)-test.