Effects of Depolymerized Sodium Alginate on Serum Total Cholesterol in Healthy Women with a High Cholesterol Intake

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The effects of DSA (depolymerized sodium alginate with a low molecular weight) on the serum lipid level were investigated in healthy women with a high cholesterol intake. The subjects in the test group were given two bottles of a test drink (containing 2 g of DSA per bottle) per day for 3 weeks. The subjects in the control group were given apparently the same drink without DSA. Blood samples were collected 4 times, the first 2 days before the experiment and then weekly during the 3-week experiment. The serum total cholesterol (T-Ch) level of the control group tended to increase, although there was no significant difference in T-Ch level between the test and control groups. The T-Ch level for 6 subjects in the control group with T-Ch of more than 180 mg/dl from the pre-experimental measurement, however, increased with the last two measurements. In contrast there was no change in the T-Ch level of eight equivalent subjects in the test group. The increment in T-Ch concentration due to a dietary excess of cholesterol was significantly suppressed by the concomitant intake of DSA. These results suggest that DSA stimulated cholesterol excretion to protect from an increase in T-Ch due to the dietary excess of cholesterol, especially in those subjects with a relatively high level of serum cholesterol.

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Keywords: serum total cholesterol, depolymerized alginate, women, dietary cholesterol, dietary fiber.

Dietary fiber is known to induce many physiological effects: i.e., hypocholesterolemia, modification of blood glucose and insulin, depressed risk of colon or breast cancer, dissolution of constipation, and so on. Among these physiological activities, the effects of dietary fiber on the serum cholesterol level have been noted by many investigators. The serum cholesterol level in indigenous South Africans (Bantu) (Walker and Arvidsson 1954) and in vegetarians (Sacks et al. 1975) has been reported to be lower than that in ordinary English people. Water-soluble dietary fiber (pectin: Tsuji et al. 1968; glucomannan: Tsuji et al. 1968; and indigestible dextrin: Nomura et al. 1992) has also been recently shown to inhibit the absorption of sterols and carbohydrates, and to suppress the increase of serum cholesterol in rats and men.

Alginate, the main constituent of brown sea weed, is an indigestible carbohydrate (Humphrey and Triffitt 1968) that has also been reported to have the characteristic activities of dietary fiber: it decreased the serum cholesterol level (Tsuji et al. 1968) and accelerated the excretion of heavy metal into the feces (Sutton 1967; Kojima et al. 1980; Cowry et al. 1982).

Sodium alginate is widely used by food manufacturers as a thickener and stabilizer. An aqueous solution of commercially available sodium alginate, however, is too viscous to take an amount that would be expected to exert sufficient effect as dietary fiber. The application of sodium alginate in the food industry is thus limited.

Watanabe et al. (1992) have recently shown that feeding depolymerized sodium alginate (DSA with an average molecular weight of 50,000) to rats caused
accelerated cholesterol excretion into the feces. Kimura and Okuda (1992) have shown a suppression of saccharide uptake in the rat small intestine by DSA feeding.

We report here the effects of DSA on the serum cholesterol and other lipid levels in healthy women with a high cholesterol intake.

**METHOD**

Thirty-one healthy women were selected from among junior college students and staff, briefed well about the purpose of the experiment, and their informed consent obtained. The experiment was conducted according to the Helsinki declaration and regulated by a medical doctor according to the protocol shown in Fig. 1.

The subjects were divided into two groups at random, i.e., a test group and control group. Each subject in the test group (15 women) was given daily two bottles of a test drink containing 2 g of DSA, once after breakfast and once after lunch (4 g/day), for 3 weeks. The control group subjects (16 women) were apparently given the same drink, but without DSA. The experiment was conducted as a single blind test.

DSA (Solgin® produced by Biomedical Division of Sumitomo Metal Industries Ltd.) was supplied as the test drink (see Table 1). The average molecular weight of DSA was 50,000, this being measured by gel-filtration HPLC with pullulan as the molecular weight standard.

Blood samples were collected weekly between 3:30 and 4:30 p.m. on four occasions. The first samples were collected 2 days before the start of the experiment (June 2, 1992), and the 2nd, 3rd and 4th samples were collected on June 10, 17 and 24, 1992, respectively. The total cholesterol (T-Ch), high-density lipoprotein cholesterol (HDL-Ch) and triglyceride (TG) levels in the blood samples were measured at SMI-Bristol Meyer Laboratory in Sapporo within 3 h of their collection, along with the biochemical indices (GOT, GPT, BUN, creatinine-S and total protein), electrolytic components (Fe, Mg, Table 1. Composition of the test drink

<table>
<thead>
<tr>
<th>Component</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fructose, glucose mixture (liquid)</td>
<td>6.0 g</td>
</tr>
<tr>
<td>Reduced malt sugar (liquid)</td>
<td>6.0 g</td>
</tr>
<tr>
<td>Depolymerized sodium alginate</td>
<td>2.0 g</td>
</tr>
<tr>
<td>Vitamin C</td>
<td>0.4 g</td>
</tr>
<tr>
<td>Citric acid</td>
<td>0.14 g</td>
</tr>
<tr>
<td>Sodium citrate</td>
<td>0.03 g</td>
</tr>
<tr>
<td>Food dye</td>
<td>0.1 ml</td>
</tr>
<tr>
<td>Guarana extract</td>
<td>0.1 ml</td>
</tr>
<tr>
<td>Fragrance</td>
<td>a little</td>
</tr>
<tr>
<td>Added water to 100 ml</td>
<td></td>
</tr>
<tr>
<td>Energy</td>
<td>18 kcal/100 ml</td>
</tr>
</tbody>
</table>

Blood collection (3:30-4:30 p.m.)

1992

May 25 26 27 28 29 30 31

June 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24

Test group

Given two bottles daily of the test drink, each containing 2g of DSA*

Control group

Given two bottles daily of apparently the same drink without DSA*

Dietary survey

Life and health survey

Fig. 1. Experimental protocol

*DSA: depolymerized sodium alginate.
Effect of Depolymerized Alginate on Serum Cholesterol in Healthy Women

Ca, Na, K and Cl) and glucose.

During the experimental period, the subjects were instructed to eat cholesterol-rich food, e.g., egg, butter and meat, to increase their dietary cholesterol intake. They ate the same lunch prepared in the cooking course of the college program from Monday through Friday. Except for this common daily meal, the subjects were allowed to eat their usual meals before and during the experiment. Each subject was obligated to record all the food eaten for 7 days before the experiment (May 25 to 31, 1992), and for 3 days during the experiment (June 22 to 24, 1992) to confirm the cholesterol intake. We calculated the intake of average energy, protein, lipid, carbohydrate, cholesterol and dietary fiber from the dietary record. The subjects were also obligated to report their menstrual state and general health condition.

Each value is presented as the mean and standard deviation (SD) or standard error (SE). Significant differences between two groups were determined by Student's t-test and Welch's test. The results are considered statistically significant at $p<0.05$.

RESULTS

Among the 31 subjects, two dropped out, one because of a leg injury and the other after catching a cold, leaving those in the test and control groups as 14 and 15, respectively. The age, height, weight and obesity indices are summarized in Table 2, there being no significant differences between the two groups.

1. Nutritional conditions

The average energy, protein, lipid, carbohydrate, cholesterol and dietary fiber intake before and during the experiment are shown in Table 3. The cholesterol intake by the two groups during the experiment was about 1.8 times more than that before the experiment. The dietary fiber intake by the test group during the experiment was 15.4 g/day (11.4 g/day plus 4 g/day from the test drink), and that by the control group was 12.3 g/day. There was no difference in any other nutritional elements, including energy intake, before and during the experiment.

Table 2. Age, height, weight and obesity index of the subjects

<table>
<thead>
<tr>
<th>Group</th>
<th>Test</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of subjects</td>
<td>15</td>
<td>14</td>
</tr>
<tr>
<td>Age (years)</td>
<td>27±14</td>
<td>30±17</td>
</tr>
<tr>
<td>19–20:</td>
<td>10 subjects</td>
<td>9 subjects</td>
</tr>
<tr>
<td>21–40:</td>
<td>2 subjects</td>
<td>2 subjects</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>156±6</td>
<td>157±6</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>51±8</td>
<td>52±6</td>
</tr>
<tr>
<td>Obesity index*</td>
<td>0.98±0.13</td>
<td>0.98±0.10</td>
</tr>
</tbody>
</table>

Mean ± SD. *Height < 150 cm: weight / [height - 100]. 150 cm ≤ height < 160 cm: weight / [50 + (height - 150) × 1.1]. Height ≥ 160 cm: weight / [(height - 100) × 0.9].

Table 3. Nutritional intake during experimental period

<table>
<thead>
<tr>
<th></th>
<th>Test group</th>
<th>Control group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before experiment</td>
<td>During experiment</td>
</tr>
<tr>
<td></td>
<td>(per day)</td>
<td>(per day)</td>
</tr>
<tr>
<td>Energy (kcal)</td>
<td>1,650±300</td>
<td>1,750±300</td>
</tr>
<tr>
<td>Protein (g)</td>
<td>64.7±11.9</td>
<td>78.7±12.8</td>
</tr>
<tr>
<td>Lipid (g)</td>
<td>53.0±13.0</td>
<td>57.1±11.1</td>
</tr>
<tr>
<td>Carbohydrate (g)</td>
<td>231±42</td>
<td>236±44</td>
</tr>
<tr>
<td>Cholesterol (mg)</td>
<td>275±82</td>
<td>497±114</td>
</tr>
<tr>
<td>Dietary fiber (g)</td>
<td>10.7±2.8</td>
<td>11.4±2.4</td>
</tr>
</tbody>
</table>

Mean ± SD. 1) From May 25 to 31, 1992. 2) From June 22 to 24, 1992. 3) Higher-cholesterolemic subjects (8 in the test group, 6 in the control group) with total cholesterol of more than 180 mg/dl by the 1st measurement. 4) This value does not contain sodium alginate from the test drink.

(227)
2. Analytical accuracy

The accuracy of blood analysis was monitored during the experiment by using a standard (Monitor Ix and ISE-Ix). There was no significant variation in the results of each measurement, so the test values were adopted without adjustment.

3. Serum lipid level

The T-Ch, HDL-Ch, low-density lipoprotein-cholesterol (LDL-Ch, calculated from [T-Ch]—[HDL-Ch]—0.2×TG) and TG levels of the two groups are summarized in Table 4. There was no difference in the HDL-Ch, LDL-Ch and TG levels between the test and control groups.

The average T-Ch level for the control group tended to increase from 178 to 186 mg/dl, while the SD values for the control group also increased during the experiment. On the other hand, the average T-Ch level for the test group was 182-185 mg/dl during the experiment, with an SD value of 24-29. Three women at the menopause of each group showed higher T-Ch levels. A slight fluctuation of the serum T-Ch level was observed with the younger subjects due to the menstrual period. As their menstrual cycles were not synchronized, this fluctuation was averaged for the test group. No significant difference between the T-Ch levels in either the test or control group was recognized at any point in the experimental period.

The tendency for T-Ch to increase in the control group was most marked in those subjects with a relatively high initial T-Ch level (more than 180 mg/dl from the 1st measurement). A comparison among these subjects (8 and 6 women in the test and control groups, respectively) showed a significant increase of T-Ch in the control group of 106.5% after 2 weeks and of 109.0% after 3 weeks (each \( p < 0.02 \) in a paired \( t \)-test), that of the 1st measurement being taken as 100% (Fig. 2). There was no change in T-Ch level in the test group. No influence from the effects of the menstrual cycle or differences in dietary intake (Table 3) were apparent between the groups.

There was no apparent effect on the serum electrolyte level, liver and kidney functions, and serum glucose level during the 3-week intake of the DSA-containing drink (data not shown).

DISCUSSION

The subjects were loaded with dietary cholesterol in this experiment, the cholesterol intake during the experimental period being 1.80-1.85 times as much as that during the pre-experimental period (500-530 mg/day for 3 weeks, Table 3). The average T-Ch level for the test group (DSA intake of 4 g/day) showed no change; however, that for the control group (no DSA intake) increased from 178 to 186 mg/dl. Tsuji and Suzuki (1981) have reported that a dietary cholesterol load on 7 subjects (about 1 g/day for 7 days) caused an average increase in T-Ch level from 180 to 192 mg/dl. The increased T-Ch level in the control group

Fig. 2. Variation of serum total cholesterol level in those subjects with total cholesterol of more than 180 mg/dl by the first measurement

Mean±SE. □, test group (8 subjects), ●, control group (6 subjects). * Significantly different from the corresponding test group at \( p < 0.05 \).

Table 4. Serum total cholesterol, HDL-cholesterol, LDL-cholesterol and triglyceride concentrations in healthy women with a high cholesterol intake

<table>
<thead>
<tr>
<th>Duration (weeks)</th>
<th>Original (mg/dl)</th>
<th>Test group</th>
<th></th>
<th>Control group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Total cholesterol</td>
<td></td>
<td>182±27</td>
<td>183±24</td>
<td>185±29</td>
</tr>
<tr>
<td>HDL-cholesterol</td>
<td></td>
<td>63±12</td>
<td>64±12</td>
<td>61±14</td>
</tr>
<tr>
<td>LDL-cholesterol</td>
<td></td>
<td>94±17</td>
<td>100±18</td>
<td>101±16</td>
</tr>
<tr>
<td>Triglyceride</td>
<td></td>
<td>125±116</td>
<td>99±79</td>
<td>126±101</td>
</tr>
</tbody>
</table>

Mean±SD. *Two days before starting the DSA drink.
is, therefore, presumed to have been due to the dietary cholesterol load. Six subjects with a relatively high T-Ch level in the control group (more than 180 mg/dl from the 1st measurement) were found to be sensitive to an excess cholesterol intake, especially with two older subjects. On the other hand, such subjects in the test group showed no particular response to a dietary excess of cholesterol. This difference in response to dietary cholesterol between the two groups is assumed to have been due to the DSA intake.

The effects of intact sodium alginate on cholesterol metabolism in rats have been studied by Tsuji et al. (1968, 1978), and the serum and liver cholesterol levels in rats fed with a hypercholesterolemic diet were decreased by the addition of 5% sodium alginate to the diet. The same effects are presumed to occur in humans, but there has been no report on the effects of sodium alginate itself on cholesterol metabolism in humans.

The serum cholesterol level is known to be affected by 1) cholesterol absorption from the small intestine, 2) cholesterol biosynthesis and catabolism, 3) resorption and excretion of bile acid, and 4) release and uptake of lipoprotein. In experiments on rats (Watanabe et al. 1992; Nishizawa et al. in press), DSA, as well as intact sodium alginate, has been shown to accelerate the fecal excretion of cholesterol, and its minimum effective dose was presumed to be between 50 and 100 mg/kg of body weight. It can be expected to inhibit the absorption of cholesterol from the small intestine.

In conclusion, the present results suggest that DSA suppressed the increase in serum cholesterol level due to a dietary cholesterol load, and that this effect may have been due to the accelerated fecal excretion of cholesterol. Moreover, DSA has high solubility in water and low viscosity in comparison with sodium alginate. It may therefore be a useful food material to control cholesterol metabolism.

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高コレステロール食を摂取した健常女性の血清コレステロールに及ぼす
低分子化アルギン酸ナトリウムの影響

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平成8年7月29日受理

コレステロールを負荷した健常女性の血清総コレステロール（T-Ch）に及ぼす低分子化アルギン酸
ナトリウム（DSA）摂取の影響を調べた。試験群にはDSA 2 g を含むドリンクを1日2本ずつ3週間
摂取させ、対照群にはDSA を含まない以外は外見、含有成分の同じドリンクを摂取させた。血液検
査は摂取開始前 2 日前、摂取開始後 1, 2, 3 週間後の 4 回おこなった。対照群の T-Ch は上昇の傾向を
示したが、有意な差は認められなかった。しかし、対照群のなかで摂取前の T-Ch が180 mg/dl 以上
の被験者では、2 週目と 3 週目の T-Ch が上昇していた。一方、試験群のなかで同様の条件の被験者
ではT-Ch の上昇が認められず、対照群との間に有意差が認められた。DSA はコレステロールの排泄
促進作用を有し、通常 T-Ch の比較的高い人では、食物に負荷されたコレステロールによる T-Ch の上
昇を抑制する作用が有意に現れるものと示唆された。

キーワード: 血清総コレステロール，低分子化アルギン酸，女性，食事コレステロール，食物纖維。