Royal Jelly Supplementation Improves Lipoprotein Metabolism in Humans

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Summary Royal jelly (RJ) has several physiological effects and is widely used in commercial medical products and health foods. We examined the effects of RJ supplementation on serum lipoprotein metabolism in humans. Fifteen volunteers were divided into an RJ intake group (n=7) and a control group (n=8). The RJ group took 6 g per day for 4 wk. Their serum total cholesterol (TC) and serum low-density lipoprotein (LDL) decreased significantly compared with those of the control group (p<0.05). There were no significant differences in serum high-density lipoprotein (HDL) or triglyceride concentrations. Moreover, the relationship between the serum cholesterol and lipoprotein levels was investigated. Among the lipoprotein fractions, small very-low-density lipoprotein was decreased (p<0.05) after RJ intake. Our results suggest that dietary RJ decreases TC and LDL by lowering small VLDL levels.

Key Words royal jelly, serum lipoprotein metabolism, small VLDL.

Royal jelly (RJ), which is secreted by the hypopharyngeal and mandibular glands of worker honeybees, is a necessary food for the growth of the queen honeybee. RJ contains a mix of proteins (12–15%), sugars (10–16%), lipids (3–6%), free amino acids, vitamins, minerals, and fatty acids. Several researchers have found that RJ has anti-tumor (1), anti-inflammatory (2), antioxidant (3), and cell proliferative activities (4). RJ reduces total cholesterol levels in experimental animals (5) and atherosclerosis in humans (6). RJ significantly affects lipid metabolism in rats and prevents the development of atherosclerosis in rabbits fed a cholesterol-rich diet (7, 8). Moreover, both oral administration and injection of RJ significantly reduce serum lipid and cholesterol levels in atherosclerosis patients with moderately high cholesterol levels (9, 10). A high blood cholesterol level is considered a health risk factor in cardiovascular diseases (11). To elucidate the effects of RJ supplementation on serum lipoprotein metabolism in humans, we focused on the relationship between serum cholesterol and lipoprotein levels.

MATERIALS AND METHODS

Subjects. All subjects were healthy adult volunteers, recruited mainly among the staff of the Research and Development Center of Nippon Meat Packers. The purpose and expectations of the study were fully explained to each volunteer. All subjects gave their informed consent before admission. Subjects showed no evidence of any chronic disease (hepatic, renal, or cardiac dysfunction) or obesity, and were not participating in unusually high levels of physical activity (e.g., sports training). None of the subjects took medications or vitamin supplements before or during the study. The study was approved by the Ethics Committee of the Research and Development Center of Nippon Meat Packers, and written informed consent was obtained from all participants.

Experimental design. Fifteen healthy adult volunteers were randomly separated into two groups: one group (5 males and 2 females, 39.0±9.9 y) was given royal jelly (RJ); the other group was assigned as control (6 males and 2 females, 36.9±12.3 y). The RJ group was given 6 g RJ (Maruwa Co. Ltd., Tokyo, Japan) daily for 4 wk. The control group received nothing. Each participant was instructed to maintain the same dietary pattern the evening before each test and the same lifestyle pattern the evening and morning before each test. Blood for biochemical analyses and serum TC, HDL, and LDL analyses was obtained from each subject immediately before and after the experimental period. To study the relationship between serum cholesterol and lipoprotein levels before and after supplementation with RJ, we analyzed each lipoprotein fraction by high-performance liquid chromatography (HPLC) (12).

Laboratory analyses. Blood samples were collected for biochemical tests. Hematological variables (white blood cells, red blood cells, and hemoglobin) were measured with an SE-9000 analysis system (Sismex, Kobe, Japan) using blood with anticoagulant (EDTA). Serum was obtained by centrifuging the blood without anticoagulant at 1,250 ×g for 15 min at 4°C. Biochemistry
parameters (total protein, A/G, albumin, TC, HDL, LDL, triglycerides, GOT, GPT, γ-GTP, creatinine, and fasting blood glucose) were measured with a 7450 Auto Analysis System (Hitachi, Tokyo, Japan) at the BML blood laboratory (Saitama, Japan). The remaining serum was stored at −80°C for lipoprotein analysis. Eighteen lipoprotein subfractions were measured by HPLC using a column of TSK gel Lipopropak XL (Tosoh, Tokyo, Japan) at the Skylight Biotech Laboratory (Tokyo, Japan): large VLDL1, large VLDL2, large VLDL3, medium VLDL, small VLDL, large LDL, medium LDL, small LDL, very small LDL1, very small LDL2, very small LDL3, very large HDL1, very large HDL2, large HDL, medium HDL, small HDL, very small HDL1, and very small HDL2.

Statistical analyses. Values were obtained as means ± standard deviations (SD). Differences between the groups were evaluated by Student’s t-test. p-values less than 0.05 were considered statistically significant.

RESULTS AND DISCUSSION

Subject characteristics and blood biochemical analyses
There were no significant differences in body weight, body fat percentage, body mass index, hematology, or biochemistry before and after RJ intake (Table 1).
### Table 3. Effect of long-term intake of royal jelly (RJ) on serum lipoprotein concentration in healthy subjects. \(^1,2\)

<table>
<thead>
<tr>
<th></th>
<th>Before</th>
<th>After</th>
<th>Particle diameter (nm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Large VLDL(_1) (mg/dL)</td>
<td>1.14±0.84</td>
<td>1.42±0.92</td>
<td>64.0</td>
</tr>
<tr>
<td>Large VLDL(_2) (mg/dL)</td>
<td>3.49±1.81</td>
<td>4.59±2.15</td>
<td>53.6</td>
</tr>
<tr>
<td>Large VLDL(_3) (mg/dL)</td>
<td>9.74±3.02</td>
<td>11.82±4.38</td>
<td>44.5</td>
</tr>
<tr>
<td>Medium VLDL (mg/dL)</td>
<td>10.68±4.51</td>
<td>10.99±4.49</td>
<td>36.8</td>
</tr>
<tr>
<td>Small VLDL (mg/dL)</td>
<td>16.4±4.35</td>
<td>0.07±2.43*</td>
<td>31.3</td>
</tr>
<tr>
<td>Large LDL (mg/dL)</td>
<td>32.5±8.19</td>
<td>27.37±4.47 (p=0.09)</td>
<td>28.6</td>
</tr>
<tr>
<td>Medium LDL (mg/dL)</td>
<td>32.7±7.19</td>
<td>32.98±10.57</td>
<td>25.5</td>
</tr>
<tr>
<td>Small LDL (mg/dL)</td>
<td>18.59±3.95</td>
<td>21.3±9.81</td>
<td>23.0</td>
</tr>
<tr>
<td>Very small LDL(_1) (mg/dL)</td>
<td>7.11±1.44</td>
<td>8.42±4.03</td>
<td>20.7</td>
</tr>
<tr>
<td>Very small LDL(_2) (mg/dL)</td>
<td>2.71±0.46</td>
<td>3.00±1.10</td>
<td>18.6</td>
</tr>
<tr>
<td>Very small LDL(_3) (mg/dL)</td>
<td>1.12±0.15</td>
<td>1.13±0.27</td>
<td>16.7</td>
</tr>
<tr>
<td>Very large HDL(_1) (mg/dL)</td>
<td>1.64±0.29</td>
<td>1.52±0.26</td>
<td>15.0</td>
</tr>
<tr>
<td>Very large HDL(_2) (mg/dL)</td>
<td>3.03±1.28</td>
<td>3.18±1.70</td>
<td>13.5</td>
</tr>
<tr>
<td>Large HDL (mg/dL)</td>
<td>12.43±5.34</td>
<td>12.67±7.70</td>
<td>12.1</td>
</tr>
<tr>
<td>Medium HDL (mg/dL)</td>
<td>19.91±1.57</td>
<td>20.34±4.47</td>
<td>10.9</td>
</tr>
<tr>
<td>Small HDL (mg/dL)</td>
<td>15.06±1.01</td>
<td>15.56±2.40</td>
<td>9.8</td>
</tr>
<tr>
<td>Very small HDL(_1) (mg/dL)</td>
<td>5.34±0.42</td>
<td>5.08±1.29</td>
<td>8.8</td>
</tr>
<tr>
<td>Very small HDL(_2) (mg/dL)</td>
<td>2.67±0.14</td>
<td>2.58±0.34</td>
<td>7.6</td>
</tr>
</tbody>
</table>

\(^1\) Subjects received or did not receive 6 g RJ daily for 4 wk. \(^*\) Differences between before and after RJ intake. p<0.05.

\(^2\) Values are means±SD. n=7.

**Serum lipoprotein metabolism**

At the end of the experimental period, serum TC and LDL concentrations in the RJ group were significantly reduced (p<0.05) compared with those in the control group (Table 2). There were no significant differences in serum HDL or triglyceride concentrations (Table 2). RJ significantly affects lipid metabolism in rats and mice (7, 8). Clinical studies have demonstrated that RJ significantly reduces serum TC levels by about 14% and total serum lipids by about 10% in atherosclerotic patients with moderately high cholesterol levels (9, 10). Our results also show a cholesterol-lowering effect of RJ in humans. Serum TC levels were reduced by about 6.0% and LDL levels by 9.1% during the RJ diet (Table 2). Among lipoprotein subfractions, small VLDL (p<0.05) was decreased after RJ intake (Table 3). However, no significant difference was found in the other subfractions.

The major plasma lipids include cholesterol, triglycerides, and phospholipids. Lipoproteins are macromolecular complexes that play important roles in the transport and metabolism of lipids. LDL is the main cholesterol-carrying lipoprotein in the circulation. High serum levels of cholesterol are usually due to excessively high levels of LDL cholesterol. A high LDL level can result from excess formation of LDL due to failure of the liver to remove VLDL, the precursor of LDL. LDL is a breakdown product of VLDLs (large, medium, and small VLDL). In the plasma, large VLDL particles are either eliminated as such or catabolized to small VLDL through the lipolysis of triglycerides by lipoprotein lipase bound to the endothelium. The metabolism of VLDL appears to be one factor regulating serum concentrations of LDL cholesterol. Moreover, VLDL gives rise to LDL, which has been proven to be atherogenic. Therefore, RJ may decrease TC, LDL, and VLDL levels.

How RJ affects the regulation of plasma cholesterol concentration is not yet known. One possible mechanism is the large number of proteins in RJ, which may decrease plasma levels of cholesterol, LDL, and small VLDL. Dietary protein has been shown to affect plasma cholesterol concentration (13). Dietary soybean protein lowers plasma triglyceride concentrations and apolipoprotein levels and increases VLDL uptake by hepatocytes (14, 15). RJ decreases liver cholesterol levels in animals (15) and total serum cholesterol serum lipids in humans (6, 10). More recent data have shown that RJ decreases the levels of cholesterol biosynthesis enzyme and influences the activity of the hepatic lipoprotein receptors that regulate VLDL uptake in mice (16). These data suggest that dietary RJ decreases small VLDL levels. In humans, RJ protein may increase small VLDL uptake by active hepatic lipoprotein receptors. Another possible mechanism is the suppression of hepatic sterol synthesis. The estrogen-like effects of RJ may decrease the concentrations of plasma cholesterol and LDL in vivo and in vivo (17–19). In addition, unsaturated fatty acids in RJ, such as trans-10-hydroxy-2-decenolic acid, essential fatty acids, arachidonic acid, and royal jelly (20), probably regulate lipid metabolism.

Recent studies suggest that small VLDL is the strongest independent predictor of disease progression and is more directly involved in atherosclerosis progression than LDL particles, which have been traditionally considered to be the major atherogenic lipoproteins (21). RJ may decrease the risk of atherosclerosis by lowering small VLDL levels.

In conclusion, RJ benefits lipoprotein metabolism in humans. We believe that dietary RJ may help prevent lifestyle-related diseases in humans.
Acknowledgments

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REFERENCES


