JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY

Effects of Dietary Herring Roe Lipids on Plasma Lipid, Glucose, Insulin, and Adiponectin Concentrations in Mice

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The aim of this study was to evaluate the effects of dietary Kazunoko (salted herring roe) lipids, which contain large amounts of cholesterol, phosphatidylcholine, and n-3 polyunsaturated fatty acids, such as eicosapentaenoic acid (EPA, 20:5n-3) and docosahexaenoic acid (DHA, 22:6n-3), on lipid and glucose metabolism in mice. Male Crlj:CD-1 (ICR) mice were fed one of four experimental diets which contained 6% lard, 1% Kazunoko lipids + 5% lard, 3% Kazunoko lipids + 3% lard, and 6% Kazunoko lipids for 12 weeks. Plasma total cholesterol, triacylglycerol, phospholipid, and glucose concentrations were significantly lower in the 3% and 6% Kazunoko lipid diet groups than in lard and 1% Kazunoko lipid diet groups ($p < 0.05$). Plasma adiponectin concentrations of mice fed the 6% Kazunoko lipid diet were higher than those of animals fed the lard diet group. These results suggest that EPA and DHA rather than cholesterol in the Kazunoko lipids influence the plasma total cholesterol level. The constituent Kazunoko lipids may not only decrease the levels of plasma lipids but also decrease glucose concentrations by enhancing plasma adiponectin levels in mice.

KEYWORDS: Kazunoko; n-3 polyunsaturated fatty acid; cholesterol; plasma lipids; plasma glucose; insulin; adiponectin

INTRODUCTION

Although caviar is the most well-known salted fish roe product in the world, there are various other salted fish roe products, such as Ikura (salmon roe), Tarako (pollock roe), Tobiko (flyingfish roe), and Kazunoko (herring roe), that have been traditionally consumed in Japan. Fish roe products are rich in cholesterol (*1*, *2*), and it is generally thought that an excess of cholesterol intake increases the risks of coronary heart disease (CHD) (*3*). Thus, it has been considered possible that fish roe products might also increase this risk. It has been shown that a reduction in the intake of some typical cholesterol-rich foods such as eggs decreases the plasma cholesterol level (*4*). However, fish roe lipids also contain a large amount of n-3 polyunsaturated fatty acids (PUFAs), such as eicosapentaenoic acid (C20:5n-3, EPA) and docosahexaenoic acid (C22:6n-3, DHA) (*1*, *2*), which could exert beneficial effects on CHD.

Previous studies have shown that an intake of n-3 PUFAs decrease plasma lipid concentrations and improve insulin resistance (*5*, *6*), thereby reducing the risk of cardiovascular disease and metabolic syndrome (*7*, *8*). In one study the ingestion of salmon roe (n-3 PUFA enriched in phosphatidylcholine) appeared to improve lipid metabolism in humans as administration to normolipidaemic patients with chronic liver disease significantly increased the plasma high-density lipoprotein concentration (*9*). However, there is little documented information on the effects of fish roe lipids on cardiovascular disease and metabolic syndrome.

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We have reported the detailed lipid classes and fatty acid composition of various fish roe products (*2*). The percentages of EPA and DHA in Kazunoko lipids were 15.0 ± 0.6 and 22.6 ± 1.0 (mean ± SD), respectively, which are similar to those of fish oil. Kaitaranta also reported that the fatty acid pattern of total lipids from fish roe was similar to that of fish flesh (*1*). An intake of n-3 PUFA decreases blood glucose levels and insulin resistance (*6*, *10*), and recently it was also reported that the ingestion of fish oil increased plasma adiponectin levels (*11*). However, the cholesterol content of Kazunoko lipids is higher than that in fish oil, and it is not clear whether the beneficial effects of the n-3 PUFA in Kazunoko lipids on lipid and glucose metabolism counteract, or indeed supersede, the deleterious effects of the cholesterol. The aim of this study was to investigate the effects of Kazunoko lipids on lipid and glucose metabolism in mice.

MATERIALS AND METHODS

Animals. Male mice of Crlj:CD1 (ICR) strain (4 weeks old) were obtained from Charles River Japan Inc. (Atsugi, Kanagawa, Japan). All animals were switched from a laboratory chow, MF (Oriental Yeast Co., Ltd., Tokyo, Japan), to experimental diets at 5 months of age. Total lipid content in MF was 6%, and percentages of main fatty acids were as follows: 16:0, 14.3; 18:1n-9, 23.7; 18:2n-6, 48.3; 18:3n-3, 3.9; 20:4n-6, ND; 20:5n-3, 0.9; 22:6n-3, 1.4. Forty mice were randomly divided into 4 groups of 10 animals each, and they were housed in suspended stainless steel cages with wire mesh bottoms. The animal room was kept at 24 ± 0.5 °C and the relative humidity at 65 ± 5%. Room lighting consisted of 12 h periods of light and dark. The diets and water were given ad libitum. The diet given to each group had

10.1021/jf0531712 CCC: $33.50
Published on Web 04/19/2006

Table 1. Composition of Experimental Diets (%)

	dietary group			
	lard	1% Kazunoko lipids	3% Kazunoko lipids	6% Kazunoko lipids
corn starch	47.8	47.8	47.8	47.8
casein	20	20	20	20
granulated sugar	15	15	15	15
cellulose powder	5	5	5	5
salt mixture[a]	4	4	4	4
vitamin mixture[b]	2	2	2	2
L-methionine	0.2	0.2	0.2	0.2
lard	6	5	3	–
Kazunoko lipid	–	1	3	6

[a] The mineral and vitamin mixtures were purchased from Oriental Yeast Co., Ltd. (Tokyo, Japan), and the compositions were previously described by Kohashi et al. (*14*). The mineral mixtures contained per kilogram: $CaHPO_4 \cdot 2H_2O$, 14.56 g; KH_2PO_4, 25.72 g; NaH_2PO_4, 9.35 g; NaCl, 4.66 g; Ca-lactate, 35.09 g; Fe-citrate, 3.18 g; $MgSO_4$, 7.17 g; $ZnCO_3$, 0.11 g; $MnSO_4 \cdot 4H_2O$, 0.12 g; $CuSO_4 \cdot 5H_2O$, 0.03 g; KI, 0.01 g. [b] The vitamin mixtures contained per kilogram: retinyl acetate, 0.1 g; cholecalciferol, 0.00025 g; α-tocopheryl acetate, 0.5 g; menadione, 0.52 g; thiamin·HCl, 0.12 g; riboflavin, 0.4 g; pyridoxine·HCl, 0.08 g; cyanocobalamine, 0.00005 g; ascorbic acid, 3 g; biotin, 0.002 g; folic acid, 0.02 g; calcium pantothenate, 0.5 g; *p*-aminobenzoic acid, 0.5 g; niacin, 0.6 g; inositol, 0.6 g; choline chloride, 20 g; cellulose powder, 73.1 g.

similar energy content. All mice were fed experimental diets for 12 weeks. Body weight was measured once every 2 weeks. All mice were maintained according to the guidelines for experimental animals of the National Food Research Institute, Japan.

Diet. The lard was kindly supplied from NOF Co., Ltd., Tokyo, Japan. Kazunoko lipids were extracted as follows: salted Kazunoko (20 kg) from Canada was immersed in distilled water overnight. The resultant desalted Kazunoko was broken by a vertical cutter blender (Robot Coupe R-1000, FMI, Osaka, Japan) at 3000 rpm for 1 min, and then it was processed, to a visually homogeneous paste, using a power blender (model 91400, Hamilton Beach, Washington, NC). The paste (15.8 kg) was combined with 35 L of 1/1 (v/v) hexane−ethanol, stirred for 30 min, and passed through a paper filter under suction. The residue was treated, using the same procedures, with 30 L of 1/1 (v/v) hexane−ethanol, and the two filtrates were combined. The hexane−ethanol was removed by evaporation, and the consequent residue (0.45kg) was used as the Kazunoko lipid sample (*12*, *13*). The extraction of Kazunoko lipids was performed by Nippon Chemical Feed Co., Ltd. (Hakodate, Hokkaido, Japan). The composition of Kazunoko lipid and lard diets is presented in **Table 1**. To prevent oxidative changes in fatty acid composition during storage, each experimental diet was stored below −40°C.

The fatty acid composition of each experimental diet is shown in **Table 2**. Percentages of 18:0, 18:1n-9, and 18:2n-6 in Kazunoko lipid diets were lower than those in the lard diet. Fatty acids 20:4n-6, 20:5n-3, and 22:6n-3 were detected in Kazunoko lipid diets. The n-3/n-6 ratio and cholesterol content increased with increasing amounts of Kazunoko lipids in the experimental diets.

Preparation of Plasma and Liver Homogenates. At the end of the feeding trials, i.e., week 12, all mice were fasted for 24 h before being anesthetized with diethyl ether. Blood was then collected from the inferior vena cava with a heparinized syringe and put into ice-cold tubes. After the blood was collected, the livers were removed and homogenized with 1/15 mol/L phosphate buffered saline (pH 7.4, Mitsubishi Kagaku latron, Tokyo, Japan) using a Teflon-glass homogenizer. The plasma was separated by centrifugation at 900*g* for 20 min at 4 °C. Plasma samples and liver homogenates were stored at −40 °C until required for analysis.

Lipid, Glucose, Insulin, and Adiponectin Analyses. Total cholesterol, triacylglycerol, phospholipid, and nonesterified fatty acid concentrations in plasma samples and liver homogenates were determined by the enzymatic methods of Allain et al. (*15*), Spayd et al. (*16*), Takayama et al. (*17*), and Shimizu et al. (*18*), respectively. Plasma glucose was measured by the method of Trinder using an oxidase−peroxidase system (*19*). Plasma insulin and adiponectin were measured with a mouse insulin ELISA kit (Morinaga Institute of Biological Science, Yokohama, Japan) and a mouse/rat adiponectin ELISA kit (Otsuka Pharmaceutical Co. Ltd., Tokyo, Japan), respectively.

Table 2. Main Fatty Acid Composition (%) and Cholesterol Content (mg/100 g Diet) of the Experimental Diets[a]

	dietary group			
	lard	1% Kazunoko lipids	3% Kazunoko lipids	6% Kazunoko lipids
SFA[b]				
14:0	2.1	2.1	2.3	2.8
15:0	0.2	0.2	0.3	0.4
16:0	26.1	25.7	26.6	29.1
17:0	0.6	0.5	0.4	0.3
18:0	13.4	12.2	9.5	2.5
total	42.2	40.8	39.1	35.1
MUFA[b]				
16:1n-9	0.3	0.3	0.4	0.7
16:1n-7	3.0	3.2	3.9	5.6
18:1n-9	41.8	38.8	31.6	13.9
18:1n-7	2.9	3.2	3.8	5.0
20:1	0.7	0.7	0.7	0.6
total	48.7	46.2	40.3	25.9
PUFA[b]				
18:2n-6	8.6	7.8	5.8	1.0
18:3n-3	0.5	0.5	0.5	0.5
20:4n-6	–	0.2	0.5	1.1
20:5n-3	–	1.7	5.5	14.7
22:6n-3	–	2.8	8.4	21.6
total	9.0	13.0	20.6	38.9
n-3/n-6	0.1	0.6	2.3	17.5
cholesterol (mg/100 g diet)	9	71	219	432

[a] Values are means, and <0.1% of total fatty acids are not reported. [b] SFA, saturated fatty acid; MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid.

Fatty Acid Analyses. Lipid extraction from the experimental diets was carried out by the method of Folch et al. (*20*). Lipid extraction and fatty acid derivatization from plasma and liver samples were done by the method of Shirai et al. (*21*). The fatty acids were measured on a gas chromatograph (GC-18A, Shimadzu Co., Ltd., Kyoto, Japan) equipped with a fused silica capillary column, Supelcowax 10 (30 m × 0.25 mm i.d., Supelco Co., Ltd., Bellefonte, PA) and fitted with a Class 10 integrator (Shimadzu Co., Ltd., Kyoto, Japan). The carrier gas was helium (flow 1 mL/min) with a split injection of 40:1. The temperature profiles were as follows: initial temperature, 175 °C; heat rate, 1 °C/min; final temperature, 220 °C; injector temperature, 250 °C; detector temperature, 270 °C. The total run time was 60 min. The fatty acids were identified by comparison of the retention times with those of standard purified fatty acids and marine fish oil already identified (*22*, *23*). The measurement of the cholesterol content in experimental diets was performed by Japan Food Research Laboratories.

Statistical Analyses. All results were expressed as mean ± SEM. The statistical significance of differences in lipid components, glucose, hormone concentrations, and fatty acid composition between dietary groups was determined by one-way analysis of variance (ANOVA) and Spjotvoll/Stoline test using the Statistica statistical program package (Statsoft, Tulsa, OK); the significance was set at $p < 0.05$.

RESULTS

Food Intakes and Body Weight. There were no differences in the average food consumption between dietary groups. The food intake (mean ± SEM) in each group was as follows: lard diet group, 4.1 ± 0.0 g/day; 1% Kazunoko lipid diet group, 4.1 ± 0.0 g/day; 3% Kazunoko lipid diet group, 4.1 ± 0.0 g/day; 6% Kazunoko lipid diet group, 4.1 ± 0.0 g/day. The time

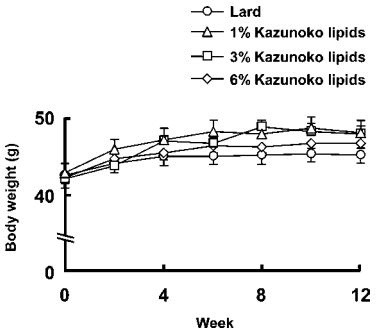

Figure 1. Time courses of changes in body weights of mice ($n = 10$/group). The statistical significance of differences between each dietary groups were determined at $p < 0.05$ by the Spjotvoll/Stoline test.

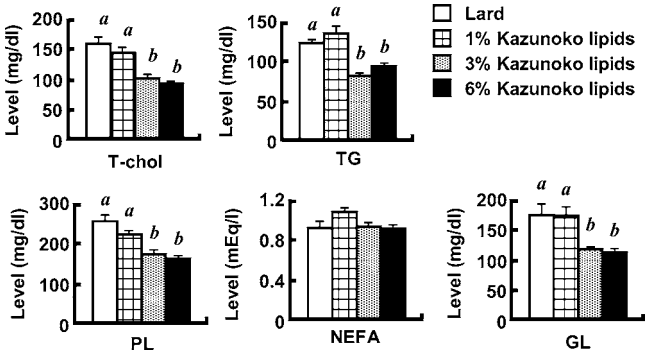

Figure 2. Plasma glucose, total cholesterol, triglyceride, phospholipid, and nonesterified fatty acid concentrations of mice fed experimental diets for 12 weeks ($n = 10$/group). Values for each sample with different italic letters in the same lipid class and glucose were significantly different at $p < 0.05$ by the Spjotvoll/Stoline test. T-chol, total cholesterol; TG, triacylglycerol; PL, phospholipid; GL, glucose; NEFA, nonesterified fatty acid.

courses for changes in body weights are shown in **Figure 1**. Body weights at each time point tended to be greater in all Kazunoko lipid diet groups than in the lard diet group. Final body weights were as follows: the lard diet group, 45.1 ± 1.1 g; 1% Kazunoko lipid diet group, 48.1 ± 1.5 g; 3% Kazunoko lipid diet group, 47.8 ± 1.1 g; 6% Kazunoko lipid diet group, 46.7 ± 0.5 g. However, there were no statistically significant differences in the final body weights between any of the dietary groups.

Concentrations of Plasma Lipid, Glucose, and the Lipid Components of Liver. The concentrations of plasma total cholesterol, triacylglycerol, phospholipid, nonesterified fatty acid, and glucose in mice are shown in **Figure 2**. Plasma total cholesterol, triacylglycerol, phospholipid, and glucose concentrations were significantly lower in the 3% and 6% Kazunoko lipid diet groups than in the lard and 1% Kazunoko lipid diet groups. There were no significant differences in the plasma concentrations of these components between 1% Kazunoko lipid and lard diet groups. There were no differences in plasma nonesterified fatty acid levels between dietary groups.

The levels of liver total cholesterol, triacylglycerol, and phospholipid in mice are shown in **Figure 3**. There were no marked differences in liver total cholesterol levels between any of the dietary groups. The liver triacylglycerol level of mice fed Kazunoko lipid diets tended to be higher than those of animals fed the lard diet. In particular, the triacylglycerol level of the 1% Kazunoko lipid diet group was significantly higher than that of all other groups. The level of liver phospholipid in

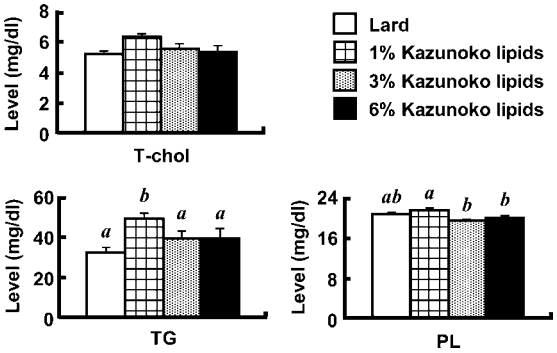

Figure 3. Liver total cholesterol, triglyceride, and phospholipid levels of mice fed experimental diets for 12 weeks ($n = 10$/group). Values for each sample with different italic letters in the same lipid class were significantly different at $p < 0.05$ by the Spjotvoll/Stoline test. T-chol, total cholesterol; TG, triacylglycerol; PL, phospholipid.

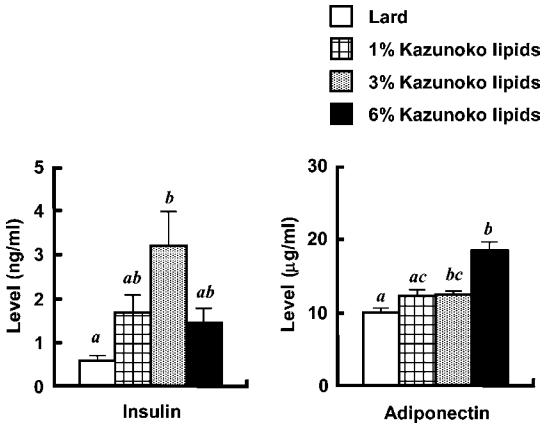

Figure 4. Plasma insulin and adiponectin concentrations of mice fed experimental diets for 12 weeks ($n = 10$/group). Values for each sample with different italic letters in the same lipid class and glucose were significantly different at $p < 0.05$ by the Spjotvoll/Stoline test.

mice fed Kazunoko lipid diets was similar to that of animals fed the lard diet.

Concentrations of Plasma Insulin and Adiponectin. The plasma insulin and adiponectin concentrations of mice in each dietary group are shown in **Figure 4**. The plasma insulin concentrations tended to be higher in mice fed the Kazunoko lipid diets than in animals fed the lard diet but this was only significant for the 3% Kazunoko lipid diet group. The plasma adiponectin concentration was significantly higher in the 3% and 6% Kazunoko lipid diet groups than the lard diet group. The plasma adiponectin concentration tended to be higher with increasing Kazunoko lipid intakes.

Fatty Acid Composition in Plasma and Liver. The plasma main PUFA composition of the mice fed each diet is shown in **Figure 5A**. The percentages of 20:4n-6 were significantly lower in the 1%, 3%, and 6% Kazunoko lipid diet groups than in the lard diet group. The 18:2n-6 percentage of the 1%, 3%, and 6% Kazunoko lipid diet groups tended to be higher than that of the lard diet group. The percentages of 20:5n-3 and 22:6n-3 in mice fed the 1%, 3%, and 6% Kazunoko lipid diets were significantly higher than those of animals fed the lard diet, and the increase in the percentage of plasma 22:6n-3 correlated with the amount of n-3 PUFA intake. The Σ(n-3) and n-3/n-6 ratio of the 1%, 3%, and 6% Kazunoko lipid groups were significantly higher than those of the lard group. The percentages of

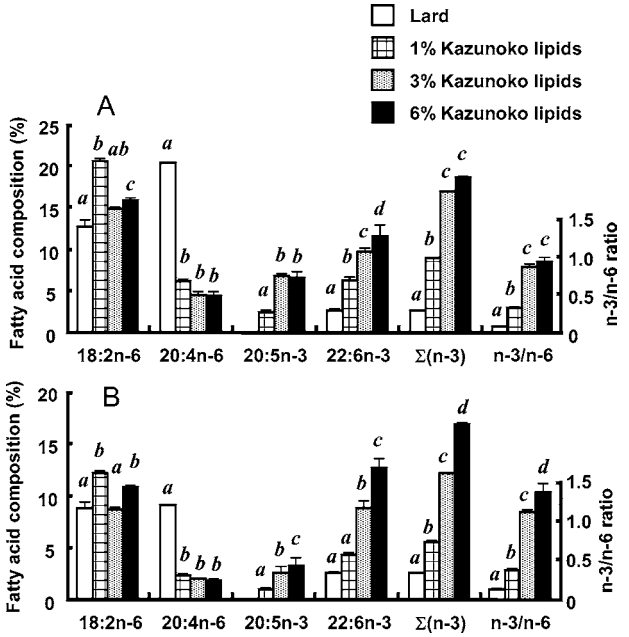

Figure 5. Percentages of plasma (**A**) and liver (**B**) 18:2n-6, 20:4n-6, and 20:5n-3, 22:6n-3, Σ(n-3), and n-3/n-6 ratio of mice fed experimental diets for 12 weeks ($n = 10$/group). Values for each sample with different italic letters in the same lipid class and glucose were significantly different at $p < 0.05$ by the Spjotvoll/Stoline test.

20:5n-3 and 22:6n-3, Σ(n-3), and n-3/n-6 ratio were higher in 3% and 6% Kazunoko lipid groups than in 1% Kazunoko lipid group.

The PUFA composition in the livers of mice fed each diet is shown in **Figure 5B**. The percentages of 18:2n-6, 20:4n-6, 20:5n-3, and 22:6n-3 in liver lipids followed a pattern similar to that seen in plasma. The Σ(n-3) and n-3/n-6 ratio of each dietary group were dependent on the percentages of Kazunoko lipids in the diet.

DISCUSSION

It is generally thought that a large amount of dietary cholesterol ingestion increases the risk of CHD and atherosclerosis since accumulation of low-density lipoprotein (LDL)-derived cholesterol in the inner layer of the arterial wall leads to the development of atherosclerotic lesions (*3*). In early 1970s, the American Heart Association had recommended that the consumption of cholesterol, for example from egg, should be restricted less than 300 mg/day in order to prevent the development of CHD. However, the effect of dietary cholesterol on increases in plasma cholesterol levels has recently been reappraised from the outcome of many cholesterol feeding studies over the past 30 years. It has been suggested that plasma cholesterol levels increase by approximately 2 mg/dL when an intake of dietary cholesterol in humans fed for more than 14 days increases 100 mg/day (*24*, *25*). Therefore, it has now been suggested that dietary cholesterol intake may have a limited influence on plasma cholesterol levels and the consequent development of atherosclerosis and CHD. As shown in **Table 2**, the cholesterol content in 1% and 6% Kazunoko lipids was respectively 7.9-fold and 48-fold larger than that in the lard diet. Nevertheless, plasma total cholesterol concentration in Kazunoko lipid diet groups was not higher than that in the lard diet group (**Figure 2**). These results indicate that dietary cholesterol in Kazunoko lipids had little influence on the plasma total cholesterol concentration. It has also been shown that n-3 PUFA have a beneficial effect on cholesterol metabolism in mice (*26*, *27*). Previously, we reported that plasma total cholesterol and phospholipid concentrations of mice were reduced by n-3 PUFA intakes (*28*, *29*). The reduction of cholesterol levels by fish oil intake may be dependent on the inhibition of absorption and/or on the enhancement of cholesterol excretion (*30*, *31*). Therefore, it is possible that, in the present study, the n-3 PUFA in Kazunoko lipids rather than the dietary cholesterol influences the plasma total cholesterol concentration of the mice. We previously showed that an intake of n-3 PUFA reduced the plasma total cholesterol concentration of mice after 6 weeks (*32*). From the present results, it would appear that a reduction in plasma total cholesterol concentrations in mice on a Kazunoko lipid diet requires a longer period of time than 6 weeks.

As shown in **Figure 3**, an intake of Kazunoko lipids did not markedly decrease liver total cholesterol, triacylglycerol, and phospholipid levels in mice compared with those in animals fed a lard diet. This contrasts with the plasma lipid concentrations in the Kazunoko diet groups which were much lower than those in the lard diet group. n-3 PUFA reduces the hepatic cholesterol level of mice (*27*, *32*). n-3 PUFA can down-regulate intestinal absorption of cholesterol, hepatic cholesterol synthesis, and/or enhance the cholesterol excretion (*30*, *31*, *33*). Nevertheless, the liver cholesterol level in mice fed the Kazunoko lipid diet did not reduce compared to animals fed the lard diet (**Figure 3**). It seems that a large amount of cholesterol derived from the Kazunoko lipids tend to remain in the liver of mice because the rate of cholesterol excretion from the liver is maybe lower than that of the cholesterol supply to the liver. Cholesterol absorption of mice is higher than that of humans (*34*), and the cholesterol in circulation of mice is mainly provided from the diet. Therefore, it is possible that the effect of dietary Kazunoko lipid on cholesterol homeostasis is larger in mice than in humans. Further, a detailed study is necessary to clarify the plasma cholesterol lowering mechanism by Kazunoko lipids intake in human and mice. The liver triacylglycerol level of the 1% Kazunoko lipid diet group was significantly higher than that of all other groups. There have been reports that triacylglycerol accumulation in the liver of rats fed a cholesterol-rich diet resulted from increased synthesis and decreased secretion of triacylglycerol (*35*, *36*). However, other results have indicated that n-3 PUFA reduces triacylglycerol synthesis in the liver of rodents by decreasing the expression of liver lipogenic enzymes (*37*, *38*). The effect of dietary cholesterol in Kazunoko lipids on liver triacylglycerol levels could be greater in the 1% Kazunoko lipid diet group than in the 3% and 6% Kazunoko lipid diet groups since amount of n-3 PUFA in the 1% Kazunoko lipid diet is low compared to the 3% and 6% Kazunoko lipid diets.

The plasma glucose concentrations were significantly lower in mice fed 3% and 6% Kazunoko lipid diets than in animals fed the lard and 1% Kazunoko lipid diets (**Figure 2**). A reduction in plasma glucose concentrations is associated with various hormones and/or cytokines. In this study, the plasma insulin concentrations of mice in Kazunoko lipid diet groups tended to be higher than the lard diet group, and there were significant increases in plasma adiponectin concentrations of mice fed Kazunoko lipids (**Figure 4**). Although it has been reported that the n-3 PUFA intake increases plasma insulin concentrations in mice (*39*), our results indicate that the plasma glucose concentration of each diet group was not dependent on the insulin concentration. Further, it is not clear why the plasma insulin concentration of the 3% Kazunoko diet group was higher

than all other dietary groups including the 6% Kazunoko diet group. It has been reported that plasma nonesterified fatty acid level increases when insulin resistance appears (*40*). We consider that insulin resistance does not appear in the 3% Kazunoko diet group since body weights and plasma nonesterified fatty acid levels of the 3% Kazunoko diet group are not markedly higher than all other dietary groups.

It has been reported that plasma adiponectin concentration in mice fed a fish oil diet is higher than in those fed a control diet (*11*). Plasma adiponectin level is negatively correlated with body mass index (*41*). The negative correlation is stronger between adiponectin levels and visceral adiposity than between the protein and subcutaneous adiposity. However, body weights of mice in the Kazunoko diet groups were not lower than in the lard diet group (**Figure 1**). It is possible that mice fed the Kazunoko diet tend to gain the subcutaneous adiposity but not the visceral adiposity. Adiponectin stimulates glucose utilization and fatty acid oxidation by activation of adenosine monophosphate-activated protein kinase (AMPK) (*42*, *43*). Suchankova et al. have proposed that PUFAs enhance hepatic AMPK activity in vivo (*44*). In contrast, Dobrzyn et al. reported that PUFAs do not activate AMPK in mouse liver, skeletal muscle, and heart (*45*). However, this latter study was only for 14 days, and in a previous study we showed that n-3 PUFA intake only reduced the plasma glucose concentration of mice after 8 weeks (*32*). Thus, it is possible that the mechanism by which plasma glucose concentrations in mice fed Kazunoko lipids are reduced may be partially mediated by adiponectin-induced AMPK activation.

As shown in **Figure 5**, the percentages of plasma and liver 20:4n-6 in Kazunoko lipid diet groups were significantly lower than that in lard diet group. The 18:2n-6 percentages in plasma and liver of mice fed the Kazunoko lipid diet tended to be higher than those of animals fed the lard diet despite the percentage of 18:2n-6 in Kazunoko lipid being markedly lower than that of lard. Results indicate that 18:2n-6 could be a precursor in the synthesis of 20:4n-6 in mammalian cells, and the synthesis of 20:4n-6 is suppressed by 22:6n-3 intake (*46*). This would suggest that ingestion of 22:6n-3 in Kazunoko lipids would inhibit the synthesis of 20:4n-6, resulting in an accumulation of 18:2n-6. However, the aims of this particular study did not allow the elucidation of a detailed mechanism.

In conclusion, we showed that plasma cholesterol, triacylglycerol, phospholipid, and glucose concentrations were reduced, and plasma adiponectin level increased in mice fed the Kazunoko lipid diet. Moreover, an intake of Kazunoko lipids markedly influenced the plasma and liver PUFA profiles. The ingestion of Kazunoko lipids may contribute to the improvement of lipid and glucose metabolism by increasing plasma adiponectin concentrations in mice.

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Received for review December 19, 2005. Revised manuscript received March 14, 2006. Accepted March 20, 2006. This study was supported by grant from the Canadian Pacific Kazunoko Association.

JF0531712