cis-バクセン酸経口投与は膵臓と心臓の脂肪酸組成を変化させる

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Oral Administration of *cis*-Vaccenic Acid alters the Fatty Acid Composition of the Pancreatic and Heart Tissues

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Persimmon fruit has a characteristic fatty acid (FA) composition with a high *cis*-vaccenic acid (*cis*-VA: C18:1, n-7) ratio; however, the effect of ingesting *cis*-VA is unknown. Therefore, to elucidate the effect of *cis*-VA upon ingestion, it was orally administered to normal (C57BL/6JJcl) and diabetic (KK-A^y/TaJcl) mice for 7 d. The FA composition of each tissue was analyzed to identify the tissues in which *cis*-VA acts, as well as those that may be affected by FA metabolism. *cis*-VA administration altered the FA composition of the pancreas in normal mice and the hearts of diabetic mice. Multiple FA ratios were altered, with five FA showing common changes between the heart and pancreas. This suggests that *cis*-VA ingestion may affect the pancreas and heart, and cause common changes in FA metabolism. Overall, *cis*-VA may have unique actions that differ from those of other monounsaturated FA.

Keywords: *cis*-vacceninc acid, fatty acid composition

1. Introduction

Persimmon fruit is consumed globally, and contains abundant amounts of vitamin C and β-carotene, which have antioxidant properties. Persimmon fruit contains β-cryptoxanthin, which acts against type 2 diabetes and osteoporosis (Sugiura *et al.* 2008, 2012, 2015), and tannins, which have a blood pressure-lowering effect and an antiviral effect (Sugawara & Igarashi 2014, Ueda *et al.* 2013). Mature persimmon fruits often remain unused because of their over-ripeness. In addition, some young persimmon fruits are harvested to allow the remaining fruits to grow sufficiently and are discarded without being used. If novel uses are discovered for these unused fruits, the persimmon industry can be improved by reducing the number of discarded fruits.

In persimmon fruit, *cis*-vaccenic acid (*cis*-VA, 18:1, n-7) accounts for approximately 30% of the total fatty acid (FA) content and 95% of the C18 monounsaturated FAs (Shibahara *et al.* 1987). This FA composition is unique to persimmon fruit. We previously reported the lipid content and FA profiles of immature and mature fruits from 18 persimmon cultivars and determined that both the content and percentage of *cis*-VA were higher in mature fruits than in immature fruits (Katsuki & Izuchi 2018)[7]. Focusing on this FA composition may lead to the development of new and distinctive processed products.

cis-VA is synthesized from palmitoleic acid (POA) (16:1, n-7) by FA elongation of very long-chain FA protein 5 (ELOVL5) in vivo. In patients with human coronary heart disease, the percentage of *cis*-VA in the FA composition of the erythrocyte cell membrane is low (Djoussé *et al.* 2012), and the higher the blood *cis*-VA concentration, the lower the incidence of diabetes (Djoussé *et al.* 2014). Therefore, a relationship between *cis*-VA and coronary heart disease has been proposed. In addition, ELOVL5 over-expression mice have improved glucose tolerance, which has been suggested to be associated with *cis*-VA and diabetes (Tripathy & Jump 2013). However, no studies have reported the dietary intake of *cis*-VA, and the effects of ingestion are unknown. An improved understanding of the effects of *cis*-VA intake may increase the value of persimmon fruit as a food source.

It is not clear in which tissues *cis*-VA ingestion occurs and what effects it exerts. Previous studies in which FAs were administered to mice evaluated tissue FA composition, suggesting effects on FA metabolism (Shinohara *et al.* 2012, Casey *et al.* 2013). Therefore, we hypothesized that VA administration may also affect FA metabolism and alter FA composition in both tissues. To explore the tissues in which *cis*-VA acts and evaluate the accompanying changes in FA metabolism, we orally administered *cis*-VA to C57BL/6JJcl

mice and obese type 2 diabetes model mice (KK-A^y/TaJcl), which are thought to have abnormalities in FA metabolism (Adachi *et al.* 2017, Teraoka *et al.* 2011, Kon *et al.* 2010). We focused on the tissues involved in energy metabolism and analyzed their FA composition.

2. Materials and methods

2-1. Preparation of *cis*-VA test samples

The test samples were prepared according to a method previously described (Yang *et al.* 2011). Polyglycerol ester (1.5%; Mitsubishi-Chemical Foods, Tokyo, Japan) were prepared using ultrafiltered water. Chemically synthesized *cis*-VA (98.3% purity; Intellim, Tokyo, Japan) was suspended in 1.5% polyglycerol ester to a final concentration of 30 mg/mL and vortexed for 30 s.

2-2. Experimental animals

Nine-week-old C57BL/6JJcl (normal) and KK-A^y/TaJcl (diabetic) male mice were purchased from CLEA Japan (Tokyo, Japan). Animals were individually housed in plastic cages under controlled conditions: 22–23˚C and 40–60% humidity with a 12 h-light/dark cycle. Animals had free access to distilled water and laboratory chow (CRF1; Oriental Yeast, Tokyo, Japan). This animal study was approved by the Animal Experiment Committee of Toyo Institute of Food Technology (No. 2017-A-004).

2-3. *cis*-VA administration

After acclimatization for 1 week, normal mice were divided into two groups: control (NC group, n=3) and *cis*-VA-administered (NV group, n=4) groups. Diabetic mice were also divided into control (DC group, n=3) and a *cis*-VA-administered (DV group, n=4) groups. The NC and DC groups were orally gavaged with a 1.5% polyglycerol ester solution, and the NV and DV groups were administered 300 mg/kg *cis*-VA daily for 7 d. On day 7 after administration, the mice were fasted for 3 h. Mice were euthanized by whole blood collection from the posterior vena cava under isoflurane anesthesia. The liver, pancreas, heart, and epididymal white adipose tissue (eWAT) were collected, frozen by liquid nitrogen, and stored at -80˚C. The collected blood was kept at 4˚C overnight and then centrifuged at 1000 × g to prepare serum. Serum blood glucose, triglyceride, free FAs, low-density lipoprotein (LDL), high-density lipoprotein (HDL) cholesterol, aspartate aminotransferase (AST), and alanine aminotransferase (ALT) levels in the DC and DV groups were measured using an automatic biochemistry analyzer (7180 Clinical Analyzer, Hitachi High-tech, Tokyo, Japan).

2-4. Lipid extraction

Lipid extraction was performed according to the Bligh-Dyer method (Bligh & Dyer 1959). Each tissue sample was transferred to a 1.5 mL Eppendorf tube, and 500 µl of calcium- and magnesium free phosphate-buffered saline (PBS (-)) was added, after which the tissues were crushed and homogenized with plastic homogenizer pestles in 1.5 mL tubes. The entire suspension was transferred to a Teflon centrifuge tube and PBS (-) was added until the liquid volume reached 2 mL. Next, 5 mL special grade methanol (Fujifilm Wako, Tokyo, Japan) and 2.5 mL special grade chloroform (Fujifilm Wako) were added, and the mixture was stirred vigorously for 2 min. After incubation at room temperature (15–25˚C) for 10 min, 2.5 mL chloroform was added and the mixture was vigorously stirred for 30 s. The mixture was then centrifuged (1000 × g, 25˚C, 10 min), and the chloroform layer was collected and transferred to pear-shaped glass flasks. Chloroform (2.5 mL) was added to the centrifuge tube, the mixture was vigorously stirred for 30 s, centrifuged (1000 × g, 25˚C, 10 min), and the chloroform layer was collected again and transferred to the same pear-shaped flask. The same process was repeated one to three times. The collected chloroform layer was vacuum-dried through rotary evaporation (EYELA, Tokyo, Japan), dissolved in 200 µL of chloroform: methanol (2:1) solution, and stored at -20˚C until analysis.

2-5. FA analysis by gas chromatography-mass spectrometry (GC-MS)

FA methylation and GC-MS analyses were performed according to the methods described by Morison and Smith (Morrison & Smith 1964). In short, 50 µL of the extracted lipid solutions were transferred to glass tubes with screw caps, and 1 mg of heptadecanoic acid was added to each tube as an internal standard. The solvent was completely volatilized using nitrogen gas in a 60˚C water bath, after which the glass tubes were cooled to room temperature using cold water. Sodium hydroxide-methanol (1.5 mL, 0.5 M) was added to each tube, and the mixtures were allowed to react at 105˚C for 9 min after adding nitrogen gas to the glass tubes. After cooling the tubes to room temperature, 2 mL of boron trifluoride methanol complex-methanol solution (Sigma-Aldrich, St. Louis, USA) was added, and the mixtures were allowed to react at 105˚C for 7 min after replacing the air with nitrogen gas in the glass tubes. After cooling to room temperature, 3 mL of special-grade hexane (Fujifilm Wako) was added, and the tubes

were shaken vigorously. Furthermore, 5 mL of saturated saline solution was added, and the mixture was gently mixed by inversion. After standing at room temperature for 5 min, the upper layer was collected, filtered with 13HP045AN syringe filters (Advantec, Tokyo, Japan), and stored at -20˚C until analysis.

For FA analysis, an Agilent 7890A GC (Agilent Technologies Japan, Tokyo, Japan) with an SP2380 column (100 m × 0.25 mm; 0.2 μm film thickness, Supelco, Tokyo, Japan) was used. Analyses were performed under the following conditions; injection volume: 1 μl, inlet temperature: 250˚C, split ratio: 20:1, carrier gas: helium (1 mL/min), column temperature: held at 50˚C for 1 min, increased to 140˚C at 20˚C/min, increased to 240˚C at 4˚C/min, and held at 240˚C for up to 50 min. The individual FAs were identified from MS obtained by JMS-T100GC (JEOL, Tokyo, Japan) and the retention times of FAs in the 37 Component FAME Mix (Supelco), which was used as the standard. Furthermore of each tissue type was quantified using standard curves created from standards of palmitic acid (PA), POA, stearic acid (SA), oleic acid (OA), *cis*-VA, linoleic acid (LA), arachidonic acid (AA), and docosahexaenoic acid (DHA) (Sigma-Aldrich). "Total" FA content was calculated as the sum of the seven FAs that were measured. The composition ratio of each measured FA was calculated and is presented as a percentage of the total FA content for each tissue type.

2-6. Statistical analysis

All data are presented as mean ± standard error (SE). The comparison between more than three groups was performed using the Tukey method, and the comparison between two groups was performed using Student's t-test (significance difference: $p<0.05$).

3. Results

3-1. Effect of *cis*-VA administration on body weight, tissue weight, and blood parameters

The DC group showed significantly higher food intake; body, liver, and eWAT weights; and lower pancreatic, brain, and testis weights than the NC group (Table 1). In turn, the NV group had a significantly lower pancreatic weight than the NC group. In addition, the liver weight of the DV group was significantly lower than that of the DC group, with no significant difference compared with that of the NC group. No differences were observed between the serum parameters measured in the DV and DC groups (Table 2).

Table 1 Body weight, food intake, and tissue weight

	NC	NV	DC	DV
body weight (g)	24.08±0.33^{b}	23.53±0.41^{b}	37.19±1.39^{a}	36.18±0.96^{a}
food intake (g/d)	3.42±0.09^{bc}	3.15±0.15^{c}	4.71±0.23^{a}	4.21±0.28^{ab}
organ weights (mg/g body weight)				
liver	50.02±0.61^{b}	47.23±0.80^{b}	56.37±1.73^{a}	48.88±0.90^{b}
pancreas	9.93±0.19^{a}	8.99±0.05^{b}	6.75±0.45^{c}	6.97±0.06^{c}
heart	5.20±0.43	5.89±0.47	6.04±0.57	4.74±0.30
brain	19.51±0.21^{a}	19.92±0.16^{a}	11.26±0.44^{b}	11.35±0.43^{b}
kidneys	5.90±0.16^{ab}	6.43±0.36^{a}	5.70±0.08^{ab}	5.42±0.14^{b}
eWAT	6.45±0.94^{b}	8.81±0.77^{b}	18.40±1.02^{a}	16.96±1.26^{a}
testes	4.54±0.10^{a}	4.75±0.15^{a}	2.75±0.20^{b}	2.92±0.15^{b}

Body weight, average food intake, and organ weight 7 d after *cis*-VA administration to C57BL/6JJcl and KK-A^{y} mice. Body weight was measured on the seventh day, and the average food intake over 7 days and organ weight (mg/g body weight) on day 7 were calculated. The significance test was performed using Tukey's method, and different characters indicate statistically significant differences ($p < 0.05$).

Table 2 Serum biochemical parameters

	DC	DV
glucose (mg/dlL)	226.3±89.2	272±40.0
triglycerides (mg/dL)	101.3±42.4	93.5±9.1
FFAs (μEq/L)	799.3±168.3	934.3±64.8
LDL-cholesterol (mg/dL)	16.7±4.9	13.5±1.9
HDL-cholesterol (mg/dL)	112.7±11.1	99.3±4.2
AST (IU/L)	58.7±7.1	46.3±3.9
ALT (IU/L)	25.0±5.3	20.8±2.3

Levels of serum biochemical parameters (glucose, triglycerides, FFAs, HDL cholesterol, LDL cholesterol, AST, and ALT) were measured 7 d after *cis*-VA administration to KK-A^y mice. Statistically significant differences were determined using the Student's t-test * ($p < 0.05$).

3-2. Change of FA composition by *cis*-VA administration

To investigate the effect of *cis*-VA administration on the tissue FA composition, we quantified seven FAs (PA, POA, SA, OA, *cis*-VA, LA, AA, and DHA) and calculated the composition ratio of each measured FA as a percentage of the total FA content for the specific tissue type. First, we compared these ratios between normal and diabetic mice. In the liver, the DC group had significantly lower SA, AA, and DHA ratios and significantly higher OA and *cis*-VA ratios than the NC group (**Table 3**). In the pancreas, the mice in the DC group had a significantly lower POA ratio and higher *cis*-VA and LA ratios than those in the NC group. The DC group exhibited significantly higher SA and AA ratios in the heart, and a higher PA ratio and lower POA, AA, and DHA ratios in the eWAT than the NC group. Next, we investigated the effects of *cis*-VA administration.

Table 3 FA composition of the liver, pancreas, heart, and eWAT lipids

		NC (%)	NV (%)	DC (%)	DV (%)
liver	PA (16:0)	25.5±0.5	24.9±0.7	23.3±0.4	22.9±0.7
	POA (16:1)	$2.2±0.2^{ab}$	$1.9±0.3^{a}$	$3.6±0.7^{ab}$	$3.6±0.4^{b}$
	SA (18:0)	$12.3±0.2^{a}$	$12.1±0.5^{a}$	$8.4±0.6^{b}$	$9.7±0.9^{ab}$
	OA (18:1, n-9)	$12.0±0.8^{a}$	$11.1±1.1^{a}$	$28.5±0.1^{b}$	$21.4±2.8^{b}$
	cis-VA (18:1, n-7)	$2.6±0.2^{a}$	$2.4±0.2^{a}$	$5.2±0.5^{b}$	$5.5±0.5^{b}$
	LA (18:2)	18.6±0.0	20.0±0.8	18.2±0.8	19.5±1.1
	AA (20:4)	$14.2±0.7^{a}$	$14.0±1.2^{a}$	$6.0±0.2^{b}$	$8.6±1.0^{b}$
	DHA (22:6)	$12.5±0.4^{a}$	$13.6±0.8^{a}$	$6.8±0.1^{b}$	$8.7±0.8^{b}$
pancreas	PA (16:0)	$28.3±0.2^{a}$	$27.0±0.1^{b}$	$28.2±0.2^{ab}$	$30.0±0.4^{c}$
	POA (16:1)	$5.6±0.4^{a}$	$2.2±0.3^{b}$	$2.8±0.4^{b}$	$2.6±0.2^{b}$
	SA (18:0)	$9.3±0.6^{a}$	$13.8±0.6^{b}$	$9.2±1.5^{a}$	$11.6±0.1^{ab}$
	OA (18:1, n-9)	$19.1±1.2^{a}$	$11.1±1.1^{b}$	$21.3±2.3^{a}$	$16.7±0.4^{a}$
	cis-VA (18:1, n-7)	$2.9±0.1^{a}$	$3.2±0.1^{ab}$	$3.4±0.1^{b}$	$3.4±0.1^{b}$
	LA (18:2)	$22.4±0.8^{a}$	$20.7±0.3^{a}$	$27.5±1.0^{b}$	$25.8±0.4^{b}$
	AA (20:4)	$9.6±1.4^{a}$	$17.4±0.9^{b}$	$5.6±1.5^{a}$	$7.2±0.3^{a}$
	DHA (22:6)	$2.9±0.3^{a}$	$4.7±0.2^{b}$	$1.9±0.4^{a}$	$2.7±0.1^{a}$
heart	PA (16:0)	$19.9±2.0^{ac}$	$15.9±0.2^{b}$	$23.6±0.6^{a}$	$16.6±0.3^{bc}$
	POA (16:1)	$2.8±0.5^{ab}$	$1.1±0.6^{a}$	$3.7±0.4^{b}$	$1.8±0.2^{ab}$
	SA (18:0)	$15.2±1.1^{a}$	$16.9±0.5^{a}$	$12.3±0.5^{b}$	$16.0±0.2^{a}$
	OA (18:1, n-9)	$12.8±2.4^{ab}$	$9.0±0.7^{a}$	$18.0±1.0^{b}$	$10.8±0.5^{a}$
	cis-VA (18:1, n-7)	$3.3±0.1^{ac}$	$4.2±0.0^{b}$	$3.2±0.2^{a}$	$3.6±0.1^{c}$
	LA (18:2)	17.7±0.3	17.1±0.5	17.9±1.9	16.3±0.1
	AA (20:4)	$5.6±0.8^{a}$	$7.2±0.3^{a}$	$3.6±0.4^{b}$	$5.7±0.3^{a}$
	DHA (22:6)	$22.6±3.2^{ab}$	$28.5±1.1^{a}$	$17.7±2.2^{b}$	$29.3±1.0^{a}$
eWAT	PA (16:0)	$25.0±0.0^{a}$	$24.3±0.4^{a}$	$28.5±0.6^{b}$	$28.1±0.2^{b}$
	POA (16:1)	$5.8±0.1^{a}$	$6.2±0.4^{a}$	$3.7±0.2^{b}$	$3.9±0.2^{b}$
	SA (18:0)	2.8±0.2	2.9±0.1	3.3±0.1	3.2±0.1
	OA (18:1, n-9)	28.6±0.3	29.2±0.1	28.8±0.7	28.8±0.2
	cis-VA (18:1, n-7)	$3.1±0.1^{a}$	$3.7±0.1^{b}$	$3.6±0.2^{ab}$	$3.8±0.0^{b}$
	LA (18:2)	32.6±0.3	32.1±0.6	31.0±1.3	31.3±0.2
	AA (20:4)	$0.8±0.2^{a}$	$0.6±0.0^{ab}$	$0.4±0.0^{b}$	$0.4±0.0^{b}$
	DHA (22:6)	$1.3±0.2^{a}$	$1.0±0.1^{ab}$	$0.6±0.0^{b}$	$0.6±0.0^{b}$

FA composition (%) of the liver, pancreas, heart, and eWAT of C57BL/6JJcl and KK-A^y mice 7 d after *cis*-VA administration. The significance test was performed using Tukey's method, and different characters indicate statistically significant differences ($p < 0.05$).

In the pancreas, the NV group showed significantly lower PA, POA, and OA ratios, and higher SA, AA, and DHA ratios than the NC group (**Table 3**). In the heart tissue, the NV group had a significantly lower PA ratio and a higher *cis*-VA ratio than the NC group. In eWAT, the NV group also showed a significantly higher *cis*-VA ratio than the NC group. There were no significant differences in the liver FA ratios between the NC and NV groups (**Table 3**). In the pancreas, the DV group exhibited a significantly higher PA ratio than the DC group. In the heart, the DV group showed significantly lower PA, POA, and OA ratios and higher SA, AA, and DHA ratios than the DC group. No significant differences were observed in the FA ratios in the liver and eWAT between the DC and DV groups.

3-3. Change of OA/SA ratio by *cis*-VA administration

cis-VA administration altered the SA and OA ratios in normal mice pancreas tissues and in diabetic mice heart tissues; therefore, one possible cause was considered to be that stearoyl-CoA desaturase 1 (SCD1), which is an enzyme involved in the synthesis of SA from OA, was activated in these tissues. To investigate the effects on SCD1 activity, the OA/SA ratios for each group and tissue type were calculated, which are used as indicators of SCD1 activity (Attie *et al.* 2002). First, we compared C57 mice with KK-A^y mice. The DC group showed a significantly higher OA/SA ratio in the liver and heart than the NC group. Next, we investigated the effect of *cis*-VA administration on this ratio. In the pancreas, the NV group exhibited a significantly lower OA/SA ratio than the NC group. Similarly, in the heart, the DV group showed a significantly lower ratio than the DC group (**Fig. 1**).

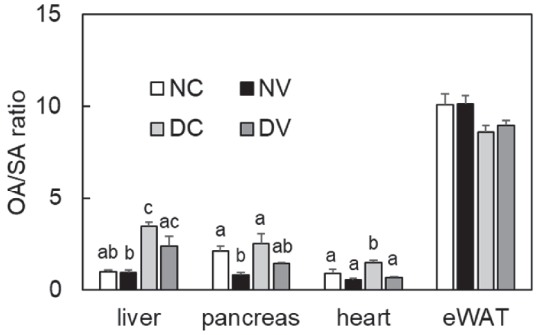

Fig. 1 OA/SA ratio.

The average OA/SA ratios were calculated from the FA composition of each tissue type after *cis*-VA administration to C57BL/6JJcl and KK-A^y mice for 7 d. □, NC group (n = 3); ■, NV group (n = 4); ■, DC group (n = 3); and ■, DV group (n = 4). Error bars indicate SE. The significance test was performed using Tukey's method, and different characters indicate statistically significant differences ($p < 0.05$).

4. Discussion

4-1. Toxicity with *cis*-VA administration

In this study, *cis*-VA was administered at 300 mg/kg daily for 7 d, and body weight did not change after 7 d in normal and diabetic mice. Furthermore, as no administration of *cis*-VA had any effect on the average food intake over a 7-d period, it was considered that *cis*-VA was not toxic.

4-2. Tissues acted upon by *cis*-VA administration and their possible changes in FA metabolism

Tissues in which multiple FA ratios were altered by *cis*-VA administration were the pancreas in normal mice and the heart in diabetic mice, with common changes including decreased percentages of PA and OA and increased percentages of SA, AA, and DHA. This suggests that *cis*-VA ingestion may affect the pancreas and heart, and cause common changes in FA metabolism. No reports of monounsaturated FAs exerting common effects on the pancreas and heart currently exist, and the effects of *cis*-VA administration may be unique compared to those of other monounsaturated FAs. In the present study, no statistically significant differences in FA composition were observed in the hearts of normal mice and the pancreas of diabetic mice; however, the trend of increase or decrease in mean values due to *cis*-VA administration was consistent between normal and diabetic mice, suggesting that similar effects occurred. Therefore, we plan to further increase the population size and evaluate whether there are clear differences. Furthermore, after fractionating the lipids in tissues into triglycerides and phospholipids, we plan to analyze the FA composition and examined whether the FA composition accumulated in tissues or was related to the composition of tissues, such as cell membranes.

4-3. Inference on the effect on SCD1

One common change in the FA composition of the pancreas and heart was a decrease in the OA/SA ratio. One factor in this change may be the suppression of SCD1 activity, which is involved in the synthesis of OA from SA (Flowers & Ntambi 2008). In a study in which POA, another n-7 monounsaturated FA, was fed to low-density lipoprotein receptor-deficient mice via diet, SCD1 expression in the liver was reduced (Yang *et al.* 2019). Although *cis*-VA, the same n-7 FA as POA, may also suppress SCD1 expression, we hypothesized that it may act in tissues other than POA. We plan to evaluate whether *cis*-VA treatment reduces SCD1 expression and clarify the tissue specificity of *cis*-VA.

β-oxidation is suppressed in the hearts of SCD1 deficient mice compared to wild-type mice (Dobrzyn *et al.* 2008). This suggests that SCD1 significantly regulates the FA metabolism in the heart. Our results showed that the OA/SA ratio was higher in diabetic mice than in normal mice, suggesting that the diabetic state may have altered the FA composition by suppressing SCD1 activation. Although it has been reported that SCD1 deficiency improves cardiac function in *ob/ob* mice (Dobrzyn *et al.* 2010), an obese murine model of type 2 diabetes, activation of SCD1 in pancreatic β cells is effective in enhancing insulin secretion and protecting cells from saturated FAs (Janikiewicz *et al.* 2015), and induction of β cell death by saturated FAs may cause diabetes (Marafie *et al.* 2019). Thus, the inhibition of SCD1 function may have both positive and negative effects on some tissues. If *cis*-VA administration is determined to be involved in the suppression of SCD1 expression, its effects on each tissue should be evaluated with caution.

4-4. Effect of *cis*-VA administration on diabetes

In this study, no change in the FA composition of the liver was observed after *cis*-VA ingestion, suggesting that the effect of *cis*-VA on FA metabolism in the liver was minimal. However, the liver weight of diabetic mice, which was higher than that of normal mice, decreased after *cis*-VA administration. The lipid content of the liver was higher in type 2 diabetes model mice than in normal mice (Nakadate *et al.* 2014). This suggests that *cis*-VA may inhibit fat accumulation in the enlarged liver under diabetic conditions and may exert a potential antidiabetic effect. In a study in which POA, the same n-7 monounsaturated FA, was administered for 4 weeks, a tendency to improve the diabetic state was observed along with a decrease in hepatic lipid accumulation (Yang *et al.* 2011). In this study, no effect of *cis*-VA administration was observed in blood biochemistry tests; however, a long-term administration study may be expected to improve the diabetic status in a manner similar to POA We plane to administrate the *cis*-VA to diabetic mice with an extended test period.

5. Conclusion

cis-VA administration altered the FA composition of the pancreas in normal mice and the hearts of diabetic mice. Multiple FA ratios were altered, with five FAs showing common variations between the heart and pancreas. This suggests that *cis*-VA ingestion may affect the pancreas and heart and cause common changes in FA metabolism. *cis*-VA may exhibit unique actions that differ from those of other monounsaturated FAs.

6. References

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