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Anti-Obesity Effects of Simultaneous Intake of D-Allulose and Capsaicin in High-Fat Diet-Fed Rats

Tatsuhiro Matsuo[1*], Seiya Iwakura[1], Shunsuke Higaki[2], Reiko Inai[3], Susumu Mochizuki[1], Akihide Yoshihara[1], Kazuya Akimitsu[1]

[1]Faculty of Agriculture, Kagawa University, Miki, Japan
[2]Faculty of Human Sciences, Hokkaido Bunkyo University, Eniwa, Japan
[3]Department of Food Science and Nutrition, Nara Women's University, Nara, Japan
Email: *matsuo.tatsuhiro@kagawa-u.ac.jp

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Abstract

D-allulose is a rare calorie-free sugar with a variety of nutritional functions. Capsaicin, a major active compound in chili peppers, has demonstrated numerous beneficial effects in the treatment of obesity. This study examined whether the synergistic effects of D-allulose and capsaicin could contribute to the suppression of body fat accumulation in rats. Thirty-two male 3-week-old Wistar rats were randomized into four groups: sedentary control (C), D-allulose (A), capsaicin (CA), and D-allulose + capsaicin (ACA). Rats in the A and ACA groups were fed a 3% D-allulose-supplemented high-fat diet for 8 weeks, whereas those in the CA and ACA groups were fed a 0.014% capsaicin-supplemented high-fat. Dietary capsaicin significantly reduced abdominal fat mass, whereas D-allulose had no effect. Total body fat mass and percentage were significantly reduced by dietary capsaicin, whereas D-allulose did not have a significant effect, although a decreasing trend was observed. No two-factor interactions were identified for any of the body fat indices. The reason for the lack of a significant D-allulose effect may be that the amount of D-allulose added to the diet was too small. These two compounds did not demonstrate synergistic anti-obesity effects, and their combined effects appeared to be largely additive.

Keywords

D-Allulose, Capsaicin, Synergistic Effects, Body Fat, Rat

1. Introduction

Obesity is a chronic and complex disease characterized by excessive fat deposition

that compromises health. The obesity epidemic has become a serious public health concern. Obesity increases the risk of type 2 diabetes, heart disease, and certain cancers along with affecting the quality of life [1]. It is essential to prevent obesity to avoid metabolic syndrome, particularly in middle-aged and older adults. Rare sugars are monosaccharides and their derivatives that are inherently rarer than common sugars, such as d-glucose and d-fructose (The International Society of Rare Sugars [ISRS], 2002)[1] and can be used as supplements, functional food additives, and medicines. They have recently attracted attention as functional foods with anti-obesity properties. Previous studies have suggested that rare sugars are beneficial to human health when used as low-calorie carbohydrate sweeteners and bulking agents [2]-[4]. Particularly, D-allulose is caloric-free and has various nutritional functions. The anti-obesity effect of D-allulose is mediated by multiple factors, including suppression of hepatic lipogenesis [5] [6] and an increase in energy expenditure [7].

Capsaicin, a major active compound in chili peppers, has numerous beneficial roles in the human body, including the treatment of obesity [8]. An epidemiological study found that eating foods containing capsaicin is associated with a lower rate of obesity [9]. Several studies have shown that capsaicin helps to regulate lipid metabolism, particularly by reducing body fat levels [10]. Its effects are mediated by the activation of the transient receptor potential vanilloid 1 (TRPV1) ion channel, which is widely distributed and found in adipocytes, the liver, vascular smooth muscle, and nociceptor neurons [11].

Although D-allulose and capsaicin induce a variety of biological responses after ingestion, they all have in common that they exert their anti-obesity effects (e.g., thermogenesis, lipolysis, and feeding inhibition) via the central nervous system [8] [12]. Although the mechanisms are not yet fully understood, given that D-allulose and capsaicin increase lipid metabolism through different mechanisms, their combination may enhance their anti-obesity effects. In this study, rats were fed a high-fat diet containing D-allulose and capsaicin to determine whether their synergistic effect could contribute to the suppression of body fat accumulation.

2. Materials and Methods

All animal procedures were approved by the Animal Care and Use Committee of Kagawa University (approval number: 24624).

2.1. Materials

D-allulose was obtained from the International Institute of Rare Sugar Research and Education (Kagawa, Japan). MF, a commercial rodent diet, was purchased from Oriental Yeast Co. Ltd. (Tokyo, Japan). Capsaicin was purchased from FUJIFILM Wako Pure Chemical Industries (Osaka, Japan). Soybean oil and beef tallow were purchased from Yamakei Industry Co. Ltd. (Osaka, Japan). Mineral and vitamin mixtures (AIN-76A) were obtained from Oriental Yeast Co. Ltd. (Tokyo, Japan), with a composition: soybean oil: 10.3% palmitic acid, 3.8% stearic acid,

[1]The International Society of Rare Sugars [ISRS] 2002, https://www.isrs.kagawa-u.ac.jp/.

24.3% oleic acid, 52.7% linoleic acid, and 7.9% *α*-linolenic acid; beef tallow: 24.0% palmitic acid, 16.6% stearic acid, 46.5% oleic acid, 2.8% linoleic acid, and 0.3% *α*-linolenic acid. Other ingredients in the diet were of food-grade and were obtained from Fonterra (Auckland, New Zealand), Mitsui DM Sugar Holdings (Tokyo, Japan), Nippon Paper Industries (Tokyo, Japan), and Oji Cornstarch (Tokyo, Japan). All other reagents were obtained from FUJIFILM Wako Pure Chemical Industries (Osaka, Japan) and Nacalai Tesque (Kyoto, Japan).

2.2. Animals, Diets, and Experimental Design

Thirty-two male Wistar rats (3 weeks old) were obtained from Japan SLC (Shizuoka, Japan). They were fed MF and had access to water *ad libitum* for 4 days. Rats were randomly assigned to four groups: sedentary control (C; n = 8), D-allulose (A; n = 8), capsaicin (CA; n = 8), and D-allulose + capsaicin (ACA; n = 8). **Table 1** shows the dietary composition of each group. The A and ACA diets contained 3% D-allulose, whereas the CA and ACA diets contained 0.014% capsaicin. Dietary additions of capsaicin and D-allulose were determined with reference to previous studies [13]-[15]. In this study, the amount of D-allulose added was 3% instead of the 5% we have often used. This is because both capsaicin and d-alluolose have strong anti-obesity effects; therefore, the anticipated cumulative effect should be avoided. The 3% D-allulose diet has been employed in previous studies [14] [15] and has been reported to exert an anti-obesity effect. Furthermore, long-term consumption of a 3% D-allulose diet has been shown to be free of pathological and serum biochemical side effects in rats [16]. All experimental diets were obesity-inducing high-fat diets with high concentrations of sucrose to increase fat synthesis in the liver. The energy compositions of the experimental diets were as follows: C and CA diets; protein/fat/carbohydrate = 14.9/48.6/36.5, A and ACA diets; protein/fat/carbohydrate = 15.3/49.9/34.8 (calculated based on the energy value of D-allulose being 0 kcal/g). The rats were housed in individual cages maintained under controlled environmental conditions (temperature: 22˚C ± 1˚C, humidity: 55% ± 5%, and a 12-h light/dark cycle), and had free access to the experimental diets and water for 8 weeks. Body weight and food intake were recorded daily. After the experimental period, all rats were euthanized by decapitation at 09:00 after 12 hours of fasting. Blood was collected to obtain serum. The heart, liver, kidneys, spleen, abdominal adipose tissues (epididymal, perirenal, and mesenteric), and interscapular brown adipose tissue (IBAT) were quickly removed and stored at −80˚C until analysis. Carcass samples were obtained by removing the head and remaining intra-abdominal and intra-thoracic tissues, and were stored at −20˚C until analysis of carcass composition.

Table 1. Composition of experimental diets.

Ingredients (g/kg diet)	C	A	CA	ACA
Casein	200.0	200.0	200.0	200.0

Continued

DL-methionine	3.0	3.0	3.0	3.0
Corn starch	249.9	249.9	249.8	249.8
Sucrose	200.0	170.0	200.0	170.0
D-allulose	0.0	30.0	0.0	30.0
Soybean oil	20.0	20.0	20.0	20.0
Beef tallow	230.0	230.0	230.0	230.0
Capsaicin	0.0	0.0	0.14	0.14
Mineral mixture[1]	35.0	35.0	35.0	35.0
Vitamin mixture[1]	10.0	10.0	10.0	10.0
Cellulose	50.0	50.0	50.0	50.0
Chorine chloride	2.0	2.0	2.0	2.0
Butylhydroxytoluene	0.1	0.1	0.1	0.1
	1000.0	1000.0	1000.0	1000.0

[1]Based on the AIN-76 mixture. C, A, CA, and ACA represent the control, D-allulose, capasicin, and D-allulose + capsaicin diets, respectively.

2.3. Biochemical Analysis

Serum levels of glucose, insulin, triglyceride, total cholesterol, high-density lipoprotein (HDL)-cholesterol, and free fatty acid were determined using LabAssay™ Glucose, LBIS Rat Insulin ELISA Kit, LabAssay™ Triglyceride, LabAssay™ Cholesterol, LabAssay™ HDL-Cholesterol, and LabAssay™ NEFA (FFA) (FUJIFILM Wako Chemicals, Osaka, Japan), respectively. Homeostatic model assessment of insulin resistance (HOMA-R) was performed as described by Matthews *et al.* [17]. Liver lipids were extracted using the method described by Matyash *et al.* [18], and liver triglyceride and cholesterol content were determined using appropriate kits (LabAssay™ Triglyceride and LabAssay™ Cholesterol [FUJIFILM Wako Chemicals], respectively). Liver glucose-6-phosphate dehydrogenase (G6PD) and malate dehydrogenase (MDH) activities were determined using the QuantiChrom™ Glucose-6-Phosphate Dehydrogenase Kit and EnzyChrom™ Malate Dehydrogenase Assay Kit (BioAssay Systems, CA, USA), respectively. IBAT and perirenal adipose tissue uncoupling protein 1 (UCP1) contents were determined using the Rat Uncoupling Protein 1, MitoChondrial (UCP1) ELISA Kit (AS ONE CORPORATION, Osaka, Japan). The carcass composition was determined using the method described by Mickelsen and Anderson [19], and total body fat was calculated using the method described by Paik and Yearick [20].

2.4. Data Analysis

Data from all groups were analyzed using two-way analysis of variance (ANOVA). If the ANOVA results revealed a significant interaction, multiple comparisons of the results were performed using the Tukey-Kramer test for all groups. Statistical

significance was set at $p < 0.05$. Data analyses were performed using Excel Statistics (Social Survey Research Information Co., Ltd., Tokyo, Japan).

3. Results

Based on the ANOVA results, dietary capsaicin significantly reduced all 1 - 8 weeks body weight at all time points ($p < 0.001$, Figure 1), weight gain, and food intake (Table 2), whereas D-allulose had no effect. The decrease in food intake because of dietary capsaicin was suppressed by concurrent ingestion of D-allulose (Table 2). Food intake was significantly higher in the C and A groups than in the CA and ACA groups (Table 2). Neither D-allulose nor capsaicin affected food efficiency (Table 2). Dietary capsaicin significantly reduced the weights of the heart, liver, kidneys, and spleen, whereas D-allulose significantly increased liver and kidney weights (Table 2). Neither D-allulose nor capsaicin affected the IBAT weight (Table 2).

Dietary capsaicin significantly reduced the epididymal, perirenal, mesenteric, and total abdominal adipose tissue weights, whereas D-allulose had no effect (Table 2). The carcass and total body fat (mass and percentage) were significantly reduced by dietary capsaicin, whereas D-allulose had not significant effect, although a decreasing trend was observed in the percentage of carcass fat ($p = 0.069$) and total body fat ($p = 0.120$) (Table 2). Dietary capsaicin significantly reduced carcass protein mass but did not affect carcass protein percentage (Table 2). No two-factor interactions were identified for any of body weight, tissue weight, or body fat indices (Table 2).

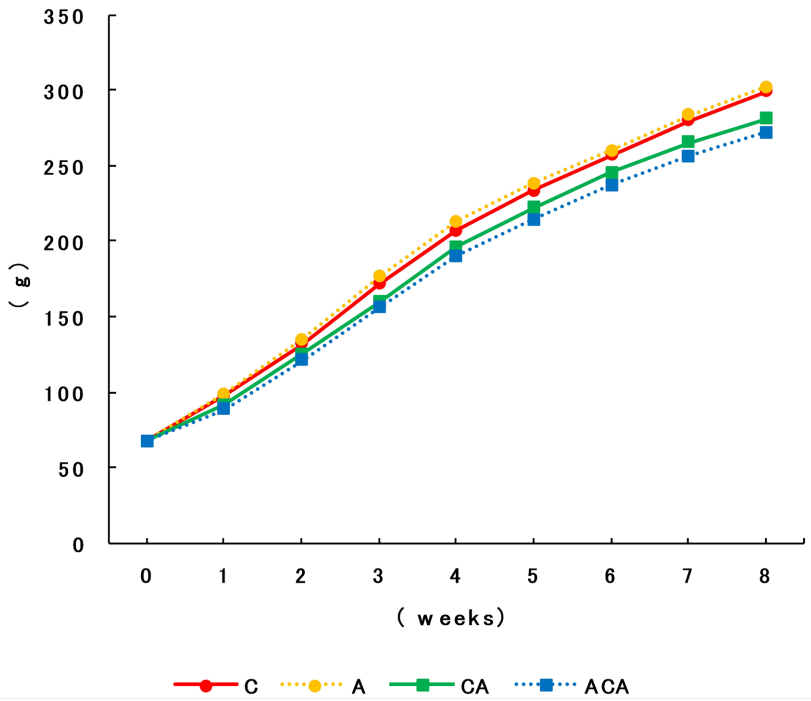

Figure 1. Weekly body weight of the rats in each group. Values are the means for eight rats. C, A, CA, and ACA represent the control, D-allulose, capsaicin, and D-allulose + capsaicin groups, respectively.

Table 2. Body and tissue weights, food intake, and body fat.

		C	A	CA	ACA	p-value*		
						A	CA	AxCA
Body weight								
Initial	(g)	67.6 ± 1.6	67.5 ± 1.5	67.2 ± 1.4	66.4 ± 1.4	-	-	-
Final	(g)	298.6 ± 3.8	301.8 ± 5.1	280.6 ± 5.3	271.6 ± 5.0	0.581	**<0.001**	0.251
Gain	(g)	231.0 ± 3.8	234.3 ± 3.8	213.4 ± 6.1	205.2 ± 5.0	0.637	**<0.001**	0.272
Food intake	(kcal/day)	58.9 ± 0.7[a]	62.3 ± 1.2[a]	53.9 ± 0.8[b]	52.2 ± 1.1[b]	0.406	**<0.001**	**0.022**
Food efficiency	(mg/kcal)	70.0 ± 0.0	67.2 ± 1.2	70.6 ± 1.2	70.1 ± 0.8	0.148	0.119	0.298
Visceral tissue weights								
Heart	(g)	0.756 ± 0.008	0.734 ± 0.026	0.686 ± 0.012	0.667 ± 0.013	0.257	**<0.001**	0.932
Liver	(g)	8.54 ± 0.24	9.73 ± 0.23	8.37 ± 0.27	8.51 ± 0.35	**0.032**	**0.025**	0.088
Kidneys	(g)	1.83 ± 0.08	2.04 ± 0.03	1.63 ± 0.05	1.74 ± 0.05	**0.010**	**<0.001**	0.375
Spleen	(g)	0.611 ± 0.021	0.616 ± 0.011	0.571 ± 0.010	0.565 ± 0.026	0.962	**0.026**	0.781
IBAT weight	(g)	0.364 ± 0.023	0.489 ± 0.052	0.397 ± 0.042	0.376 ± 0.042	0.248	0.372	0.110
Intra-abdominal adipose tissue weights								
Epididymal	(g)	9.88 ± 0.30	9.47 ± 0.71	8.67 ± 0.42	8.37 ± 0.39	0.494	**0.032**	0.912
Perirenal	(g)	9.35 ± 0.13	9.06 ± 0.58	7.88 ± 0.41	7.63 ± 0.35	0.538	**0.002**	0.965
Mesenteric	(g)	6.54 ± 0.28	5.88 ± 0.35	5.26 ± 0.32	5.24 ± 0.28	0.317	**0.007**	0.339
Total	(g)	25.77 ± 0.49	24.41 ± 1.55	21.81 ± 1.06	21.24 ± 0.89	0.409	**0.004**	0.731
Carcass fat	(g)	31.2 ± 1.4	29.2 ± 1.9	25.8 ± 1.8	22.3 ± 1.1	0.117	**0.001**	0.664
	(%)	19.7 ± 0.7	17.6 ± 0.9	16.6 ± 1.1	15.3 ± 0.5	0.069	**0.006**	0.611
Carcass protein	(g)	30.4 ± 1.0	30.8 ± 0.7	28.2 ± 0.7	26.5 ± 0.9	0.498	**0.001**	0.232
	(%)	19.3 ± 0.8	18.7 ± 0.3	18.1 ± 0.4	18.3 ± 0.5	0.718	0.172	0.538
Total body fat	(g)	53.1 ± 1.6	49.9 ± 3.1	44.4 ± 2.7	40.4 ± 1.8	0.168	**0.001**	0.871
	(%)	19.9 ± 0.7	16.2 ± 0.9	17.2 ± 0.8	19.3 ± 0.8	0.120	**0.017**	0.803

Values are the mean ± SE for eight rats. n.s., not significant. Within a row, values with different superscripts are significantly different ($p < 0.05$). C, A, CA, and ACA represent the control, D-allulose, capasicin, and D-allulose + capsaicin groups, respectively. IBAT: interscapular brown adipose tissue. *The significant p-values are shown in bold (two-way ANOVA).

Dietary capsaicin significantly reduced HDL-cholesterol levels, but neither dietary D-allulose nor capsaicin affected any of the other serum indices, and no two-factor interactions were identified (Table 3). The liver triglyceride content was not affected by dietary D-allulose or capsaicin. Liver cholesterol content was significantly increased by dietary capsaicin but was suppressed by concurrent ingestion with D-allulose (Table 3).

Dietary capsaicin significantly reduced liver G6PD activity and increased liver MDH activity, whereas dietary D-allulose had no effect (Figure 2). Neither dietary D-allulose nor capsaicin affected UCP1 levels in the IBAT and perirenal adipose tissue (Figure 2). No two-factor interactions were identified for liver G6PD and MDH activities or the UCP1 levels in the IBAT and perirenal adipose tissue (Figure 2).

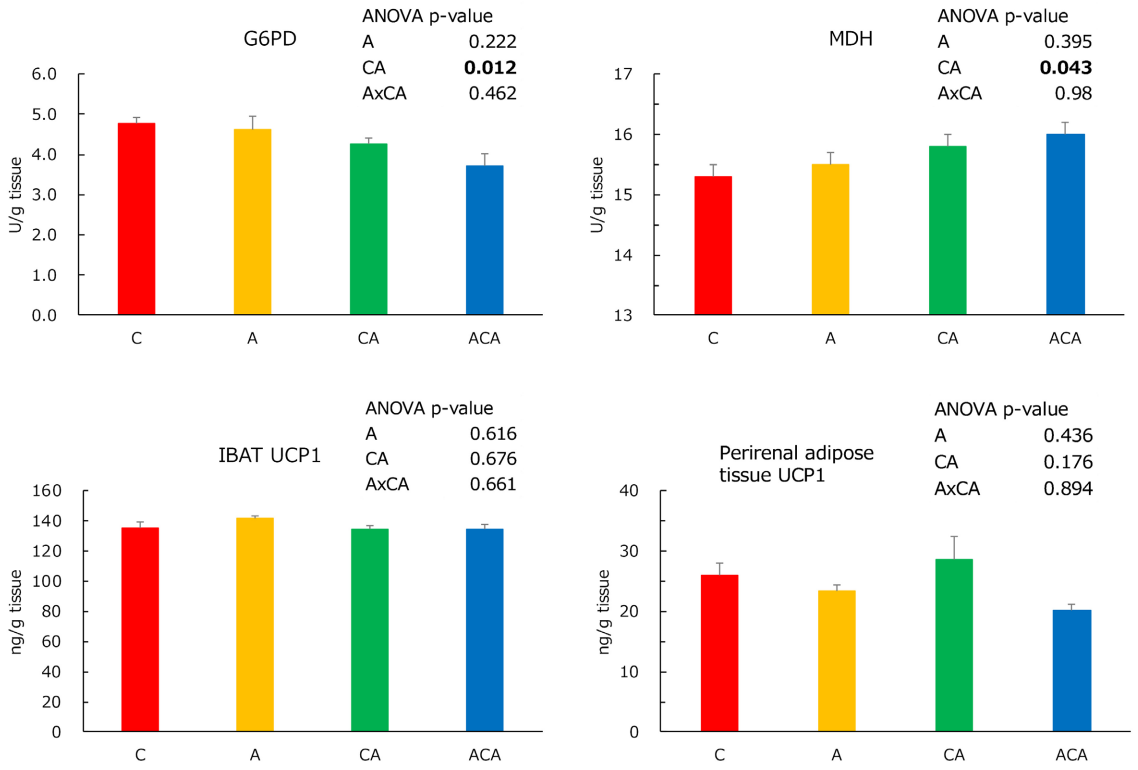

Figure 2. Liver enzyme activities and tissue UCP1 contents. Values are the means and SE for eight rats. C, A, CA, and ACA represent the control, D-allulose, capasicin, and D-allulose + capsaicin groups, respectively. IBAT: interscapular brown adipose tissue. G6PD: glucose-6-phosphate dehydrogenase, MDH: malate dehydrogenase, UCP1: uncoupling protein 1. The significant p-values are shown in bold (two-way ANOVA).

Table 3. Serum and liver components.

		C	A	CA	ACA	p-value*		
						A	CA	AxCA
Serum								
Glucose	(mg/dL)	153.5 ± 6.2	161.5 ± 1.9	153.1 ± 4.4	175.2 ± 9.7	0.085	0.450	0.444
Insulin	(ng/mL)	4.13 ± 1.07	2.42 ± 0.23	3.09 ± 0.33	2.73 ± 0.44	0.062	0.500	0.265
HOMA-R		32.3 ± 5.0	25.0 ± 2.3	30.8 ± 4.1	31.1 ± 5.7	0.167	0.650	0.252
Triglycerides	(mg/dL)	164.8 ± 12.4	167.0 ± 9.0	144.6 ± 7.3	158.8 ± 8.4	0.609	0.524	0.735
Total cholesterol	(mg/dL)	133.7 ± 7.4	139.2 ± 5.9	127.1 ± 5.5	130.8 ± 7.4	0.475	0.367	0.769
HDL-cholesterol	(mg/dL)	88.4 ± 4.9	83.8 ± 5.0	75.4 ± 3.4	74.4 ± 4.1	0.601	**0.015**	0.544
Non-HDL-cholesterol	(mg/dL)	45.3 ± 3.1	55.4 ± 4.9	51.7 ± 3.1	56.5 ± 5.3	0.114	0.221	0.859
Free fatty acids	mEq/L	0.99 ± 0.05	0.99 ± 0.08	0.95 ± 0.04	1.09 ± 0.06	0.577	0.649	0.142
Triglyceride	(mg/g tissue)	59.1 ± 5.0	70.0 ± 4.7	73.1 ± 4.7	63.8 ± 3.7	0.848	0.378	**0.026**
Cholesterol	(mg/g tissue)	4.49 ± 0.58^{b}	7.22 ± 0.65^{a}	4.44 ± 0.39^{b}	4.87 ± 0.42^{ab}	**0.003**	0.051	**0.031**

Values are the mean ± SE for eight rats. n.s., not significant. Within a row, values with different superscripts are significantly different ($p < 0.05$). C, A, CA, and ACA represent the control, D-allulose, capasicin, and D-allulose + capsaicin groups, respectively. IBAT: interscapular brown adipose tissue, G6PD: glucose-6-phosphate dehydrogenase, MDH: malate dehydrogenase, UCP1: uncoupling protein 1. *The significant p-values are shown in bold (two-way ANOVA).

4. Discussion

Therapeutic approaches to address obesity involve lifestyle changes such as avoiding a sedentary lifestyle and a balanced diet. Numerous experimental and clinical studies have explored potential dietary and exercise therapies to reduce and prevent obesity [21]-[23]. According to Olateju *et al.* [22], the best approach for managing obesity in adults involves a tailored low-calorie diet that considers the metabolic requirements and general health of the individual, along with a combination of strength and endurance exercises for at least 3 hours per week. However, sustaining a low-calorie diet and active exercise for prolonged periods can be challenging. Therefore, alternative anti-obesity treatments that are easy to sustain, effective, safe, and widely available are required. Dietary D-allulose and capsaicin are functional ingredients recognized as easily implemented and sustained anti-obesity therapies. In this study, we determined whether the combined use of these two dietary therapies exerted a synergistic effect by suppressing body fat accumulation. Dietary capsaicin suppressed body fat accumulation as well as that of carcass (reflecting subcutaneous fat) and intra-abdominal fat. In contrast, a trend toward the body fat accumulation inhibition by D-allulose was observed, but was not significant (carcass fat percentage: $p = 0.069$; total body fat percentage: $p = 0.120$); additionally, these two factors did not exert synergistic anti-obesity effects. However, the ACA group exhibited the lowest accumulation of intra-abdominal, carcass, and total body fat, indicating an additive effect of combining these two therapies.

Several studies have reported the anti-obesity effects of D-allulose [4]-[7] [24] [25]. Notably, D-allulose had a more significant effect on body fat reduction than d-fructose, its C-3 epimer [26]. These effects are attributed to a combination of factors, including the inhibition of fatty acid synthesis in the liver, promotion of lipid metabolism, increase in energy expenditure, and a decrease in the synthesis of chylomicrons in small intestinal mucosal epithelial cells. However, the present study confirmed that dietary D-allulose only slightly inhibits body fat accumulation and does not affect the activities of liver G6PD and MDH, which are lipogenic and oxidative enzymes, respectively. This may be because the addition of 5% D-allulose used in previous studies [5] [15] [27] was reduced to 3% in this study. Therefore, it is necessary to revisit the effects of 5% D-allulose in the future.

In this study, dietary capsaicin reduced food intake but did not affect feeding efficiency. Thus, the anti-obesity effects of capsaicin may be partly attributed to reduced food intake. Capsaicin or capsaicin-rich peppers have been reported to suppress energy intake and regulate macronutrient intake by modulating appetite and satiety [28]. Yoshioka *et al.* [29] examined the effects of capsaicin on eating behaviors and energy intake. The authors found that adding red pepper to breakfast significantly reduced protein and fat intake at lunch, and adding red pepper to an appetizer significantly reduced energy and carbohydrate intake for the rest of the lunch course. These effects may be related to increased sympathetic activity [29]. Another possibility is TRPV1 receptor-mediated feeding inhibition, as sev-

eral capsaicin-induced effects are mediated by stimulation of the TRPV1 receptor [8] [11]. TRPV1 plays a pivotal role in the action of leptin, an appetite-suppressing hormone, in the hypothalamus [30]. Capsaicin suppresses feeding by affecting TRPV1 [31]. Although the effects of capsaicin on appetite remain poorly explored, neural circuits in the hypothalamus may be important targets of capsaicin. The underlying cause of this effect is unknown; however, the involvement of complex energy balance regulatory mechanisms must be considered.

Brown adipose tissue (BAT) plays a crucial role in adaptive thermogenesis, and research has shown that BAT activity can help protect against obesity and metabolic diseases [32]. Saito *et al.* [33] reported that BAT is activated by cold exposure, as well as various foods or spices such as capsaicin-rich-chili peppers. This activation may involve an increase in energy usage, stimulation of fat breakdown in BAT, an increase in the levels of cyclic adenosine monophosphate and the activity of protein kinase A in BAT. In a recent study in rats [34], capsaicin offset the negative effects of a high-energy diet, such as glucose intolerance, high cholesterol levels, and reduced BAT activity. The main reason for these effects is the increased expression of key thermogenic genes in BAT, such as UCP1 and zinc finger protein 16. However, in the present study, dietary capsaicin did not influence IBAT and perirenal adipose tissue UCP1 levels. High-fat diets have been reported to increase UCP1 expression [35], which could explain why no additional impact of capsaicin was observed. Recently, several thermogenic mechanisms have been identified based on ATP sinks centered on creatine, lipid, or calcium cycling, along with fatty acid-mediated UCP1-independent leakage pathways driven by ADP/ATP carriers [36]. In addition, dietary capsaicin significantly reduced liver G6PD activity and increased liver MDH activity, indicating an increased hepatic lipid metabolic turnover. It has been reported that the liver is also involved in heat production [37]. Therefore, the effects of dietary capsaicin on thermogenesis warrant further investigation.

Dietary D-allulose increased liver cholesterol content. Although our previous studies showed similar results [15] [27] [38], the underlying reasons for these observations remain poorly understood. It is noteworthy that combining dietary D-allulose with capsaicin suppressed hepatic triglyceride and cholesterol levels. In addition, dietary D-allulose significantly increased liver and kidney weights, despite the invariance in final weight and weight gain; similar results have been reported in previous studies [4] [5] [7]. In our previous chronic toxicity study using rats, 1- and 1.5-year administration of D-allulose in the diet resulted in liver and kidney weight gain without inducing any adverse health effects [16]. We suggested that feeding rats a diet containing D-allulose for 4 weeks could increase liver and kidney weights without any pathological impairment, and 10-week D-allulose cessation reversed these effects [39]. In a human study evaluating 12 weeks of ingesting a rare sugar syrup containing 6% D-allulose, Hayashi *et al.* [3] found no adverse effects or abnormalities in blood parameters when assessing lipid and carbohydrate metabolism, as well as hepatic and renal functions. The results of these studies suggest that D-allulose is a safe monosaccharide in animals and humans.

D-allulose has been approved and is generally recognized as safe as a food (GRAS Notice No. GRN 498, Food and Drug Administration, USA, 2017) for use in various foods and dietary supplements.

In conclusion, we confirmed that both dietary D-allulose and capsaicin treatment reduced body fat accumulation in rats fed a high-fat diet, although the effect of D-allulose was not significant. The reason for the lack of significant D-allulose effect may be that the amount of D-allulose added to the diet was too small. These two factors did not induce synergistic anti-obesity effects, and their combined effects appeared to be largely additive. Additionally, the anti-obesity effect of dietary capsaicin appears to be partly owing to the suppression of food intake. However, the mechanisms underlying the anti-obesity effects of dietary D-allulose and capsaicin remain unclear, and warrant clarification in additional investigations.

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Conflicts of Interest

No potential conflict of interest was reported by the authors.

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