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Research Article

Body Weight Management in Healthy Humans Using Low-Sugar and High-Dietary Fiber Noodles : A Single Group Pre-Post Trial

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Background. The recommendation of the low-carbohydrate diet by the American Diabetes Association (2013) has popularized its use as a nutritional treatment. Previously, we evaluated the effects of a novel strategy to reduce dietary intake based on low-sugar, high-dietary fiber noodles (LS-HDFNs) composed of okara and konjac on blood glucose levels in healthy animals, animal models of type 2 diabetes, and healthy humans (the single meal test). In this study, a single group pre-post trial for 28 days administration was carried out to investigate the body weight management in healthy humans using LS-HDFNs. *Methods*. Nine healthy subjects were requested to eat LS-HDFNs once (180 g) daily for 28 days. Physical characteristics and blood biochemical parameters were measured before (0 day) and after (28 days) the consumption of the noodles. Qualitative analysis of compounds in the noodles was investigated by the HPLC system and the UPLC/qTOF-MS system. *Results*. The LS-HDFNs group did not exhibit any complications or adverse effects. Furthermore, the body weights, body fat percentage, total cholesterol, and low-density lipoprotein cholesterol were significantly reduced after 28 days of LS-HDFNs consumption. Some isoflavones, amino acids, peptides, and phospholipids were contained in the LS-HDFNs. *Conclusion*. As per our knowledge, this is the first study of the usefulness of consumption of LS-HDFNs for 28 days for body weight management in healthy humans. LS-HDFNs may be useful for body weight management. This trial is registered with number 2020002, registered on 2nd March 2020.

1. Introduction

Overweight and obesity predispose to a number of chronic diseases, such as type 2 diabetes, cardiovascular disease, hypertension, and several cancers [1]. The World Health Organization (WHO) stated that obesity nearly tripled between 1975 and 2016 [2], and one-fifth of the adults around the globe will have obesity in 2025 [3]. Therefore, obesity-related diseases are important issues.

Type 2 diabetes mellitus is becoming increasingly common worldwide and leads to significant negative effects on health and associated economic burden [4]. The American Diabetes Association recommends that monitoring carbohydrate intake should be a component of diabetes therapy [5]. Diabetes UK proposed that low-carbohydrate diets may provide an effective treatment option [6]. The prevalence of obesity combined with diabetes is increasing and will increase by 51% by 2045 [7].

Tubers, such as potato and cassava, and grains, such as rice and wheat, are typical staple foods [8]. Rice are widely used globally [9] and are the main carbohydrate sources in Asia [10]. Moreover, noodles, originating from China, are traditional staple foods in China, Korea, and Japan. Several noodle products are produced from refined wheat [11]. Frequent noodle consumption predisposes to type 2

diabetes, similar to frequent rice consumption, because both noodles and rice are carbohydrate sources [12]. Dietary strategies to lower postprandial blood glucose levels are important to prevent the progression of type 2 diabetes [13].

Therefore, we explored the relationships of health with food intake and *Glycine max* (commonly called "okara"), a byproduct of soybean processing. Previously, we explored the effect of fermented okara with *Rhizopus oligosporus* in obesity/overweight dogs [14]. Moreover, we developed low-sugar, high-dietary fiber noodles (LS-HDFNs) composed of okara and *Amorphophallus konjac* (commonly called "konjac") for individuals with frequent noodle consumption (Figure 1). We demonstrated the impact of LS-HDFNs consumption on blood glucose levels in type 2 diabetes mouse and rat models in previous studies [15]. In addition to these reports, we described the impact of LS-HDFNs on glycemic response in healthy individuals in a crossover trial using a single meal test and reported that individuals who consumed LS-HDFNs had significantly reduced postprandial blood glucose and insulin levels than healthy individuals who consumed normal wheat noodles [16]. Nevertheless, there is no experimental evidence on the body weight of healthy humans who consume LS-HDFNs for 28 days.

In this preliminary research, we explored the impact of LS-HDFNs consumption for 28 days on body weight management in healthy humans as a single group pre-post trial for the first time. Moreover, we qualitatively analyzed the compounds in noodles using the HPLC system and the UPLC/qTOF-MS system.

2. Materials and Methods

2.1. Materials. This study used commercial LS-HDFNs Healthy Noodles^{TM} (Kibun Foods Inc., Japan). The details of LS-HDFNs have been previously reported in [16]. The LS-HDFNs (180 g) had energy (kcal), proteins (g), fats (g), and carbohydrates (g) of 35.0, 2.4, 1.4, and 11.3 (sugar: 0.0, dietary fiber : 11.3), respectively.

2.2. Study Design. In this single group pre-post trial, 10 subjects (females, 5; males, 5) aged 24–59 years, with a body mass index of 21.8–30.0 kg/m^2 and glucose levels of 95–166 mg/dL, were enrolled from the Kyushu area, including Fukuoka, Japan (Table 1). The study eligibility criteria were similar to those used by Nagae et al. [17], with certain modifications (Table 2). The experiments were performed at the Kinki University Faculty of Humanity-Oriented Science and Engineering Ethics Committee (number: 2020002). The study was conducted in complete accordance with the Declaration of Helsinki. Written informed consent was obtained from the study participants. The administration period of LS-HDFNs was set to 28 days. The reason was as follows: (1) In the previous studies, we demonstrated the impact of LS-HDFNs consumption on blood glucose levels in type 2 diabetes mouse and rat models for 28 days administration [15] and (2) Isnawati et al. reported the effect of tempeh (which is made from fermented tofu from *Rhizopus oligosporus* and containing high fiber) administration on blood glucose in obese women, and this research was an experimental study with a pre-post randomized control group design for 28 days administration [18]. Of the ten eligible individuals, nine were enrolled in this study. All subjects consumed a bag of LS-HDFNs (180 g) once a day for 28 days. Each subject visited the research laboratory twice (at 0 and 28 days of administration) for efficacy measurements. One (male) out of the 10 subjects did not continue the research because of personal reasons. Therefore, the study was continued in nine healthy subjects (females, 5; males, 4).

Figure 1: Low-sugar and high-dietary fiber noodles (Kibun Healthy Noodle^{TM}).

2.3. Measurement of Physical Characters and Blood Biochemical Parameters. We used body composition analyzer (Tanita Corporation, Tokyo, Japan) to determine the body weight and body fat percentage. Visceral fat meter EW-FA90 (Panasonic Corporation, Osaka, Japan) was used to analyze visceral fat. The blood samples were stored at −80°C until further analyses. Total protein (TP), albumin (ALB), blood urea nitrogen (BUN), creatinine (CRE), uric acid (UA), aspartate aminotransferase (AST), alanine transaminase (ALT), γ-glutamyl transpeptidase (γ-GT), alkaline phosphatase (ALP), hemoglobin A1c (HbA1c), glycated albumin (GA), total cholesterol (T-CHO), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) were measured using Spotchem D-Concept SD-4810 (Arkray Inc., Kyoto, Japan). Glucose (GLU) levels were analyzed using glycohemoglobin analyzers A1c iGear K (Sakae Co., Ltd., Tokyo, Japan).

2.4. Statistical Analysis. Mean ± standard error (SE) was calculated for the data. The paired t-test was used to compare the data. $P < 0.05$ was used to indicate statistical significance.

Table 1: Characteristics of study subjects ($n = 9$).

Age (years)	Sex		Weight (kg)	Height (cm)	BMI (kg/m^2)	Glucose (mg/dL)
	Females	Males				
46.0 ± 3.8	5	4	67.71 ± 4.69	162.50 ± 2.87	25.37 ± 0.95	112.56 ± 6.97

Table 2: Inclusion and exclusion criteria.

Inclusion criteria
(i) Persons judged as healthy
Persons not currently going to the hospital and not taking medication
Persons with no history of serious medical and nervous system disease
(ii) Persons with high fasting blood glucose levels (100–125 mg/dL)
(iii) Persons who give voluntary written consent to participate in the trial
Exclusion criteria
(i) Persons who take any dietary supplements, quasi drugs, or medicines, which can cause the same or similar effects as the supplements evaluated in this study
(ii) Persons who have changed their habits with respect to supplement or cosmetic use within the past 4 weeks
(iii) Persons who work in the night shift or both day and night shift
(iv) Persons who have been treated for their condition or prevention in a clinic with their informed consent
(v) Persons with the following medical histories: skin disease or atopic dermatitis, serious diseases of glucose metabolism, lipid metabolism, or hepatic function, and abnormal renal, cardiovascular, circulatory, respiratory, endocrine, or immune function, or mental illness
(vi) Persons with a medical history of alcoholism or drug addiction
(vii) Persons at risk of an allergic reaction to food
(viii) Persons who are pregnant, breast-feeding, or hope to become pregnant during the study period
(ix) Persons who are participating in or will participate in any other clinical trial
(x) Persons who are not judged suitable for participation by the investigator

The inclusion and exclusion criteria were similar to those described by Nagae et al. [17] with some modifications.

2.5. Composition Analysis of LS-HDFNs. Commercial LS-HDFNs were lyophilized by freeze-drying. For the analysis of isoflavones, amino acids, and peptides, powdered lyophilized LS-HDFNs were mixed with methanol at 23–27°C and extracted by sonication for 30 min. The extracted solution was centrifuged at 1,710 × g at 25°C.

Lipid extraction was performed using the Folch method [19]. Methanol (0.4 mL) was added to 100 mg of lyophilized LS-HDFNs powder and extracted by sonication for 3 min. Furthermore, chloroform (0.8 mL) was added. After shaking the solution, 0.2 mL of water was added. The solution was shaken for 1 min followed by centrifugation at 16,000 × g for 2 min. The organic lower phase was collected separately and shifted to a glass vial. Re-extraction of the aqueous phase was extracted with 0.9 mL of chloroform/methanol/water (86 : 14 : 1, v/v). The organic lower phase obtained from centrifugation was collected. The two organic lower phases were combined and, after drying, redissolved in 0.1 mL of methanol/chloroform (9 : 1, v/v). It was filtered through 0.20 μm PTFE membrane (Millex-LG, Japan).

2.6. HPLC Analysis of the LS-HDFNs Extract for Isoflavone Levels. The isoflavone levels in LS-HDFNs were measured as reported by Kudou et al. [20]. LS-HDFNs extracts were analyzed using a Chromaster DAD system (Hitachi, Tokyo, Japan) and an InertSustain C18 (4.6 i.d. × 150 mm) HPLC column (GL Sciences, Tokyo, Japan). The column oven temperature and the flow rate were set at 35°C and 1.0 mL/min, respectively. The mobile phase consisted of solvent A (0.1% acetic acid in water) and solvent B (0.1% acetic acid in acetonitrile). The linear gradient program was set as follows: 0 min, 15% solvent B; 8 min, 15% solvent B; and 42 min, 35% solvent B. In total, 10 μL was injected. The quantity of isoflavones in LS-HDFNs was determined using standard curves based on authentic standards.

2.7. Analysis of the LS-HDFNs Extract by UPLC/qTOF-MS. An Agilent 1290 Infinity II LC system equipped with a 1290 photodiode array detector (DAD) (Agilent Technologies, Santa Clara, CA, USA) combined with an Agilent 6545 q-TOF hybrid mass spectrometer (MS) and a dual electrospray ionization (ESI) was used for analysis of the extract of LS-HDFNs dissolved in methanol or methanol/chloroform (9 : 1, v/v). The analytes were efficiently separated on an Agilent InfinityLab Poroshell 120 EC-C18 column (100 × 2.1 mm i.d.; 2.7 μm particle size) (Agilent Technologies, Santa Clara, CA, USA), and 2 μL of the sample (10 mg/mL) was injected. The column temperature was set at 50°C. The gradient method for isoflavones and peptide was as follows: The mobile phases were 0.1% (v/v) formic acid aqueous solution (phase A) and 0.1% (v/v) formic acid in acetonitrile (phase B) at a flow rate of 0.2 mL/min. The solvent gradient program was as follows: 15% B for 0 min, increased to 40% B for 10 min, increased to 100% B for 15 min, and maintained for 5 min. The gradient method for lipids was as follows: The mobile phases were 10 mM ammonium acetate in water/methanol (9 : 1, v/v) (phase A) and 10 mM ammonium acetate in acetonitrile/methanol/isopropanol (2 : 3 : 5, v/v) (phase B) at a flow rate of 0.25 mL/min. The solvent gradient program was as follows:

70% B for 0 min, maintained for 1 min, increased to 86% B for 3.5 min, maintained for 2.5 min, increased to 100% B for 7 min, maintained for 19 min, decreased to 70% B for 0.1 min, and maintained for 3.9 min.

A dual ESI source was performed in negative ionization under the following conditions: nebulizer gas at 35 psi with the drying gas flow rate and the temperature at 10 L/min and 325°C, respectively. The capillary voltage was set at 3,500 V, whereas the fragmentor, skimmer, and octapole voltages were fixed at 130, 65, and 750 V, respectively. Data were obtained in the centroid mode in the extended dynamic range (2 GHz). The complete scan was performed at 1.5 spectra per second within the m/z range of 100–1,700.

2.8. HPLC Analysis of the LS-HDFNs Extract for Phospholipids. The phospholipid levels in LS-HDFNs were determined according to the methods described by Shafiq-ur-Rehman et al. [21]. The lipid extract of LS-HDFNs was analyzed using a Chromaster DAD system (Hitachi, Tokyo, Japan) equipped with a TSK-gel Silica-60 (4.6 i.d. × 250 mm) column (Tosoh, Tokyo, Japan) and InertSustain Amide (4.6 i.d. × 250 mm) column (GL Sciences, Tokyo, Japan). Analyses of phospholipids were performed using acetonitrile/methanol/phosphoric acid (100 : 10 : 1.8, v/v) under isocratic conditions at a flow rate of 1.0 mL/min for the TSK-gel Silica-60 column and 0.8 mL/min for the InertSustain Amide column. The column oven temperature was set at 35°C and UV detection at 205 nm. In total, 10 μL was injected. The amounts of phospholipids in LS-HDFNs were calculated using standard curves.

3. Results

3.1. Effect of LS-HDFNs Administration for 28 Days in Healthy Humans. In total, nine participants completed the study. LS-HDFNs consumption was not associated with any abnormalities or adverse effects.

The physical characteristics before (0 day of administration) and after (28 days after administration) treatment with LS-HDFNs are shown in Table 3. The body weight before and after LS-HDFNs consumption was 67.71 ± 4.69 and 66.26 ± 4.47 kg, respectively. After 28 days of LS-HDFNs consumption, the body weight decreased significantly ($p = 0.006$). The body fat percentage was significantly decreased after 28 days of LS-HDFNs consumption (32.41 ± 1.68%) compared to that before LS-HDFNs consumption (31.67 ± 1.80%). The waist circumference and visceral fat area levels were lower after 28 days of LS-HDFNs administration than those before LS-HDFNs administration.

Table 4 presents a comparison of blood biochemical parameters before and after LS-HDFNs consumption. None of the parameters showed any significant difference. T-CHO and LDL-C levels were significantly reduced after LS-HDFNs consumption compared to those before LS-HDFNs consumption (T-CHO, $p = 0.003$; LDL-C, $p = 0.011$).

Table 3: Physical characteristics before and after treatment with LS-HDFNs.

		Before 0 day of administration	After 28 days of administration
Body weight	kg	67.71 ± 4.69	66.26 ± 4.47*
Body fat percentage	%	32.41 ± 1.68	31.67 ± 1.80*
Waist circumference	cm	91.76 ± 2.27	90.67 ± 2.55
Visceral fat area	cm^2	124.44 ± 14.36	113.89 ± 15.62

Results are expressed as the mean ± standard error. Statistical significance was evaluated using Student's *t*-test. * $p < 0.01$ vs. before LS-HDFNs consumption.

Table 4: Blood biochemical parameters before and after treatment with LS-HDFNs.

		Before 0 day of administration	After 28 days of administration
TP	g/dL	9.18 ± 0.24	8.86 ± 0.24
ALB	g/dL	5.28 ± 0.10	5.30 ± 0.15
BUN	mg/dL	13.33 ± 1.08	13.00 ± 1.17
CRE	mg/dL	0.66 ± 0.03	0.69 ± 0.03
UA	mg/dL	6.23 ± 0.33	6.72 ± 0.35
AST	IU/L	31.44 ± 4.16	25.89 ± 2.16
ALT	IU/L	38.78 ± 12.16	26.89 ± 4.63
γ-GT	IU/L	43.44 ± 8.46	39.67 ± 9.62
ALP	IU/L	88.11 ± 10.01	93.33 ± 10.51
GLU	mg/dL	112.56 ± 6.97	108.11 ± 6.67
HbA1c	%	5.88 ± 0.18	5.78 ± 0.14
GA	%	14.06 ± 0.80	13.14 ± 0.47
T-CHO	mg/dL	265.22 ± 14.62	226.11 ± 15.78*
TG	mg/dL	108.89 ± 49.16	115.67 ± 49.60
HDL-C	mg/dL	70.44 ± 8.69	59.33 ± 9.02
LDL-C	mg/dL	173.00 ± 13.53	143.67 ± 10.99*

TP, total protein; ALB, albumin; BUN, blood urea nitrogen; CRE, creatinine; UA, uric acid; AST, aspartate aminotransferase; ALT, alanine transaminase; γ-GT, γ-glutamyl transpeptidase; ALP, alkaline phosphatase; GLU, glucose; HbA1c, hemoglobin A1c; GA, glycated albumin; T-CHO, total cholesterol; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol. Results are expressed as the mean ± standard error. Statistical significance was evaluated using Student's *t*-test. * $p < 0.01$ vs. before LS-HDFNs consumption.

3.2. HPLC Analysis of Isoflavone in LS-HDFNs. The HPLC chromatogram of isoflavones in LS-HDFNs is presented in Figure 2. The analysis identified daidzin, glycitin, genistin, daidzein, glycitein, and genistein.

3.3. UPLC/qTOF-MS Analysis of LS-HDFNs. The components of LS-HDFNs were qualitatively analyzed using UPLC and qTOF-MS.

Table 5 summarizes the MS data for amino acids. We detected 12 amino acids (nos.: A1–A12 in Table 5). Moreover, we measured the dipeptides and oligopeptides in LS-HDFNs. LS-HDFNs contained 20 peptides (P1–P20 in Table 6). The MS data of lipids are presented in Table 7 (positive mode) and Table 8 (negative mode). LS-HDFNs contained 37 lipids.

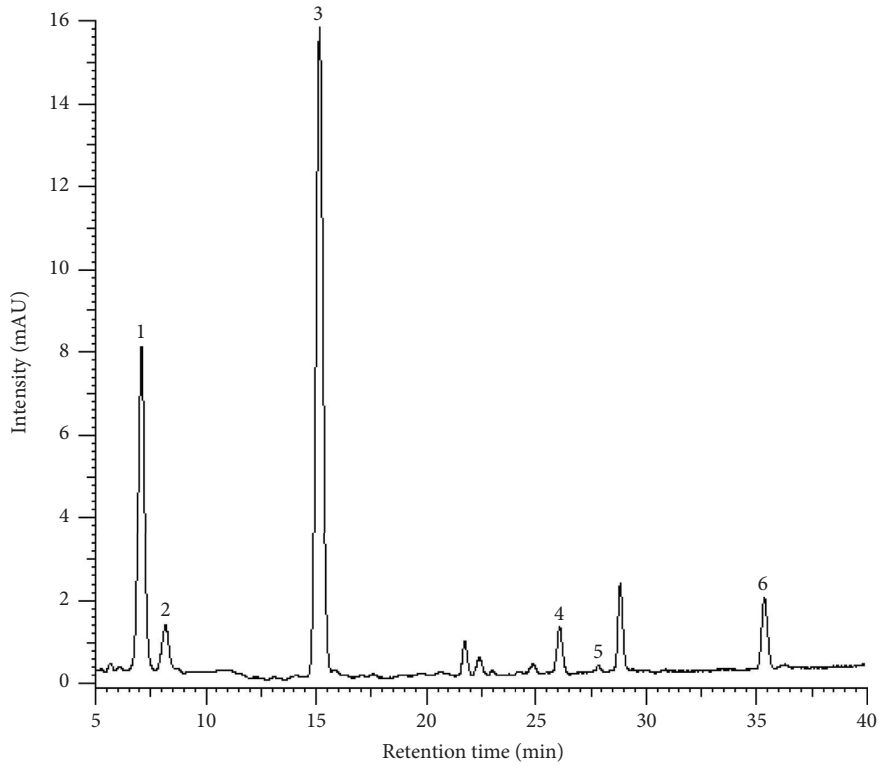

Figure 2: HPLC chromatogram of isoflavones in LS-HDFNs. 1, daidzin; 2, glycitin; 3, genistin; 4, daidzein; 5, glycitein; 6, genistein.

Table 5: UPLC/qTOF-MS data of amino acids in LS-HDFNs.

Nos.	Retention time (min)	MS (m/z)	Molecular formula	Suggested compound
A1	1.24	197.1008	$C_6H_{14}N_4O_2$	Arg
A2	1.26	133.0607	$C_4H_8N_2O_3$	Asn
A3	1.26	155.0696	$C_6H_9N_3O_2$	His
A4	1.26	106.0501	$C_3H_7NO_3$	Ser
A5	1.27	134.0444	$C_4H_7NO_4$	Asp
A6	1.27	169.0584	$C_5H_{10}N_2O_3$	Gln
A7	1.33	148.0606	$C_5H_9NO_4$	Glu
A8	1.62	118.0862	$C_5H_{11}NO_2$	Val
A9	2.17	182.0810	$C_9H_{11}NO_3$	Tyr
A10	2.43	132.1017	$C_6H_{13}NO_2$	Ile
A11	2.64	132.1019	$C_6H_{13}NO_2$	Leu
A12	7.51	205.0970	$C_{11}H_{12}N_2O_2$	Trp

4. Discussion

Obesity is a serious metabolic disorder. Obesity and overweight have a growing prevalence globally [22]. Obesity and overweight are associated with several chronic diseases, including hyperglycemia, hyperlipidemia, low-grade inflammation, cardiovascular diseases, and type 2 diabetes [23]. For this reason, it is important to develop safe and healthy methods of weight loss and prevention of obesity and its complications.

Diabetes mellitus is a significant public health issue globally and a leading cause of motility and morbidity [24]. Diabetes affected 537 million worldwide in 2021, and its prevalence is expected to increase from 643 million in 2030 to 783 million by 2045 [25], which may be explained by the population growth, aging, urbanization, physical inactivity, and obesity [4]. Consumption of refined carbohydrates, including rice and noodles, leads to abnormal glucose metabolism [26]. Rice and noodles are major staple foods of the Asian population, such as the Chinese, Korean, and Japanese. For this reason, we produced LS-HDFNs composed of okara and konjac for individuals with high consumption of noodles. A previous research explored the effects of LS-HDFNs on the glycemic response in healthy individuals using a single meal test as a crossover trial. The study found that the postprandial blood glucose and insulin levels in the LS-HDFNs group remained stable for 120 min after the consumption of LS-HDFNs [16]. The main predisposing factors of type 2 diabetes are overweight and obesity. Weight loss is the main treatment of type 2 diabetes

Table 6: UPLC/qTOF-MS data of peptides in LS-HDFNs.

Nos.	Retention time (min)	MS (m/z)	Molecular formula	Suggested compound
P1	1.38	360.1501	$C_{16}H_{23}N_3O_5$	Tripeptide
P2	8.88	371.2272	$C_{17}H_{30}N_4O_5$	Tetrapeptide
P3	11.80	236.1622	$C_9H_{18}N_2O_4$	Dipeptide
P4	12.37	250.1782	$C_{10}H_{20}N_2O_4$	Dipeptide
P5	12.39	266.1516	$C_{10}H_{20}N_2O_3S$	Dipeptide
P6	12.88	387.1802	$C_{15}H_{26}N_6O_4S$	Tripeptide
P7	12.99	250.1776	$C_{10}H_{20}N_2O_4$	Dipeptide
P8	13.66	250.1775	$C_{10}H_{20}N_2O_4$	Dipeptide
P9	14.32	266.1517	$C_{10}H_{20}N_2O_3S$	Dipeptide
P10	15.28	362.2393	$C_{15}H_{31}N_5O_5$	Tripeptide
P11	15.94	502.3738	$C_{23}H_{44}N_6O_5$	Tetrapeptide
P12	15.94	502.3738	$C_{23}H_{47}N_7O_5$	Tetrapeptide
P13	17.07	554.1758	$C_{23}H_{31}N_5O_7S_2$	Tetrapeptide
P14	17.53	536.1665	$C_{20}H_{30}N_4O_6S_3$	Tetrapeptide
P15	17.53	538.1650	$C_{22}H_{27}N_5O_9S$	Tetrapeptide
P16	17.53	538.1650	$C_{19}H_{29}N_7O_8D$	Tetrapeptide
P17	17.53	539.1645	$C_{21}H_{32}N_4O_7S_2$	Tetrapeptide
P18	17.53	540.1626	$C_{22}H_{29}N_5O_7S_2$	Tetrapeptide
P19	17.53	540.1626	$C_{19}H_{31}N_7O_6S_2$	Tetrapeptide
P20	20.67	587.3604	$C_{24}H_{46}N_{10}O_7$	Tetrapeptide

Table 7: UPLC/qTOF-MS data of lipids in LS-HDFNs (the positive mode).

Nos.	Retention time (min)	MS (m/z)	Molecular formula	Molecular species	
L1	4.92	520.3387	$C_{26}H_{50}NO_7P$	LPC	0 : 0/18 : 2
L2	5.31	520.3395	$C_{26}H_{50}NO_7P$	LPC	18 : 2/0 : 0
L3	6.16	496.3392	$C_{24}H_{50}NO_7P$	LPC	16 : 0/0 : 0
L4	6.60	522.3545	$C_{26}H_{52}NO_7P$	LPC	18 : 1/0 : 0
L5	8.16	524.3699	$C_{26}H_{54}NO_7P$	LPC	18 : 0/0 : 0
L6	10.84	788.5421	$C_{42}H_{75}O_{10}P$	PG	
L7	11.43	778.5368	$C_{44}H_{76}NO_8P$	PC	18 : 3/18 : 3
L8	11.54	764.5426	$C_{40}H_{75}O_{10}P$	PG	16 : 0/18 : 2
L9	12.13	738.5062	$C_{41}H_{72}NO_8P$	PE	18 : 2/18 : 3
L10	12.46	780.5543	$C_{44}H_{78}NO_8P$	PC	18 : 2/18 : 3
L11	13.23	714.5058	$C_{39}H_{72}NO_8P$	PE	16 : 0/18 : 3
L12	13.32	740.5227	$C_{41}H_{74}NO_8P$	PE	18 : 2/18 : 2
L13	13.68	756.5533	$C_{42}H_{78}NO_8P$	PC	16 : 0/18 : 3
L14	13.73	782.5700	$C_{44}H_{80}NO_8P$	PC	18 : 2/18 : 2
L15	13.89	630.5078	$C_{39}H_{64}O_5$	DG	18 : 3/18 : 3
L16	14.71	716.5227	$C_{39}H_{74}NO_8P$	PE	16 : 0/18 : 2
L17	15.04	742.5371	$C_{41}H_{76}NO_8P$	PE	18 : 1/18 : 2
L18	15.37	758.5702	$C_{42}H_{80}NO_8P$	PC	16 : 0/18 : 2
L19	15.69	784.5851	$C_{44}H_{82}NO_8P$	PC	18 : 1/18 : 2
L20	16.86	718.5367	$C_{39}H_{76}NO_8P$	PE	
L21	17.58	608.5237	$C_{37}H_{66}O_5$	DG	16 : 0/18 : 3
L22	17.79	634.5408	$C_{39}H_{68}O_5$	DG	18 : 2/18 : 2
L23	17.86	744.5525	$C_{41}H_{78}NO_8P$	PE	
L24	17.92	760.5838	$C_{42}H_{82}NO_8P$	PC	16 : 0/18 : 1
L25	19.02	786.6001	$C_{44}H_{84}NO_8P$	PC	
L26	26.12	638.5706	$C_{39}H_{72}O_5$	DG	18 : 0/18 : 2

PC, phosphatidylcholine; DG, diacylglycerol; PE, phosphatidylethanolamine; LPC, lysophophatidylcholine; PG, phosphatidylglycerol.

[27]. Our results showed the impact of LS-HDFNs intake for 28 days on body weight management in healthy individuals as a single group in a pre-post trial for the first time.

The nine study participants consumed a bag of LS-HDFNs (180 g) once a day for 28 days. The physical characteristics and blood biochemical parameters were measured twice (0 and 28 days after administration). After 28 days of LS-HDFNs consumption, the body weight and body fat percentage were significantly decreased compared to those before LS-HDFNs consumption, whereas the waist circumference and visceral fat area levels were lower than those before LS-HDFNs consumption. LS-HDFNs consumption was not associated with any abnormalities or adverse effects. The simple strategy of using LS-HDFNs was effective for the

Table 8: UPLC/qTOF-MS data of lipids in LS-HDFNs (the negative mode).

Nos.	Retention time (min)	MS (m/z)	Molecular formula	Molecular species	
L27	4.09	255.2330	$C_{16}H_{32}O_2$	FA	16 : 0
L28	5.89	283.2640	$C_{18}H_{36}O_2$	FA	18 : 0
L29	8.51	831.5008	$C_{43}H_{77}O_{13}P$	PI	16 : 0/18 : 3
L30	8.54	745.5008	$C_{40}H_{75}O_{10}P$	PG	16 : 0/18 : 2
L31	8.54	857.5161	$C_{45}H_{79}O_{13}P$	PI	18 : 2/18 : 2
L32	8.72	339.3269	$C_{22}H_{44}O_2$	FA	22 : 0
L33	8.76	833.5181	$C_{43}H_{79}O_{13}P$	PI	16 : 0/18 : 2
L34	9.26	861.5477	$C_{45}H_{83}O_{13}P$	PI	18 : 0/18 : 2
L35	9.41	736.4903	$C_{41}H_{72}NO_8P$	PE	18 : 2/18 : 3
L36	9.89	738.5072	$C_{41}H_{74}NO_8P$	PE	18 : 2/18 : 2
L37	10.46	714.5074	$C_{39}H_{74}NO_8P$	PE	16 : 0/18 : 2

PC, phosphatidylcholine; DG, diacylglycerol; PE, phosphatidylethanolamine; LPC, lysophophatidylcholine; PG, phosphatidylglycerol; PI, phosphatidylinositol; FA, free fatty acid.

management of body weight. The energy (kcal), proteins (g), fats (g), and carbohydrates (g) of LS-HDFNs (180 g; Healthy Noodles™ from Kibun Foods Inc., Japan) are 35.0, 2.4, 1.4, and 11.3 (sugar : 0.0, dietary fiber : 11.3), respectively. LS-HDFNs are a low-calorie, low-sugar, and high-dietary fiber product. Therefore, LS-HDFNs are effective for the management of body weight. All study participants had high blood glucose (fasting blood glucose levels : 100–125 mg/dL) before LS-HDFNs administration. The GLU, HbA1c, and GA levels were lower after compared to before LS-HDFNs consumption. In our previous study, we found that LS-HDFNs consumptions altered the blood glucose levels in a model of obese type 2 diabetes (28 days administration) in Spontaneously Diabetic Torii fatty rats. The levels of blood glucose, HbA1c, and glycated albumin were reduced in the LS-HDFNs group compared to the control group [15]. We investigated the impact of LS-HDFNs consumption on the glycemic response in healthy individuals in a crossover trial using a single meal test. We found that subjects who consumed LS-HDFNs had significant attenuation of the increase in postprandial blood glucose and insulin levels compared to subjects who consumed normal wheat noodles [16]. Our results are in line with those of our previous reports. Therefore, LS-HDFNs are useful for the management of diabetes and body weight. Moreover, the T-CHO and LDL-C levels were significantly reduced than those before LS-HDFNs consumption. Therefore, the consumption of LS-HDFNs is effective for the management of T-CHO and LDL-C.

Isoflavones, such as daidzin, glycitin, genistin, daidzein, glycitein, and genistein, were contained in LS-HDFNs from *Glycine max* (commonly called "okara"). The levels (μg/g LS-HDFNs powder) of daidzin, glycitin, genistin, daidzein, and genistein were 6.37 ± 0.05, 1.25 ± 0.05, 11.16 ± 0.07, 0.31 ± 0.01, and 0.91 ± 0.01, respectively. Isoflavones are a subgroup of flavonoids. The most abundant isoflavones in soybean are genistein, daidzein, and glycitein. These isoflavones are present in glycosylated forms, such as genistin, daidzin, and glycitin. Generally, isoflavones are not easily absorbed from the intestines and undergo hydrolysis catalysed by beta-glucosidase from intestinal microflora [28]. Isoflavones are useful as an alternative treatment of hormone-related cancers, such as breast and prostate cancer [29], cardiovascular diseases [30], osteoporosis [31], and menopausal symptoms [32]. In addition, there are some reports about the beneficial effects of genistein on weight loss [33, 34]. Based on these reports, the reduction in body weight and body fat percentage after LS-HDFNs consumption may be due to the impact of isoflavones, including genistein.

In UPLC and qTOF-MS analyses, 12 amino acids were identified in the LS-HDFNs. Using the MS (m/z) and molecular formula, we identified A1, Agr; A2, Asn; A3, His; A4, Ser; A5, Asp; A6, Gln; A7, Glu; A8, Val; A9, Tyr; A10, Ile; A11, Leu; and A12, Trp. Moreover, 20 peptides, including dipeptides and oligopeptides, were found in LS-HDFNs. The highest content among the 20 peptides was of peptide no. P4 and P14. Based on the MS (m/z) and molecular formula, P4 is a dipeptide (Ile and Thr) and P14 is a tetrapeptide (Met, Try, Cys, and Cys). Bioactive peptides are classified as specific protein fragments and are important for human health [35]. Bioactive peptides are produced during enzymatic proteolysis of proteins and during food processing, such as cooking, fermentation, and ripening [36]. Till now, more than 1,500 peptides have been identified [37]; these peptides have shown antidiabetic, cholesterol-lowering, antihypertensive, anticancer, antimicrobial, opioid, and antioxidant effects [38]. LS-HDFNs contain amino acids, dipeptides, and oligopeptides. These compounds may exhibit novel physiological effects. Moreover, Zani et al. reported that endogenous and bioactive peptides exhibit antiobesity properties [39]. In the future, we will attempt to perform a comprehensive analysis for the identification of active peptides and amino acids.

In UPLC and qTOF-MS analyses, 37 lipids were contained in LS-HDFNs. Of the 37 lipids, the highest ion strength was noted for no. L14 and L33. The MS (m/z) and molecular formula showed that L14 is phosphatidylcholine (PC; molecular formula, $C_{44}H_{80}NO_8P$) and L33 is phosphatidylinositol (PI; molecular formula, $C_{43}H_{79}O_{13}P$). Based on the results of quantitative analysis of phospholipids, PC and PI were detected. The levels (μg/g LS-HDFNs powder) of PC and PI were 388.24 ± 1.87 and 91.43 ± 4.21, respectively. Phospholipids (PLs) have biological therapeutic activity

against chronic diseases, such as cardiovascular and cerebrovascular diseases [40]. Cardiovascular and cerebrovascular diseases, including Alzheimer's disease, may be improved by PLs [41]. PLs, particularly PC, phosphatidylethanolamine (PE), and phosphatidylserine (PS), lower the lipid levels and improve brain function [42]. A study found that dietary PI reduces the hepatic and serum cholesterol levels via the enhancement of fecal bile acid excretion in the metabolic syndrome model rats [43]. Moreover, Su et al. reported that PLs substantially reduced body weight gain, adipose gain, fasting blood glucose, serum insulin, and serum and liver lipid levels [44]. Based on these reports, the loss of body weight and body fat percentage after LS-HDFNs consumption may be related to the effects of PC and PI.

5. Conclusion

In general, individuals with overweight, obesity, and type 2 diabetes consume seasoned staple foods, such as rice, bread, and noodles, which contain high quantities of carbohydrates. As a result, LCD is challenging to adapt for prolonged periods. Several strategies have been developed to manage body weight, including dietary carbohydrate restriction (e.g., using LCD). LCD has several advantages and disadvantages. Therefore, it is essential to individualize the dietary advice. In this preliminary study, we explored the effects of LS-HDFNs in healthy individuals and found that the levels of body weight, body fat percentage, T-CHO, and low-density lipoprotein cholesterol were significantly lower after 28 days of LS-HDFNs consumption. Our results provide novel information on a simple strategy for weight loss. LS-HDFNs were a low-calorie, low-sugar, and high-dietary fiber product, which contain active compounds such as isoflavones, bioactive peptides, and PLs. The detailed mechanisms by which LS-HDFNs reduce body weight remain unclear; however, our preliminary study showed that LS-HDFNs are useful for body weight management.

Data Availability

All data generated or analyzed during this study are included within this published article.

Ethical Approval

The experiments were performed at the Laboratory of Systematic Forest and Forest Products Sciences, Faculty of Agriculture, Kyushu University. The experiment was performed in complete accordance with the Declaration of Helsinki. This study was approved by the Kinki University Faculty of Humanity-Oriented Science and Engineering Ethics Committee (no.: 2020002; registered on March 2, 2020).

Consent

The participants provided written consent prior to participation in the study.

Conflicts of Interest

The authors declare that there are no conflicts of interest.

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