

Effects of promoting eating foods containing bitter vegetables on nutritional status in the elderly

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ABSTRACT

Background: Non-communicable diseases pose a considerable risk for the elderly population. This study aimed to investigate the impact of incorporating bitter vegetables into the diets of elderly individuals on their nutritional status. The study involved regular consumption of northern foods, such as Malidmai (Peka), salae, neem (neem), bitter gourd, and cassia, at least once a day for three months.

Materials and methods: A randomized clinical trial recruited eighty individuals aged 60 years and above. One group was allowed to eat ad libitum, while the other group followed a recommended menu that emphasized bitter flavors. The study assessed dietary intake, body composition, and blood biochemical parameters.

Results: The findings revealed a significant reduction in energy, saturated fat, and cholesterol intake, with the bitter group experiencing a statistically significant decrease in sugar consumption. The bitter group also demonstrated a considerable reduction in anthropometric and metabolic parameters when compared to the control group and baseline measures. These results indicate the potential benefits of bitter substances in managing or preventing obesity and type 2 diabetes in the elderly.

Conclusion: Encouraging the elderly to consume at least one bitter meal per day for 12 weeks resulted in a reduction in weight gain, adipose tissue, sugar levels, and LDL-C. The study highlights the importance of incorporating bitter vegetables into the diets of elderly individuals for better nutritional status and health outcomes.

Introduction

According to recent statistics, as of 2021, Thailand's total population is 66.7 million. There has been a significant increase in the number of elderly citizens in Thailand in recent years, with the older population growing at an unprecedented rate. Half a century ago, Thailand only had two million elderly citizens. However, as of 2021, this number has surged to 12.5 million, equivalent to 19% of the country's population. It is projected that by 2022, at least 20% of Thailand's population will be 60 years or older, making it a "completely aged society."¹

As we age, our ability to perceive taste declines. Research conducted on healthy elderly individuals has demonstrated that the taste threshold begins to increase and can lead to dysgeusia after the age of 70. Additionally, chewing difficulties caused by tooth loss or denture use can interfere with taste sensation and reduce saliva

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production.² The reduction in taste recognition ability is attributed to various causes, including the reported decrease in the number and density of taste buds on the tongue.^{3,4} The relationship between taste and diabetes is complex as several factors, including genetics, environment, behavior, and sensory perception, can influence eating habits, some of which may contribute to the development of diabetes. Patients with diabetes have been shown to have a general decrease in taste function, especially about sweet taste. Hyperglycemia has been linked to an increase in taste threshold.³

Recently, there has been an escalating interest in the ability of bitter substances to regulate energy intake and enhance glycaemic control. This interest is based on reports from preclinical models, such as studies conducted in cell cultures or animals, which have demonstrated that bitter substances have potent effects on the secretion of gastrointestinal hormones and the slowing of gastric emptying.⁵⁻⁷ Studies have established that these gut functions play crucial roles in regulating acute energy intake and postprandial glycemia.⁸⁻¹⁰ Given these findings, bitter substances may serve as a novel approach to managing or preventing obesity and its comorbidities, especially type 2 diabetes.

Over the last 4-5 years, while rendering academic services to the communities residing in Phayao Province, it has been observed that the elderly population has a predilection towards consuming bitter vegetables. As a result, it can be inferred that the sensation of bitterness in food may act as a deterrent to malnutrition and prevent obesity and type 2 diabetes.

This study is significant for the elderly population who are experiencing malnutrition or are at risk of malnutrition. It recommends regularly consuming Northern Thai foods such as Malidmai (Peka), Salae, Neem (Neem), Bitter Gourd, and Cassia at least once daily for three months. Anthropometric, biochemical, clinical, and nutritional assessments were utilized as indicators for the prevention of malnutrition and type 2 diabetes in elderly individuals.

Methods

Subjects

Eighty elderly people aged 60 years or over in Phayao Province, calculated by the G-power program. Family as t-tests and statistical tests selected as Means Difference between two independent means (two groups), specify α err prob equal to 0.05 and set Power equal to 0.87 and use effect size as recommended by Cohen (1988), effect size equal to 0.7. To calculate the total sample size, 80 subjects were required to test, divided into two groups of 40 subjects each.

Study design

This research was designed as a randomized clinical trial for 12 weeks, divided into two groups of 40 older adults with no differences, with the first group being a control group and the second group being a bitter group. Before recruitment, each participant was screened for eligibility. A flow chart of the study enrolment is demonstrated in Figure 1.

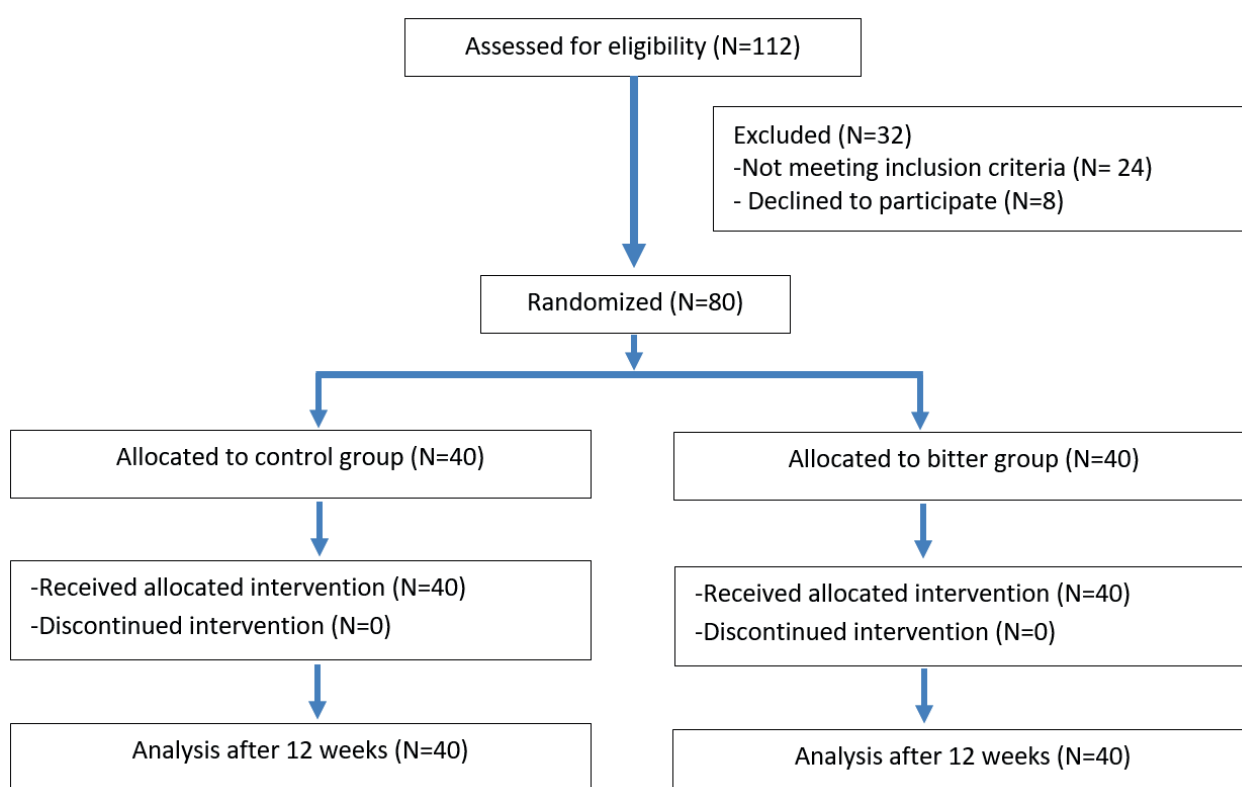


Figure 1. Flow of participants in the study.

Dietary

The control group was allowed to eat *ad libitum*. The experimental group, or the bitter group, was eating food according to the recommended menu. It is a local food menu that focuses on bitter tastes from Malidmai (Peka), salae, neem (neem), bitter gourd, cassia, sweet juice, gurma, and Marsdenia glabra Cost, one meal a day. Both groups were trained before the start of the study so that they could make the right dietary choices for the elderly.

Inclusion criteria

An elderly person aged 60 years and over in Phayao Province. Malnutrition or at risk of malnutrition as elderly with greater than 23.0 kg/m², able to read and write well and willing to participate in the project.

Exclusion criteria

Elderly people with severe communicable diseases or severe NCDs, disabilities, chewing swallowing problems, or the inability to eat bitter foods were excluded from the study.

Body composition assessment

Height was measured by using a calibrated stadiometer. Body weight (kg), body fat (% of body weight), Visceral fat (level) were assessed using Tanita BC-418 ma segmental body composition analyzer (Tanita Co.Ltd., Japan).

Biochemical assessment

Biochemical measurements were conducted in both the control and experimental groups, including fasting blood sugar, total cholesterol, HDL-cholesterol, LDL-cholesterol, and triglyceride. These parameters were analyzed using an automated blood BS-400 Chemistry Analyzer (Mindray bio-Medical Electronics Co. Ltd).

Dietary assessment

Energy and nutrient intakes were recorded 24 hrs. Dietary intake was calculated using INMUCAL-Nutrients version 3 software provided by the Institute of Nutrition, Mahidol University (Institute of Nutrition, 2016). All subjects were recorded for three days with a food record form at week 0 and week 12.

Ethics approval and permissions

This study, including protocol and consent forms for students and their parents, was approved by the Ethics committee at the University of Phayao (UP-HEC 1.3/010/65). Written informed consent was obtained from the subjects.

Statistical Analysis

Statistical analysis was performed using SPSS statistics version 18.0 (Levesque, 2007). Nutritional status (anthropometric, biochemical, and dietary data) was presented as mean (\pm SD) or percentage. The differences in body composition, biochemical data, and dietary data in the group were determined by the paired t-test. In addition, an independent t-test was employed to test the differences between the intervention and control groups. The $p < 0.05$ was considered statistically significant.

Results

This study aimed to study the effect of encouraging the elderly to eat bitter vegetables on nutritional status. The elderly are at risk of developing non-communicable diseases. Therefore, 80 elderly people were recruited into the project to study the effects of promoting the consumption of bitter foods to reduce blood sugar and lipid levels.

At baseline, the characteristics of subjects in the two treatment groups do not differ in both body composition and biochemical assessment, as shown in Table 1.

Table 1. Baseline characteristics of subjects in the two treatment groups.

Parameters	Control group	Bitter group	p value*
Female gender, N (%)	72.5	70.8	
Age, years	68.4 \pm 5.41	67.24 \pm 4.81	0.312
Weight, kg	60.04 \pm 6.63	59.99 \pm 7.75	0.193
BMI, kg/m ²	24.88 \pm 1.75	24.37 \pm 2.44	0.076
FBS, mg/dL	92.12 \pm 11.12	92.90 \pm 17.38	0.214
Total cholesterol, mg/dL	198.83 \pm 40.06	197.54 \pm 49.57	0.907
HDL-C, mg/dL	51.20 \pm 11.08	51.88 \pm 14.49	0.924
LDL-C, mg/dL	124.20 \pm 35.16	125.83 \pm 37.63	0.298
LDL-C/HDL-C ratio	2.460 \pm 0.64	2.495 \pm 0.69	0.149
Triglyceride, mg/dL	117.83 \pm 55.05	118.15 \pm 39.77	0.658

Note: Values are presented in mean (SD), *comparison between groups at baseline using Independent t-test, *statistically significant at $p < 0.05$, FBS: fasting blood sugar, HDL-C: high-density lipoprotein cholesterol, LDL-C: low-density lipoprotein cholesterol.

Table 2 shows that at week 0, subjects in both groups received enough energy from food according to the Dietary reference intake for Thais. At the same time, sugar and cholesterol were consumed more than the recommended daily amount.

After 12 weeks, there was a statistically significant decrease in energy intake, SFA, and cholesterol intake from baseline in both the control and bitter groups. When comparing groups, the bitter group had a statistically significant reduction in sugar consumption more than the control group at $p=0.02$, as shown in Table 3.

Anthropometric and metabolic parameters, including Weight, BMI, Body weight, Visceral fat, FBS, Total cholesterol, HDL-C, LDL-C, and Triglyceride after the 12-week nutritional intervention programmed both control and bitter groups were decreased when compared at baseline period as shown in Table 4.

After the 12-week nutritional intervention program, weight, BMI, body fat, FBS, and LDL-C in the bitter group were significantly reduced compared to baseline. When compared between groups, BMI and body fat in the bitter group were statistically significantly lower than the control group, as shown in Table 5.

Table 2. Comparison of dietary intakes between control and bitter groups at week 0 and week 12.

Parameters	Control group (N=40)		Bitter group (N=40)	
	Week 0	Week 12	Week 0	Week 12
	Mean±SD	Mean±SD	Mean±SD	Mean±SD
Energy intake, kcal	1599.91±161.35	1416.89±136.65	1601.86±162.51	1405.15±121.26
Energy distribution, % of total energy				
Carbohydrate	49.28±3.65	49.56±2.23	48.18±2.92	50.68±2.50
Protein	22.86±1.49	23.01±1.31	22.77±1.32	23.15±1.43
Fat	27.84±2.99	27.41±1.73	29.04±2.24	26.16±1.64
Sugar, gm	31.59±14.89	24.00±4.91	33.20±13.33	21.35±5.13
SFA, gm	18.26±3.13	15.34±2.44	18.70±2.85	14.73±1.85
Cholesterol, mg	361.17±95.86	295.47±26.28	369.18±87.67	284.50±23.15

Note: Values are presented in mean (SD), ^acomparison between week 0 and week 12 using the paired t-test, SFA: saturated fatty acid.

Table 3. Changes in dietary intakes in response to the 12-week nutritional intervention program.

Parameters	Control group			Bitter group			Control vs bitter group differences	
	Δ 0-12 week	% Change from baseline	p value	Δ 0-12 week	% Change from baseline	p value	Mean	p value
Energy intake, kcal	-183.02	11.43	<0.001	-196.70	-12.27	<0.001	11.73	0.498
Energy distribution, % of total energy								
Carbohydrate	0.280	0.56	0.621	2.499	5.18	<0.001	1.114	0.038
Protein	0.151	0.66	0.513	0.382	1.67	1.133	0.140	0.647
Fat	-0.431	1.54	0.296	-2.881	9.92	<0.001	1.255	0.001
Sugar, gm	-7.592	24.03	0.002	-11.848	35.68	<0.001	2.647	0.020
SFA, gm	-2.920	15.99	< 0.001	-3.965	21.20	<0.001	0.605	0.212
Cholesterol, mg	-65.701	18.19	< 0.001	-84.680	22.93	<0.001	10.963	0.050

Note: Values are presented in mean (SD), Significant differences in the control vs bitter group between 0-12 weeks without adjustment for the baseline value ($p\leq0.05$), SFA: saturated fatty acid.

Table 4. Anthropometric and metabolic parameters at baseline (time=0) and after the 12-week nutritional intervention program. (Mean±SD and CV).

Parameters	Control group (N=40)				Bitter group (N=40)			
	Week 0		Week 12		Week 0		Week 12	
	Mean±SD	CV	Mean±SD	CV	Mean±SD	CV	Mean±SD	CV
Weight, kg	60.04±6.63	0.11	58.29±8.76	0.15	59.99±7.75	0.12	56.50±6.25	0.11
BMI, kg/m ²	24.88±1.75	0.07	23.90±3.09	0.12	24.37±2.44	0.10	22.36±1.51	0.06
Body fat, %	32.38±6.77	0.20	30.48±8.29	0.27	30.94±7.75	0.25	26.79±6.66	0.24
Visceral fat, level	9.70±3.28	0.33	8.45±3.46	0.40	9.58±3.21	0.33	8.82±3.50	0.39
FBS, mg/dL	92.12±11.12	0.12	89.15±13.08	0.14	92.90±17.38	0.18	86.73±10.80	0.12
Total cholesterol, mg/dL	198.83±40.06	0.20	192.90±39.35	0.20	197.54±49.57	0.25	185.36±38.79	0.20
HDL-C, mg/dL	51.20±11.08	0.21	51.45±11.31	0.21	51.88±14.49	0.27	50.22±11.99	0.23
LDL-C, mg/dL	124.20±35.16	0.28	119.08±33.86	0.28	125.83±37.63	0.29	112.20±33.33	0.29
LDL-C/HDL-C ratio	2.46±0.64	0.26	2.33±0.52	0.22	2.49±0.69	0.27	2.27±0.61	0.26
Triglyceride, mg/dL	117.83±55.05	0.46	112.50±36.61	0.32	118.15±39.77	0.33	115.20±36.62	0.31

Note: Values are presented in mean (SD), ^acomparison between week 0 and week 12 using the Paired t-test, FBS: fasting blood sugar, HDL-C: high-density lipoprotein cholesterol, LDL-C: low-density lipoprotein cholesterol, coefficient of v(CV).

Table 5. Changes in anthropometric and metabolic parameters in response to the 12-week nutritional intervention program.

Parameters	Control group			Bitter group			Control vs bitter group differences	
	Δ 0-12 week	% Change from baseline	p value	Δ 0-12 week	% Change from baseline	p value	Mean	p value
Weight, kg	-1.74	-2.89	0.209	-3.47	-5.78	0.024	1.790	0.292
BMI, kg/m ²	-0.98	-3.93	0.029	-2.00	-8.20	<0.001	1.534	0.006
Body fat, %	-1.90	-1.90	0.207	-4.15	-4.15	0.004	3.694	0.030
Visceral fat, level	-1.25	-12.88	0.102	-0.75	-7.82	0.299	0.379	0.626
FBS, mg/dL	-2.98	-3.23	0.077	-6.17	-6.64	0.016	2.418	0.366
Total cholesterol, mg/dL	-5.93	-2.98	0.169	-12.17	-6.16	0.077	7.534	0.388
HDL-C, mg/dL	0.25	0.49	0.800	-1.65	-3.18	0.306	1.230	0.636
LDL-C, mg/dL	-5.13	-4.13	0.239	-13.63	-10.83	0.008	6.879	0.360
LDL-C/HDL-C ratio	-0.12	4.87	0.149	-0.21	-8.43	0.014	0.055	0.666
Triglyceride, mg/dL	-5.33	-4.52	0.522	-2.95	-2.50	0.685	2.695	0.741

Note: Values are presented in mean (SD), Significant differences in the control vs bitter group between 0-12 weeks without adjustment for the baseline value (p≤0.05), FBS: fasting blood sugar, HDL-C: high-density lipoprotein cholesterol, LDL-C: low-density lipoprotein cholesterol, Δ 0-12: changes in anthropometric and metabolic parameters week 12 - week 0.

Discussion

Taste function in humans decreases with age. A reduction in taste recognition ability was described with increasing age. Older persons have a reduced taste of food, making them more likely to eat foods that are too sweet, salty, or fat, increasing the risk of NCDs. Encouraging older people to eat bitter foods may result in lower intakes of sugar, sodium, or fat from their diet. This reduces the risk of NCDs.

During the baseline assessment, it was observed that the elderly participants in the study exhibited an elevated body mass index while their blood sugar and lipid levels were within normal ranges.¹¹ However, the average

values for these parameters were quite high and almost exceeded the standard thresholds. These findings are consistent with previous studies which have shown that a majority of the elderly population tends to have a higher body weight that exceeds the recommended BMI.¹² This is often associated with elevated levels of blood sugar and lipids.^{13,14}

According to the 24-hr food questionnaire, it was found that the energy intake from food among the elderly was normal. However, their consumption of sugar, saturated fat, and cholesterol was higher than the recommended daily intake.¹⁵ Overconsumption of sugar, saturated fat, and cholesterol can lead to an increase in

blood sugar, cholesterol, and LDL-C levels in the elderly, similar to the study in 2020, which can exceed the normal value.¹⁶ This finding is consistent with the study conducted by Witek K *et al.*, which suggests that consuming sweet-tasting foods with high sugar content is associated with diabetes and high blood sugar levels.¹⁷

Encouraging the elderly in the bitter group to consume at least one bitter meal per day for 12 weeks resulted in a statistically significant decrease in their daily sugar intake and LDL-C blood sugar levels compared to the control group. The quantity of bitter vegetables consumed in both groups was documented. The daily consumption of bitter vegetables was recorded for three days per week. The results revealed that the experimental group consumed an average of 40-50 grams per day, whereas the control group consumed approximately 5-10 grams per day. The possible mechanism underlying the reduction of blood sugar levels after consuming bitter-tasting food may be conducted on preclinical models. It has been observed that bitter substances have a potent impact on upper gastrointestinal functions. This impact is primarily seen in the secretion of gut hormones such as CCK, GLP-1, and ghrelin. These hormones are associated with a decrease in food intake and body weight, as well as a reduction in postprandial blood glucose excursions. This beneficial effect has been observed in models of obesity and type 2 diabetes. However, when it comes to clinical studies, the outcomes have needed to be more consistent and varied. These clinical studies have only been conducted on healthy individuals. Nevertheless, the studies suggest that bitter compounds stimulate GLP-1, reduce postprandial glucose, and modestly reduce energy intake.¹⁸

In addition to the monitoring of blood glucose levels, the group who consumed bitter foods exhibited a statistically significant reduction in LDL-C levels. This reduction is believed to be due to the suppression of saturated fatty acid intake and subsequent decrease in cholesterol levels during the 12-week study period. The underlying mechanisms responsible for this effect are likely similar to those observed in previous studies.¹⁸

The study found that a decrease in energy intake from food, as well as a reduction in energy intake from fat and carbohydrates, led to a significant statistical reduction in body weight, BMI, and body fat among participants in the bitter group. Additionally, there was a noticeable decrease in abdominal fat, consistent with previous research, which concluded that weight loss of 6-7% with diet or with exercise plus diet reduced both subcutaneous and intra-abdominal fat.¹⁹

Based on the study, it can be observed that promoting the consumption of at least one bitter meal per day among the elderly can lead to a reduction in the intake of sugar, fat, and cholesterol from their diet. This reduction in consumption consequently leads to lower blood sugar and LDL-C levels, as well as a decrease in body weight and adipose tissue over a 12-week duration.

Conclusion

Encouraging the elderly to eat at least one bitter meal

daily for 12 weeks resulted in weight loss. Adipose tissue, sugar levels, and LDL-C were statistically significantly reduced.

Conflict of interest

No

Funding

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References

- [1] Pramote Prasartkul, Jongjit Rittirong, Sutthida Chuanwan, Napaphat Satchanawakul, Suporn Jaratsit, Kanchana Thianlai (2022). Situation of the Thai Older Persons 2021. Institute for Population and Social Research, Mahidol University; Nakhon Pathom. ISBN: 978-616-443-686-2.
- [2] Shilpa Amarya, Kalyani Singh and Manisha Sabharwal. Aging Process and Physiological Changes. Reviewed: March 6th, 2018 Published: July 4th, 2018 doi: 10.5772/intechopen.76249
- [3] Pugnaloni S, Alia S, Mancini M, Santoro V, Di Paolo A, Rabini RA, Fiorini R, Sabbatinelli J, Fabri M, Mazzanti L, Vignini A. A Study on the Relationship between Type 2 Diabetes and Taste Function in Patients with Good Glycemic Control. *Nutrients*. 2020; 12(4): 1112. doi: 10.3390/nu12041112.
- [4] Sergi G., Bano G., Pizzato S., Veronese N., Manzato E. Taste loss in the elderly: Possible implications for dietary habits. *Crit Rev Food Sc Nutr*. 2017; 57(17): 3684-9, doi: 10.1080/10408398.2016.1160208.
- [5] Avau B, Bauters D, Steensels S, Vancleef L, Laermans J, Lesuisse J, Buyse J, Lijnen HR, Tack J, Depoortere I. The Gustatory Signaling Pathway and Bitter Taste Receptors Affect the Development of Obesity and Adipocyte Metabolism in Mice. *PLoS One*. 2015; 10(12): e0145538. doi: 10.1371/journal.pone.0145538.
- [6] Chen MC, Wu SV, Reeve JR Jr, Rozengurt E. Bitter stimuli induce Ca²⁺ signaling and CCK release in enteroendocrine STC-1 cells: role of L-type voltage-sensitive Ca²⁺ channels. *Am J Physiol Cell Physiol*. 2006; 291(4): C726-39. doi: 10.1152/ajpcell.00003.2006.
- [7] Kim KS, Egan JM, Jang HJ. Denatonium induces secretion of glucagon-like peptide-1 through activation of bitter taste receptor pathways. *Diabetologia*. 2014; 57(10): 2117-25. doi: 10.1007/s00125-014-3326-5.
- [8] Marathe CS, Rayner CK, Jones KL, Horowitz M. Relationships between gastric emptying, postprandial glycemia, and incretin hormones. *Diabetes Care*. 2013; 36(5): 1396-405. doi: 10.2337/dc12-1609.
- [9] Steinert RE, Feinle-Bisset C, Asarian L, Horowitz M, Beglinger C, Geary N. Ghrelin, CCK, GLP-1, and PYY(3-36): Secretory Controls and Physiological Roles in Eating and Glycemia in Health, Obesity, and After

- RYGB. *Physiol Rev.* 2017; 97(1): 411-63. doi: 10.1152/physrev.00031.2014.
- [10] Murphy KG, Bloom SR. Gut hormones and the regulation of energy homeostasis. *Nature.* 2006; 444(7121): 854-9. doi: 10.1038/nature05484.
- [11] Pan WH, Yeh WT. How to define obesity? Evidence-based multiple action points for public awareness, screening, and treatment: an extension of Asian-Pacific recommendations. *Asia Pac J Clin Nutr.* 2008; (3): 370-4.
- [12] Kıskaç M, Soysal P, Smith L, Capar E, Zorlu M. What is the Optimal Body Mass Index Range for Older Adults? *Ann Geriatr Med Res.* 2022; 26(1): 49-57. doi: 10.4235/agmr.22.0012.
- [13] Bae YJ, Shin SJ, Kang HT. Body mass index at baseline directly predicts new-onset diabetes and to a lesser extent incident cardio-cerebrovascular events, but has a J-shaped relationship to all-cause mortality. *BMC Endocr Disord.* 2022; 22(1): 123. doi: 10.1186/s12902-022-01041-3.
- [14] Bai K, Chen X, Song R, Shi W, Shi S. Association of body mass index and waist circumference with type 2 diabetes mellitus in older adults: a cross-sectional study. *BMC Geriatr.* 2022; 22(1): 489. doi:10.1186/s12877-022-03145-w.
- [15] Dietary reference intake for Thais 2020. The Committee on Allowances, Recommended Daily Dietary Nutrition Division, Department of Health, Ministry of Public Health. A.V. Progressive LTD., Bangkok. 2020. (in Thai).
- [16] Carson JAS, Lichtenstein AH, Anderson CAM, Appel LJ, Kris-Etherton PM, Meyer KA, Petersen K, Polonsky T, Van Horn L; American Heart Association Nutrition Committee of the Council on Lifestyle and Cardiometabolic Health; Council on Arteriosclerosis, Thrombosis and Vascular Biology; Council on Cardiovascular and Stroke Nursing; Council on Clinical Cardiology; Council on Peripheral Vascular Disease; and Stroke Council. Dietary Cholesterol and Cardiovascular Risk: A Science Advisory from the American Heart Association. *Circulation.* 2020; 141(3): e39-e53. doi: 10.1161/CIR.0000000000000743.
- [17] Witek K, Wydra K, Filip M. A High-Sugar Diet Consumption, Metabolism and Health Impacts with a Focus on the Development of Substance Use Disorder: A Narrative Review. *Nutrients.* 2022; 14(14): 2940. doi: 10.3390/nu14142940.
- [18] Rezaie P, Bitarafan V, Horowitz M, Feinle-Bisset C. Effects of Bitter Substances on GI Function, Energy Intake and Glycaemia-Do Preclinical Findings Translate to Outcomes in Humans? *Nutrients.* 2021; 13(4): 1317. doi: 10.3390/nu13041317.
- [19] van Gemert WA, Peeters PH, May AM, Doornbos AJH, Elias SG, van der Palen J, Veldhuis W, Stapper M, Schuit JA, Monninkhof EM. Effect of diet with or without exercise on abdominal fat in postmenopausal women - a randomised trial. *BMC Public Health.* 2019; 19(1): 174. doi: 10.1186/s12889-019-6510-1.