



The second-meal effect of *Undaria pinnatifida* sporophylls (mekabu) in healthy young women: An open-label crossover study

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ABSTRACT

Background: Postprandial hyperglycemia is an early indicator of impaired glucose tolerance and an established risk factor for the development of type 2 diabetes mellitus (T2DM). While low-glycemic index (GI) foods and soluble dietary fibers have shown efficacy in modulating postprandial glycemia, their capacity to influence glycemic responses to subsequent meals—referred to as the "second-meal effect"—remains underutilized in dietary interventions.

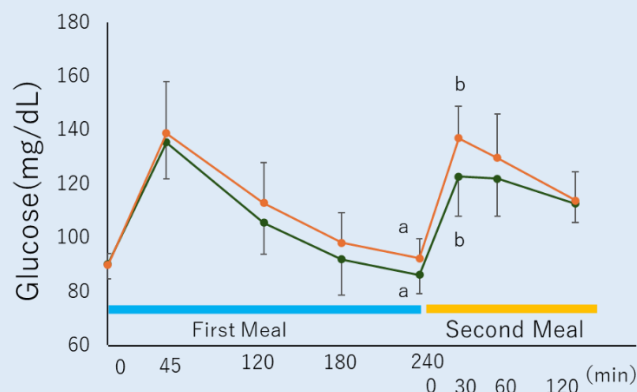
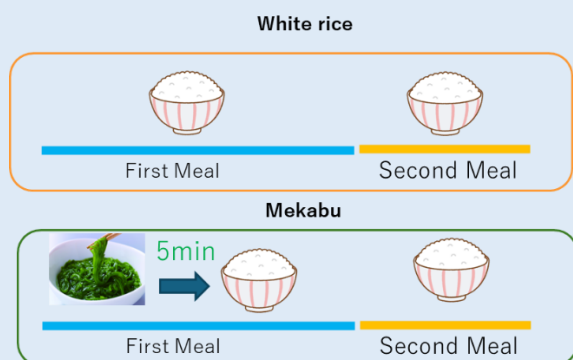
Objective: This study aimed to investigate whether breakfast consumption of *Undaria pinnatifida* (mekabu), a seaweed rich in soluble fiber and sulfated polysaccharides, could attenuate postprandial glycemic response at a subsequent meal in healthy young women.

Methods: An open-label, two-period, crossover study was conducted among healthy female participants. Subjects consumed a test breakfast with or without mekabu, followed by a standardized lunch. Capillary blood glucose levels were measured at multiple time points post-lunch to assess second-meal glycemic modulation.

Results: The findings indicated that mekabu consumption at breakfast significantly reduced postprandial blood glucose levels after lunch, compared to the control condition. These effects may be mediated, at least in part, through delayed gastric emptying and enhanced GLP-1 secretion.

Conclusion: Breakfast intake of mekabu may enhance glycemic stability over successive meals by eliciting a second-meal effect. These findings support the potential utility of mekabu as a functional dietary intervention for the early prevention of T2DM.

Keywords: Mekabu (*Undaria pinnatifida*), Second-meal effect, Soluble dietary fiber, Postprandial glycemia, Glucagon-like peptide-1 (GLP-1), functional foods, bioactive compounds



Graphical Abstract: The Second-Meal Effect of *Undaria pinnatifida* sporophylls (mekabu) in Healthy Young Women: Open-Label crossover design

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INTRODUCTION

Type 2 diabetes mellitus (T2DM) imposes a growing global burden, with an estimated 537 million adults aged 20–79 years affected in 2021, a figure projected to reach 783 million by 2045, and nearly 45% of all cases remaining undiagnosed [1]. Impaired glucose tolerance (IGT), a prediabetic state, is characterized by postprandial hyperglycemia that frequently precedes fasting hyperglycemia, underscoring the pivotal role of early glycemic dysregulation in disease development [2]. Accordingly, dietary strategies that mitigate postprandial glucose excursions are critical for delaying the progression from IGT to overt diabetes [3].

The glycemic index (GI), introduced by Jenkins et al.,

classifies carbohydrate foods according to their postprandial glycemic response [4]. The second-meal effect occurs when the glycemic index (GI) of one meal influences the glycemic response to a subsequent meal [5]. Consumption of low-GI foods slows carbohydrate digestion and absorption, thereby attenuating postprandial glycemia. In addition, the “second-meal effect”, first described by Wolever et al., refers to the modulation of the glycemic response to a subsequent meal by the composition of a prior one, offering a practical approach to maintaining glycemic stability throughout the day [6]. In patients with type 2 diabetes mellitus (T2DM), soluble dietary fibers have been

reported to attenuate postprandial glucose and insulin responses by delaying gastric emptying and reducing the rate of carbohydrate absorption [7]. Despite these benefits, fiber intake remains insufficient in many high-income nations, mainly because of increased consumption of ultra-processed foods (UPFs), which are inherently low in fiber [8]. Notably, even modest increases in dietary fiber intake are associated with substantial reductions in cardiometabolic risk [9]. Certain soluble fibers, including β -glucans and inulin, can also stimulate glucagon-like peptide-1 (GLP-1) secretion, thereby enhancing glucose-dependent insulin secretion, slowing gastric emptying, and promoting satiety [10]. Recent work has further shown that soluble dietary fibers, including seaweed-derived polysaccharides such as alginate and fucoidan, can attenuate postprandial glycemia by increasing viscosity and delaying gastric emptying [11].

Seaweed-derived bioactive compounds, including alginate and fucoidan, have been reported to modulate glucose and lipid metabolism through their functional properties, highlighting their potential as metabolic modulators [12]. As part of the broader functional foods framework, seaweed-derived soluble fibers have attracted growing interest for their potential role in metabolic regulation. Mekabu, the sporophyll of *Undaria pinnatifida*, is a traditional Japanese edible seaweed rich in soluble fiber and sulfated polysaccharides, such as fucoidan. Emerging evidence suggests that mekabu consumption may suppress postprandial glycemic elevation, potentially through GLP-1-mediated mechanisms [13].

However, its influence on glycemic regulation beyond the initial meal—specifically, its potential to

enhance the second-meal effect—has yet to be elucidated. Therefore, the present study aimed to investigate whether mekabu ingestion at breakfast could attenuate postprandial glycemic responses at a subsequent meal. Findings from this study may provide new evidence supporting the use of mekabu as a functional dietary component for the early prevention and management of T2DM.

Subjects and methods:

Subjects: A total of sixteen healthy female university students aged 20 to 22 years were enrolled in this study. All participants had normal fasting blood glucose levels and no history of metabolic or chronic diseases. The body composition of the participants is shown in Table 1. Participants were instructed to refrain from strenuous physical activity on the morning of each test day and to consume only water during the testing period.

Test Foods: The test meals were composed of 150 g of commercially packaged white rice (Sato Foods Co., Ltd., Niigata, Japan) and 40 g of mekabu (Kaneryo Sea Vegetable Corporation, Uto, Kumamoto, Japan) processed with the Takaki Heating and Cooling (THC) System developed by Takaki Shoten Corporation (Uto, Kumamoto, Japan).

The THC System is an innovative electrothermal processing technique in which an electric current is passed through mekabu to heat and sterilize it. Compared with traditional steam-based sterilization, this approach maintains the seaweed's natural green color, distinctive flavor, and crisp texture, while markedly reducing nutrient degradation caused by heat. The proximate composition of the test foods is summarized in Table 1, and the specific dietary fiber profile of mekabu is detailed in Table 2.

Table 1. Composition of test foods.

Categories	Rice	+Mekabu
Weight (g)	150	40
Energy (kcal)	222	6.9
Protein (g)	3.6	0.5
Fat (g)	0.0	0.2
Carbohydrate (g)	50.7	1.1
Dietary fiber (g)	0.45	1.0

Table 2. Dietary fiber content in mekabu. 1 The total dietary fiber content represents the combined amount of water-soluble and insoluble dietary fiber. 2 The total water-soluble dietary fiber is calculated as the sum of alginic acid and fucoidan contents.

Categories	Content (g/40g of raw mekabu)
Total dietary fiber ¹	1.0
Water-soluble dietary fiber ²	0.8
Alginic acid	0.6
Fucoidan	0.2
Insoluble dietary fiber	0.2

Protocol: In this crossover design, the white rice–only meal served as the control condition, and the mekabu + white rice meal served as the intervention condition. The two test days were separated by a 1-week washout period to minimize carryover effects. This study employed an open-label, randomized, two-period crossover design conducted over two separate test days. Participants were instructed to abstain from consuming any food or beverages other than water or unsweetened tea after 11:00 p.m. on the evening before each test session.

On each test day, participants consumed one of the two test breakfasts at 9:00 a.m. In the mekabu condition, 40 g of mekabu was consumed first, followed 5 minutes later by 150 g of white rice. Lunch was provided four hours later, at 1:00 p.m., and consisted of 150 g of white rice only, regardless of the breakfast condition. All meals were consumed within 10 minutes, and mineral water was provided ad libitum throughout the study period.

All measurements were performed using capillary fingertip blood samples. Capillary blood glucose concentrations were measured at the following time points: immediately before breakfast (0 min), and at 45,

90, 120, 180, and 240 minutes after breakfast. Following the lunch meal (at 240 minutes), additional measurements were taken at 270, 300, and 360 minutes (i.e., 30, 60, and 120 minutes post-lunch). All glucose measurements were obtained using a self-monitoring device (Glutest Neo Super; Sanwa Kagaku Kenkyusho Co., Ltd., Nagoya, Japan), and participants performed self-testing under investigator supervision. The Glutest Neo Super device has a measurement accuracy of $\pm 15\%$ in accordance with ISO 15197:2013 standards. Participants remained seated in a resting state in a temperature-controlled room (approximately 24–26°C) throughout all measurement periods. Blood glucose concentrations were expressed in milligrams per deciliter (mg/dL).

Statistical Analysis: Blood glucose concentrations were expressed as changes from baseline (0 min) and denoted as Δ blood glucose levels. The incremental area under the curve (Δ AUC) for postprandial blood glucose was calculated using the trapezoidal rule based on the time-course data. For Δ AUC, a paired t-test was performed between rice only and mekabu + rice. Statistical processing was performed using SPSS Statistics version

28 (IBM, Japan). A two-sided p -value of < 0.05 was considered statistically significant.

All results are presented as means \pm standard deviations (SD). To evaluate the effect of mekabu intake, paired t -tests were performed to compare blood glucose responses between the two test conditions (white rice only vs. mekabu + white rice) at each measurement time point. Similarly, comparisons of Δ AUC values between the two conditions were conducted using paired t -tests.

Ethical considerations: This study was carried out in compliance with the ethical principles of the Declaration of Helsinki (initially adopted in 1964 and most recently revised in October 2013). The research protocol was reviewed and approved by the Ethics Committee of Wayo Women's University (Approval No. 2144; March 2, 2021).

Before participation, all volunteers received both

oral and written explanations regarding the study's objectives, anticipated benefits, and procedures. They were assured that choosing to participate, decline, or withdraw at any time would not result in any disadvantage. The handling and confidentiality of personal information were also described in detail. Only after confirming that each participant had fully understood these points did they provide written informed consent.

RESULTS

Subjects: All sixteen participants completed both phases of the crossover study and were included in the final analysis. The mean age of participants was 21.1 ± 0.2 years, and the mean body mass index (BMI) was 19.6 ± 2.6 kg/m². The average fasting blood glucose concentration at baseline was 91.8 ± 8.5 mg/dL (Table 3).

Table 3. Characteristics of the subjects.

	mean \pm SD
Age (year)	21.1 \pm 0.2
Height (cm)	157.3 \pm 4.6
Weight (kg)	48.7 \pm 7.6
BMI (kg/m ²)	19.6 \pm 2.6
Fasting blood glucose (mg/dL)	91.8 \pm 8.5

Changes in Blood Glucose Levels: Figure 1A shows the time-course changes in blood glucose concentrations after the consumption of breakfast and lunch under the two test conditions. In both the white rice-only and the mekabu + white rice conditions, blood glucose levels increased after breakfast, peaking at 45 minutes and gradually declining thereafter. Following lunch, a secondary rise in blood glucose was observed, peaking approximately 270 minutes later.

Compared with the white rice-only condition, the mekabu + white rice condition demonstrated a consistently lower postprandial glycemic response throughout the observation period. Significant

differences between the two conditions were observed at 240 and 270 minutes ($p < 0.01$; denoted by a and b in Figure 1A).

Figure 1B presents the area under the curve (AUC) for blood glucose concentrations. The AUC after breakfast was significantly higher in the white rice-only condition compared with the mekabu + white rice condition ($p < 0.05$). A similar trend was observed for the second meal, with a lower AUC in the mekabu condition ($p < 0.01$). The total AUC (first + second meals) was also significantly lower following mekabu intake than after white rice alone ($p < 0.05$).

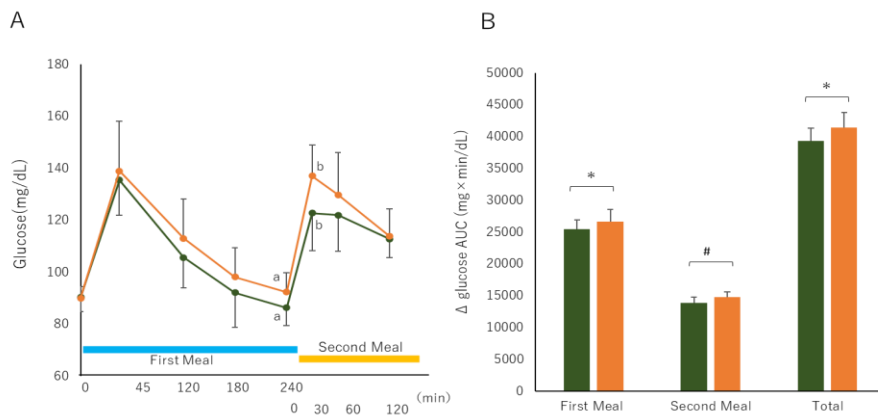


Figure 1 A: Time courses of the plasma glucose concentrations after intake of two different test meals. (Mekabu: green circles, rice: orange circles). A paired t-test analyzed the data. Significant differences were observed in the same alphabet. (a, b $p < 0.01$ respectively). **B:** The value of the plasma glucose concentration time curve after intake of two different test meals. (Mekabu: green bars, rice: orange bars.) Significant differences were observed in the symbols (* $p < 0.05$ # $p < 0.01$, respectively).

Changes in Δ Blood Glucose Levels: Figure 2A illustrates the time-course changes in Δ blood glucose levels after breakfast and lunch under both test conditions. In both the white rice-only and the mekabu + white rice conditions, Δ blood glucose levels increased after breakfast, peaked at 45 minutes, and gradually declined thereafter. A secondary rise was observed after lunch, peaking approximately 270 minutes after lunch.

Compared with the white rice-only condition, the mekabu + white rice condition showed consistently smaller postprandial increases in Δ blood glucose.

Significant differences were observed at 240 and 270 minutes ($p < 0.01$; indicated by a, b in Figure 2A).

Figure 2B presents the incremental area under the curve (ΔAUC) for Δ blood glucose levels. The ΔAUC after the first meal was significantly higher in the white rice-only condition than in the mekabu + white rice condition ($p < 0.05$). The ΔAUC for the second meal also tended to be lower in the mekabu condition ($p < 0.01$). Moreover, the total ΔAUC (sum of the first and second meals) was significantly reduced following mekabu intake compared with white rice alone ($p < 0.05$).

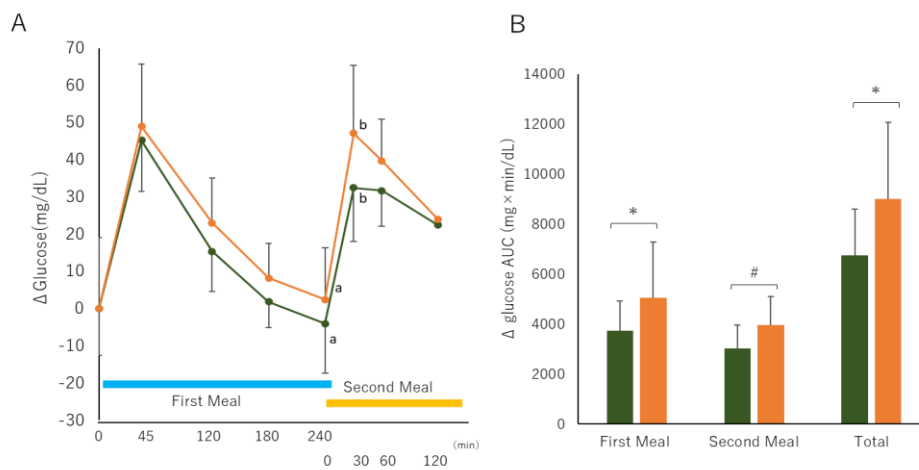


Figure 2 A: Time courses of the Δ plasma glucose concentrations after intake of two different test meals. (Mekabu: green circles, rice: orange circles). A paired t-test analyzed the data. Significant differences were observed in the same alphabet (a, b, $p < 0.01$, respectively). **B:** The value of the Δ plasma glucose concentration time curve after intake of two different test meals. (Mekabu: green bars, rice: orange bars.) Significant differences were observed in the symbols (* $p < 0.05$ # $p < 0.01$, respectively).

DISCUSSION

This study evaluated the potential of *Undaria pinnatifida* sporophylls (mekabu) to modulate postprandial glycemic responses across successive meals, with a focus on the second-meal effect. The results demonstrated that consuming mekabu before white rice significantly attenuated postprandial blood glucose elevations after both breakfast and lunch. Blood glucose and Δ blood glucose levels were significantly lower at 240 and 270 minutes compared with the rice-only condition ($p < 0.01$), and both total AUC and Δ AUC (sum of the first and second meals) were significantly reduced ($p < 0.05$). These findings indicate that mekabu exerts a measurable second-meal effect, contributing to sustained glycemic stability throughout the day.

The second-meal effect describes how the composition of one meal influences metabolic responses to the next [3][14]. Mechanistic explanations include suppression of plasma free fatty acids, improved insulin sensitivity, and modulation of incretin hormones, such as GLP-1 (glucose-dependent insulinotropic polypeptide) and GIP (glucose-dependent insulinotropic polypeptide) [15-16]. Recent evidence indicates that fermentable carbohydrates and the ensuing production of colonic short-chain fatty acids (SCFAs) are central to the second-meal effect, linking prebiotic fiber intake with improved glycemic control [17-18]. This concept is further supported by recent reviews indicating that soluble fibers can elicit a robust second-meal effect across diverse populations and food matrices [19]. This perspective complements classic work on fiber viscosity and glucose regulation by emphasizing that both fermentability (SCFA generation) and rheological properties jointly determine the metabolic benefits of dietary fibers [20-21].

Among soluble fibers, alginate—abundant in Mekabu—increases gastrointestinal viscosity, delays gastric emptying, and slows carbohydrate absorption, which together temper postprandial glycemic excursions;

recent reviews synthesize these mechanisms and human data, although post-2020 trials directly isolating alginate's acute glycemic effects remain limited [20].

Our previous human study showed that Mekabu ingestion enhanced GLP-1 secretion and suppressed postprandial hyperglycemia in healthy adults, supporting an incretin-mediated pathway [13]. In the broader literature since 2020, human interventions with prebiotic/viscous fibers report improved postprandial glycemia and modulation of gut hormones consistent with incretin involvement—even if alginate-specific GLP-1 outcomes are still sparse; for example, recent clinical work demonstrates robust GLP-1 elevations and improved postprandial tolerance after nutrient formulations designed to engage incretin pathways, aligning mechanistically with our findings [22]. Similarly, recent functional food studies have shown that dietary fibers can influence gut hormone secretion, including GLP-1 and PYY. However, the timing and magnitude of these responses vary across fiber types and formulations [23]. SCFAs produced during colonic fermentation are known to stimulate the secretion of GLP-1 and other gut hormones; this mechanism may require longer fermentation times than the time window observed in the present study. SCFAs produced during colonic fermentation are known to stimulate the secretion of GLP-1 and other gut hormones. However, this mechanism likely requires longer fermentation times than the time window of the present study. Recent reviews have further highlighted that gut microbiota and their metabolites play a key regulatory role in GLP-1 secretion and metabolic homeostasis [24]. Therefore, the attenuation of postprandial glycemia observed after Mekabu consumption is more likely explained by its physicochemical properties, such as increased viscosity, delayed gastric emptying, and reduced glucose absorption, rather than rapid SCFA-mediated hormonal responses. Further studies measuring SCFAs and gut

hormones directly are needed to clarify these mechanistic pathways. The broader literature supports this framework, as dietary fiber fermentation and the resulting SCFA production have been recognized as essential contributors to metabolic regulation in humans [25].

These fermentation products have been shown to activate G-protein-coupled receptor 43 (GPR43) on intestinal L-cells, leading to the stimulation of glucagon-like peptide-1 (GLP-1) secretion [26-27]. Activation of this receptor pathway has multiple physiological consequences: GLP-1 enhances glucose-dependent insulin secretion from pancreatic β -cells, delays gastric emptying to moderate nutrient absorption, and suppresses glucagon release, all of which contribute to more stable postprandial glucose homeostasis [26]. Through these coordinated effects, the SCFA-GPR43-GLP-1 signaling axis represents a critical pathway through which dietary polysaccharides, including alginate, exert beneficial metabolic effects. Although the present study did not directly measure GLP-1 concentrations, the attenuated post-lunch glycemic response observed after Mekabu ingestion may indicate a sustained incretin effect initiated by breakfast consumption.

This interpretation is supported by experimental evidence showing that acetate and propionate directly stimulate GLP-1 release via GPR43 signaling in intestinal L-cells, and that this response is markedly reduced in GPR43-deficient mice [27].

Taken together, these findings suggest that Mekabu's glycemic-lowering action may, at least in part, be mediated through enhanced SCFA production and the subsequent activation of the GPR43-GLP-1 pathway in the gut.

Moreover, the timing and order of food ingestion may have contributed to the observed attenuation. In the present study, Mekabu was consumed five minutes before white rice, which likely enhanced gastrointestinal

viscosity and slowed carbohydrate absorption. Recent human trials have more directly supported this concept: for example, consuming vegetables before carbohydrates significantly reduced postprandial glucose and improved GLP-1 levels in individuals with type 2 diabetes in a 2022 study [28]. Additionally, a 2024 crossover study in healthy adults found that consuming vegetables first, then proteins, and carbohydrates last (the "vegetables-first" order) significantly improved glycemic control and insulin sensitivity compared to other orders, consistent with the idea that meal sequencing affects incretin responses [29]. From a nutritional and public health standpoint, incorporating Mekabu into breakfast offers a practical, culturally integrated strategy for maintaining glycemic stability throughout the day. Seaweed-based foods are low in energy density yet rich in soluble fiber, minerals, and bioactive polysaccharides, making them suitable for functional food applications targeting early diabetes prevention [4-5][30]. Epidemiological evidence consistently supports the association between higher seaweed intake and improved cardiometabolic profiles [31].

Nevertheless, limitations should be acknowledged. The small, homogeneous sample (healthy young women) limits external validity, and the lack of biomarker measurements (GLP-1, SCFAs, insulin) precludes mechanistic confirmation. Future studies should include diverse populations, larger sample sizes, and integrate microbiome, hormonal, and metabolic data to confirm causal pathways.

In conclusion, Mekabu intake before carbohydrate-rich meals significantly reduced postprandial blood glucose responses at both breakfast and lunch, demonstrating an apparent, reproducible second-meal effect. This may be mediated by delayed gastric emptying, enhanced GLP-1 secretion, and potential gut hormone responses associated with dietary fiber

fermentation. Mekabu thus represents a traditional, yet scientifically validated, functional food with potential benefits for metabolic health and glycemic regulation.

This study is the first to demonstrate that mekabu ingestion at breakfast produces a measurable second-meal effect in healthy young women, reducing postprandial glycemia at both the first and subsequent meals. By integrating real-world food sequencing with seaweed-derived soluble fibers, this research provides novel evidence on how traditional Japanese foods can modulate glycemic dynamics across consecutive meals. The findings advance our understanding of functional food mechanisms by highlighting the potential role of viscosity-related effects and gut hormone responses in glycemic regulation.

Mekabu is an accessible, culturally integrated food that can be easily incorporated into daily meals, making it a practical strategy for stabilizing postprandial glycemia throughout the day. Consuming mekabu before carbohydrate-rich foods may help reduce post-meal glucose spikes, offering a simple dietary approach for individuals at risk of impaired glucose tolerance or early-stage metabolic dysregulation. These results support the potential use of seaweed-based functional foods in public health and preventive nutrition programs to reduce the burden of type 2 diabetes.

CONCLUSION

This study demonstrated that consuming *Undaria pinnatifida* sporophylls (mekabu) before a carbohydrate-rich meal significantly reduced postprandial blood glucose levels at both breakfast and lunch, indicating an apparent second-meal effect. The effect is likely mediated through delayed gastric emptying, enhanced GLP-1 secretion, and fermentation-derived short-chain fatty acids. Mekabu is a simple, culturally integrated functional food that helps improve glycemic control and support metabolic health.

List of Abbreviations: AUC: Area under the curve, BMI: Body mass index, GLP-1: Glucagon-like peptide-1, GIP: glucose-dependent insulinotropic polypeptide, GPR: G-protein-coupled receptor, SCFA: Short-chain fatty acid, SD: Standard deviation, T2DM: Type 2 diabetes mellitus, GI: Glycemic index

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The authors declare no conflicts of interest related to this work.

Author Contributions: M.T. designed and conducted the study, performed all analyses, interpreted the data, and wrote the manuscript. K.Y., N. H.K., and I contributed to study design, data interpretation, and critical revision of the manuscript. All authors read and approved the final version of the manuscript before submission.

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