

ORIGINAL**Changes in intestinal microbiota and biochemical parameters in patients with inflammatory bowel disease and irritable bowel syndrome induced by the prolonged addition of soluble fibers to usual drug therapy**

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Abstract : Objectives : Partially hydrolyzed guar gum (PHGG) is a soluble dietary fiber ; in addition to improving bowel movements, it maintains intestinal health by producing short-chain fatty acids. However, majority of clinical studies on PHGG have been concluded within a month and excluded usual drug therapy. Hence, this study aimed to determine the effects of long-term consumption of PHGG, in combination with drug therapy, on gut bacteria ratios, laboratory values for inflammatory response, and fecal characteristics. Methods and Results : The study was performed in patients with irritable bowel syndrome (IBS), Crohn's disease (CD), and ulcerative colitis (UC), by the administration of PHGG for six months while they continued their usual treatment. PHGG treatment caused significant changes in patients with IBS, including an increase in the abundance of short-chain fatty acid-producing bacteria, a significant decrease in *Bacteroides* abundance, and normalization of the Bristol scale of stool. In patients with UC, non-significant normalization of soft stools and decrease in fecal calprotectin were observed. Adverse events were not observed in any of the groups. Conclusion : Thus, it would be beneficial to include PHGG in the usual drug therapies of patients with IBS. *J. Med. Invest.* 71 :121-128, February, 2024

Keywords : Partially hydrolyzed guar gum (PHGG), irritable bowel syndrome (IBS), Crohn's disease (CD), ulcerative colitis (UC), short-chain fatty acid-producing bacteria

INTRODUCTION

Inflammatory bowel disease (IBD), including Crohn's disease (CD) and ulcerative colitis (UC), is characterized by chronic inflammation of the digestive tract. It has a high incidence rate in developed countries such as in Western Europe, while the incidence rate is increasing in East Asian countries such as Japan, Korea, and China (1).

The exact etiology of IBD remains unknown due to the complex interplay of genetic, environmental, and immunomodulatory factors. Hou *et al.* (2) reported an increased risk of developing IBD with high fat and meat intake, and a reduced risk with high fiber, fruit, and vegetable intake. This indicates that dietary factors, such as the increasing prevalence of a "western" diet which is high in fats and proteins but low in fruits and vegetables, may be associated with an increase in patients with IBD. These patients may undergo therapeutic interventions, such as 5-aminosalicylic acid preparations, corticosteroids, immunomodulators (azathioprine/mercaptopurine), antibacterial agents and probiotics, biological agents, nutritional therapy, including enteral and total parenteral nutrition, apheresis therapy, and surgical treatment. In dietary therapy, a low-fiber diet is recommended, particularly for patients with IBD and stenosis, because insoluble fibers irritate the intestinal tract and exacerbate

inflammation (3). Meanwhile, soluble fiber is considered an important nutrient for treatment of IBD because it can efficiently make stools more tangible and suppress diarrhea.

Guar gum is a high-molecular weight polysaccharide, consisting of one molecule of galactose for every two molecules of mannose ; it is made from the guar bean (*Cyamopsis tetragonoloba*), an annual legume, and refined from the gumminess of its endosperm (4). Due to its high viscosity, the use of guar gum as a food additive is unfeasible ; however, partially hydrolyzed guar gum (PHGG), which has reduced viscosity, is used as a water-soluble dietary fiber and as a thickening agent in food stabilizers (5). In addition to its use as a food additive, PHGG has also been studied for its pharmacological role as a health-promoting supplement. The consumption of PHGG by healthy volunteers increases the abundance of bifidobacteria in the gut and lowers fecal pH (6). Additionally, PHGG is fermented by bacteria in the colon which promotes the production of short-chain fatty acids (SCFAs), particularly butyric acid (7, 8). Moreover, SCFAs benefit human health by improving the intestinal microbial environment (7).

Thus, it is now presumed that PHGG benefits host health by regulating colon microbiota and producing SCFAs (8).

Clinical studies have reported that PHGG improves the symptoms associated with constipation and the predominant form of diarrhea in irritable bowel syndrome (IBS) (9).

Additionally, PHGG induced relief from symptoms in an animal model of loperamide-induced constipation (10), and has also improved bowel movements in healthy participants, when consumed for six weeks (11). In addition, participants with functional constipation and abdominal discomfort have shown improvement in symptoms after consuming a mixture of PHGG

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and low molecular weight sodium alginate for 4 weeks (9). Furthermore, PHGG significantly reduces colonic mucosal damage when administered to mice with dextran sulfate sodium-induced colitis, a pathological model of UC (12), and is also beneficial in the treatment of colitis (13).

In Japan, several guidelines have been established and effective treatment methods have been proposed for IBS, CD, and UC (14, 15). There are several clinical study reports, wherein PHGG has been administered alone for several weeks to patients with IBS, CD, and UC; however, only a few reports have studied the efficacy and safety of long-term topical supplementation of PHGG along with therapeutic drugs.

Therefore, this intervention study, conducted in patients with IBD and IBS, aimed to determine the effects of long-term consumption of soluble fiber, along with usual medical therapy, on gut bacteria ratios, laboratory values for inflammatory response, and fecal characteristics.

MATERIALS AND METHODS

Materials

The soluble dietary fiber used in this study was a commercial PHGG, SunFiber[®] (Taiyo Kagaku Corporation, Yokkaichi, Japan), obtained from guar gum conditioned with endo-1-4-beta-Galactanase from *Aspergillus niger*, with an average molecular weight of 20 kDa and 80% total dietary fiber content (16).

Research Design

This study was conducted as a single-arm, non-randomized, open-label study at Watanabe Hospital, in accordance with the guidelines set forth in the Declaration of Helsinki, and with the approval of the Tokushima University Ethics Review Committee (approval no. 3545-2). The study participants were patients newly diagnosed with UC, CD, or IBS between September 17, 2020 and March 31, 2022. The patients were being treated for their respective symptoms and were explained the consent form by their physicians at Watanabe Hospital. Written informed consent was obtained from all participating patients and healthy individuals (control group). The study was also registered with the University Hospital Medical Information Network Clinical Trials Registry (UMINCTR : <http://www.umin.ac.jp/ctr/index.htm>) as UMIN Study ID : UMIN000037537.

The study period was a total of six months. Fecal samples were collected from patients prior to PHGG administration and used as the initial control sample. Throughout the clinical trial, participants were instructed to consume 6–18 g of PHGG per day as a single dose or several divided doses, and continue any medications they were prescribed prior to PHGG intake. Stool samples were collected after two, four, and six months of consuming PHGG; blood samples were collected after six months to evaluate the C-reactive protein (CRP) levels, and Crohn's Disease Activity Index (CDAI). Fecal samples were collected using guanidine thiocyanate solution (fecal collection kit; Techno Suruga Lab, Shizuoka, Japan). The following participants were excluded from the study: those who did not provide consent; those who faced difficulty in collecting fecal samples; those with blood-containing stools; those in extremely poor general health due to conditions such as wasting disease; females who were lactating, pregnant, or intending to become pregnant during the study period; those prone to or having obstruction or stricture of the gastrointestinal tract; those with a history of problems with soluble fiber intake; those with limited self-determining capacity (such as in dementia and mental illness); and those who were judged to be ineligible by the responsible study physician.

The intervention was discontinued if the participant

voluntarily stopped taking soluble fiber, if he/she complained of feeling unwell during the study period and the cause was strongly attributable to the intake of soluble fiber, or if the intake of soluble fiber was presumed to affect the therapeutic effects of the intervention. Eventually, this clinical study was conducted with six healthy participants and seven patients each with IBS, CD, and UC. Among the patients studied, IBS was symptomatic and IBD (CD, UC) was in a stable condition with use of drug treatment (Supplement Table 1).

Fecal analysis

The stool samples were subjected to 16S rRNA analysis for intestinal bacteria at Takara Bio Inc. (Shiga, Japan), to determine the proportion of fecal bacteria. Fecal calprotectin levels were determined using fluorescence enzyme immunoassay at BML, Inc. (Tokyo, Japan) by collecting stool samples in F30 test tubes.

In addition, fecal characteristics were assessed using the Bristol Stool Scale as follows:

- Value 1 (hard, columbite, rabbit-feces-like stools);
- Value 2 ("sausage-shaped" but lumpy stools);
- Value 3 (sausage-shaped stools with cracked surface);
- Value 4 (smooth surface and soft sausage-like);
- Value 5 (soft, semi-solid stool with well-defined breaks);
- Value 6 (loose ends, squishy, irregularly shaped small pieces of stool, muddy stool); and
- Value 7 (watery, liquid stools with no solids) (17).

Measurement of blood parameters and assessment of IBD disease activity

Blood samples were collected with BD SSTII (with serum separator) (New Jersey, USA) blood collection tubes, and CRP levels were measured using Beckman Coulter's AU reagent CRP (California, USA). CDAI and Mayo score were evaluated according to previous reports (18, 19).

Evaluation parameters

In this experiment, patients with IBD and IBS, taking usual drug therapy, and healthy subjects, were given PHGG for six months to investigate changes in gut microbiota, blood parameters, and stool properties.

Statistical analyses

In the statistical calculation among multiple groups, when normality is satisfied, we used one-way ANOVA. However, in cases where it isn't satisfied, we utilized the Kruskal-Wallis test.

In the two-group test with correspondence, based on normality and equal variance, we utilized either the paired t-test or the Wilcoxon signed-rank test, and within-group comparisons were done using the Dunnett test.

All statistical analyses were performed using EZR (version 1.55) derived from R software (20). A p value <0.05 was considered statistically significant.

RESULTS

Overall experimental scheme

Characteristics of the study participants are shown in Table 1. Initially, seven healthy participants and eight, nine, and eight patients with IBS, UC, and CD, respectively, were selected. However, after applying the exclusion criteria, six healthy participants and seven patients each with IBS, UC, and CD were selected for the study. All patients with UC and CD were in the stable phase and no acute phase patients were included. None of the participants dropped out during the clinical trial period.

One of the seven patients with IBS and all seven patients

with UC and CD patients had been on drug therapy for at least one month prior to the clinical trial (Supplementary Table 1), and their drug therapy was continued during the PHGG intake period. There were significant differences in age between the groups ($p=0.0262$), the CD patient group being younger; however, there were no significant differences in height, weight, or body mass index between patients of each group and the healthy participants.

Table 1. Patient background

Factor	Normal	IBS	UC	CD	p-value
Number of subjects (male : female)	6 (4 : 2)	7 (6 : 1)	7 (3 : 4)	7 (6 : 1)	0.2607
Age (years)	42.8 ± 11.6	40.7 ± 12.9	49.0 ± 12.2	29.6 ± 7.0	0.0262
Height (cm)	165.8 ± 6.2	169.4 ± 9.1	162.9 ± 7.9	166.9 ± 7.0	0.3990
Weight (kg)	65.2 ± 11.9	73.1 ± 11.6	61.4 ± 9.6	70.3 ± 15.4	0.3210
BMI (kg m ⁻²)	23.5 ± 2.8	25.6 ± 3.7	23.0 ± 2.3	24.7 ± 5.7	0.6240

Each value is represented as mean ± standard deviation (SD). p-values were obtained using one-way analysis of variance (ANOVA), except for sex ratio (obtained using Kruskal–Wallis test). Abbreviations : BMI, body mass index ; IBS, irritable bowel syndrome ; UC, ulcerative colitis ; CD, Crohn’s disease

Changes in the species of intestinal bacteria following PHGG ingestion

We examined the stool samples collected from patients to determine whether PHGG intake altered the number of bacterial species in the intestine (Figure 1). The results showed that there were no significant changes in bacterial counts between the four groups (Normal, IBS, UC, and CD) studied, both before and six months after PHGG intake. In addition, no significant differences were found when the same groups were examined for bacterial counts before and after PHGG administration.

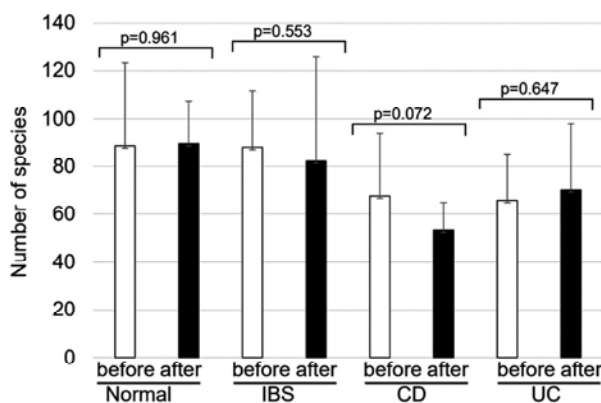


Figure 1. Effect of partially hydrolyzed guar gum (PHGG) on the number of bacterial species.

White bars represent the number of bacteria present in feces before administration of PHGG ; black bars represent the number of bacteria in feces after six months of continuous PHGG administration in four groups of participants (Normal, n = 6 ; IBS, UC, and CD, n = 7). Data are expressed as mean ± standard deviation (SD).

Changes in the alpha diversity of intestinal bacteria following PHGG ingestion

Figure 2 shows the evaluation results of alpha-diversity (Shannon Diversity Index) before and after PHGG intake for each group. Comparing the mean values (Fig. 2, closed circles) in the results, we found that patients in the CD and UC groups had lower Shannon alpha-diversity before PHGG intake, than patients in the healthy and IBS groups. Comparing the change in mean values of the indicators before and six months after PHGG intake, no statistically significant difference was observed in Shannon alpha diversity for all four groups.

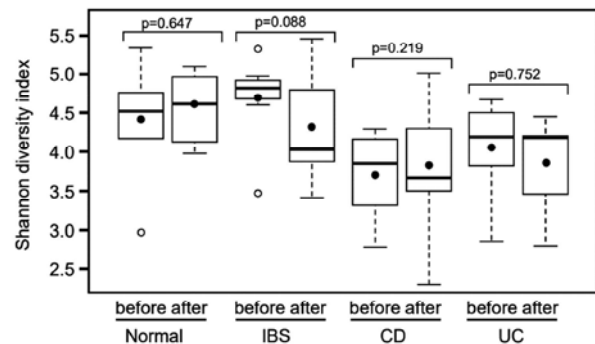


Figure 2. Boxplots of alpha diversity (Shannon Diversity Index) in four groups of participants before and six months after PHGG treatment.

Boxes represent the interquartile range between the first and third quartiles (25th and 75th percentiles); horizontal line inside the box defines the median; open circles represent outliers and closed circles indicate average.

The average alpha diversity for each group was not significantly different among patients treated with PHGG.

Changes in the proportion of bacteria at the phylum level

At the phylum level, bacteria constituting the human intestinal flora are classified into the following four main groups : Firmicutes, Bacteroidetes, Actinobacteria, and Proteobacteria (21). We examined whether the ratio of bacteria at the phylum level was altered by the ingestion of PHGG. As shown in Figure 3, the three major genera—Actinobacteria (Figure 3A), Bacteroidetes (Figure 3B), and Firmicutes (Figure 3C)—compose approximately 90% of the total intestinal bacteria. No statistically significant differences were recorded in phylum-level bacterial abundance between pre-and post-PHGG administration in both healthy participants and patient groups (IBS, UC, and CD). However, a comparative analysis of before and after PHGG administration within the same group revealed that the IBS group showed a significant decrease in Bacteroidetes abundance ($p=0.0055$) after PHGG ingestion, but the abundance of other bacteria were unchanged.

Changes in the ratio of SCFA-producing bacteria

PHGG intake increases the abundance of SCFA-producing bacteria (8, 22). Hence, in this clinical study, we investigated changes in the proportion of the genera containing representative SCFA-producing bacteria—such as Bifidobacterium (23), Eubacterium (23), Faecalibacterium (24), Lactobacillus (24), Roseburia (23), and Ruminococcus (23)— before and after PHGG administration (Figure 4). A significant increase in the percentage of SCFA-producing bacteria was observed in the IBS group after six months of oral PHGG ingestion ($p=0.025$). On the contrary,

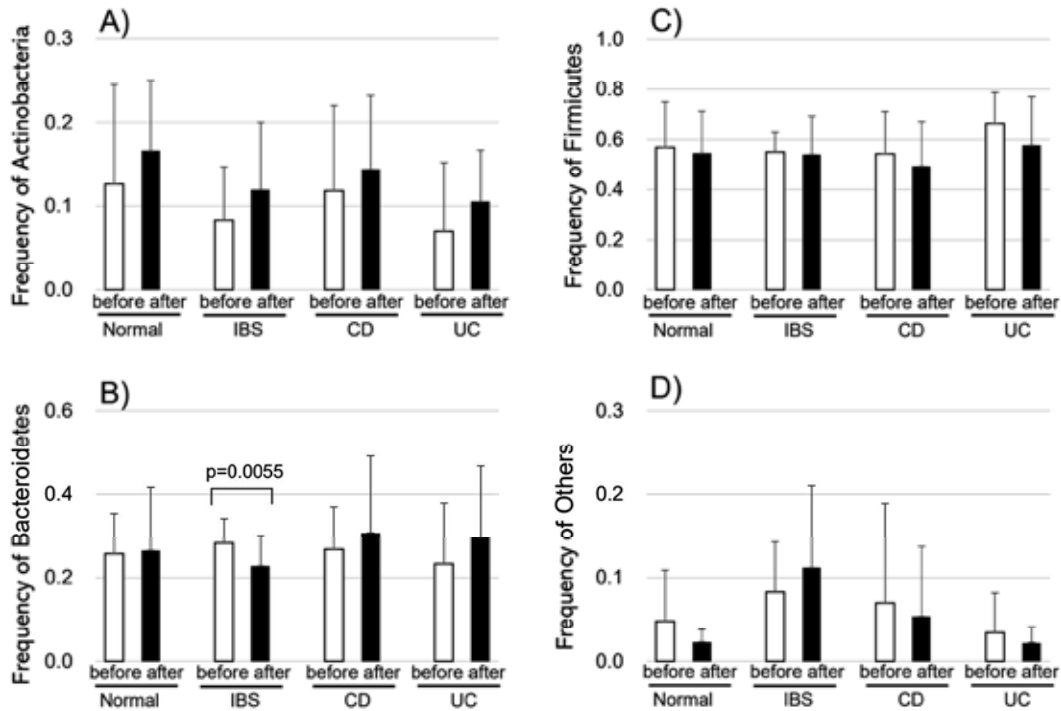


Figure 3. Effect of PHGG on the ratio of Phylum classification. White bars represent the frequency of each phylum bacteria present in feces before administration of PHGG; black bars represent the frequency of each phylum bacteria in feces after six months of continuous PHGG administration in four groups of participants (Normal, $n = 6$; IBS, UC, and CD, $n = 7$). A; *Actinobacteria*, B; *Bacteroidetes*, C; *Firmicutes* and D; remaining Phylum bacteria. Data are expressed as mean \pm SD.

no change was observed in healthy participants and patients with UC and CD.

Changes in the levels of CRP, CDAI, Mayo score, and fecal calprotectin

The Mayo sub-score (19) for patients with UC, and the CDAI (25) for patients with CD, were used to evaluate the pathophysiology of patients with IBD. In addition, inflammatory response markers in the body, such as CRP and fecal calprotectin (26), an inflammatory marker indicating gastrointestinal inflammation, have also been used empirically in recent times (27). We examined changes in these values and found no significant changes in

CRP values before and after PHGG intake in patients with UC and CD (Table 2). Similarly, no significant differences in CDAI or Mayo scores were observed in patients with CD and UC, before and after PHGG administration. Fecal calprotectin levels were not significantly altered by PHGG intake in both UC and CD patient groups.

Table 2. Changes in C-reactive protein (CRP) levels, Crohn's Disease Activity Index (CDAI), Mayo score, and fecal calprotectin levels after six months of PHGG administration

		Period		p-value
		Before	After	
CRP	UC	0.28 \pm 0.55	0.08 \pm 0.04	0.752
	CD	0.34 \pm 0.40	0.45 \pm 0.60	0.675
CDAI	CD	52 \pm 23	64 \pm 33	0.295
Mayo score	UC	0.86 \pm 1.07	0.57 \pm 0.53	0.356
Fecal calprotectin (mg/kg)	UC	284	201	0.219
	CD	37	58	0.469

Data are expressed as mean \pm SD (healthy participants group, $n = 6$; IBS, UC, and CD groups, $n = 7$) for CRP, CDAI, Mayo score, and median value ($n = 7$) for fecal calprotectin. The p-value was obtained using paired t-test (for CRP, CDAI and Mayo score) and paired Wilcoxon signed-rank sum test (for fecal calprotectin). Abbreviations: UC, ulcerative colitis; CD, Crohn's disease

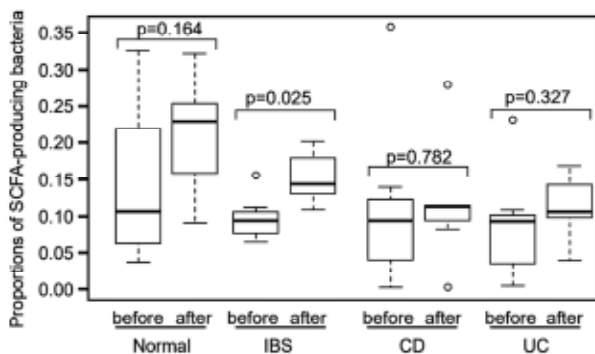


Figure 4. Boxplots for the proportion of genera containing short-chain fatty acid-producing bacteria among the four groups of participants, before and six months after PHGG treatment. Boxes represent the interquartile ranges between the first and third quartiles (25th and 75th percentiles); horizontal line inside the box defines median; open circles represent outline.

Frequency of defecation and change in stool classification

Since PHGG ingestion improves gastrointestinal function (17, 28), we examined whether this effect exists after six months of PHGG ingestion, using the Bristol scale and frequency of defeca-

tion. The frequency of defecation decreased insignificantly in patients with IBS ($p=0.089$), whereas it was unchanged in healthy individuals and patients with CD and UC (Table 3).

As evaluated using the Bristol Scale, stool properties did not change with PHGG administration in healthy participants and patients with CD and UC, while a significant change from soft to normal stools (5.8 to 4.4 ; $p=0.0034$) was observed in patients with IBS.

Table 3. Changes in (a) defecation frequency and (b) Bristol scale value after six-month PHGG administration

		Period		p-value
		Before	After	
a) Fecal defecation frequency	Normal	1.08 ± 0.20	1.08 ± 0.20	NA
	IBS	1.79 ± 1.11	1.14 ± 0.63	0.089
	UC	1.86 ± 1.21	1.71 ± 1.22	0.586
	CD	1.93 ± 0.98	1.93 ± 0.978	NA
b) Bristol scale value	Normal	4.0 ± 0.6	4.0 ± 0.0	1.000
	IBS	5.8 ± 0.3	4.4 ± 0.8	0.034
	UC	4.7 ± 0.8	4.1 ± 0.4	0.089
	CD	4.9 ± 0.4	4.9 ± 0.4	NA

Data are expressed as mean \pm SD (healthy participants group, $n = 6$; IBS, UC, and CD groups, $n = 7$), p-value was obtained using paired t-test. Abbreviations: IBS, irritable bowel syndrome; UC, ulcerative colitis; CD, Crohn's disease; NA, not applicable

DISCUSSION

This study aimed to determine the effects of prolonged consumption of soluble fibers, in addition to ongoing medical therapy, in patients with CD, IBS, and UC. The present study showed that PHGG treatment for six months significantly affected patients with IBS; the observed changes include an increase in the abundance of SCFA-producing bacteria and a decrease in the frequency of defecation. In the IBS group, the Bristol scale of stool was significantly normalized; it tended towards normalization in the UC group.

The ameliorative effects of PHGG on IBD, which includes conditions such as CD (8), UC (29), and IBS (30, 31), are well demonstrated in animal experimental models. In 1994, a study in nine healthy Japanese men who were administered soluble dietary fiber (7 g at each meal for 2 weeks) reported that the percentage of fecal bifidobacterial increased with fiber intake, but returned to normal when the intake was stopped (6). Subsequent studies have been conducted on the changes in intestinal microflora with the consumption of PHGG. However, majority of the clinical trials have been conducted with PHGG administration for a few weeks; only few studies have reported on the efficacy and safety of PHGG consumed for as long as six months.

Therefore, in this intervention study, we instructed the enrolled patients with IBD and IBS to consume PHGG for six months along with their usual drug therapy. The patients were evaluated for changes in intestinal bacteria, effects on the blood biochemical test values, Bristol scale, and frequency of defecation.

In this study, patients with CD and UC showed lower bacterial counts than those in healthy participants, before PHGG ingestion.

This may reflect the reduced diversity in the bacterial population under IBD condition (32).

In all the groups, including control, no change was observed

in the number of bacteria before or six months after PHGG administration; similar results have been reported in animal models (12).

In this study, all patients with UC and CD were taking 5-amino-2-hydroxybenzoic acid (Supplement Table 1), which is known to affect intestinal bacteria (33, 34). Therefore, it is necessary to consider the effect of this drug on bacterial growth. No clear difference was observed in the groups (Figure 2). Previous reports have indicated contradictory results, such as increased (8, 35) or decreased (36) bacterial diversity. Further studies are needed to clarify this association.

Firmicutes and *Bacteroidetes* are known to be the primary intestinal bacteria species at the phylum level (32, 37); our observations in all groups receiving PHGG in the present study corroborated this finding.

The abundances of *Firmicutes* and *Bacteroidetes* decrease, while those of *Actinobacteria* and *Proteobacteria* increase in IBD (38); however, no such propensity was observed in our study.

This may partially be because of the administration of 5-amino-2-hydroxybenzoic acid to all patients with UC and CD, which affects the distribution of bacterial species (32). In contrast, a comparative analysis of before and after PHGG ingestion showed a significant decrease in the abundance of *Bacteroidetes*, particularly in the IBS group ($p < 0.01$).

SCFAs are organic acids produced by intestinal bacteria when they break down dietary fiber; in the human gut, these include acetic, propionic, and butyric acids. The administration of an SCFA mixture, through enema, to patients with active UC improved their condition (39). These acids also contribute to the homeostasis of regulatory T cells and suppress intestinal inflammation (40). Recently, SCFAs generated in the gastrointestinal tract have been shown to improve systemic glycolipid metabolism (41), inhibit the onset and progression of colon cancer (42), maintain immune homeostasis (43), and exhibit anti-inflammatory effects (44). Thus, SCFAs are considered to be beneficial in maintaining homeostasis.

Compared to other dietary fibers, PHGG is easily fermented by intestinal bacteria, producing higher amounts of SCFAs (7). Reider *et al.* (45) reported that PHGG administration to healthy participants at 5–15 g/day for 3 weeks transiently and significantly increased SCFA levels during the first 1–2 weeks. However, since the long-term effect of PHGG intake on the ratio of SCFA-producing bacteria was unknown, in this study, we examined the effect of administering PHGG for six months. We observed an increase in the abundance of SCFA-producing bacteria in all the study groups; particularly, in the IBS group. Thus, it was speculated that the increased SCFA production was maintained even with the prolonged administration of PHGG.

There were no significant changes in CRP levels caused by PHGG intake in patients with UC and CD in this study; this could be because CRP levels increase in highly inflammatory conditions such as IBDs (46); the cases examined in this experiment were all in the stable phase, hence, a considerable change in CRP levels was not observed.

PHGG effectively improves diarrhea induced by enteral nutrition (28), and is effective in constipation, for normalizing defecation frequency (47); this is consistent with our results that defecation frequency was reduced in patients with IBS.

Similarly, the Bristol Scale results showed that PHGG intake normalized soft stools in patients with IBS (Bristol Scale: 5.8 ± 0.3 to 4.4 ± 0.8 ; $p=0.0034$) and UC (4.7 ± 0.8 to 4.1 ± 0.4 ; $p=0.089$), respectively (Table 3). These results indicate that the effects of PHGG on the normalization of stools were sustained even after long-term use of PHGG. In the present study, participants were asked to consume 6–18 g of PHGG per day to ensure no difficulty in consumption of PHGG. Therefore, it cannot be denied that

differences in intake could have affected the rigorous evaluation of the effects of PHGG in this study. Further investigations on the effects of PHGG on clinical parameters would require rigorous control of its intake by participating patients.

CONCLUSION

In this study, we evaluated the efficacy of prolonged PHGG use in patients with IBS, CD, and UC undergoing drug therapy. In IBS patients, PHGG intake significantly improved the Bristol scale from loose stools to normal stools. SCFA production was also shown to significantly increase in patients with IBS. These results suggest that sub-chronic PHGG intake can particularly be effective in patients with IBS already receiving drug therapy.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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AUTHOR CONTRIBUTIONS

Contributions to the submitted work from each author : H.W. conceived the study ; K.T., L.M., and H.W. designed and supervised the study ; T.I., Y.O., K.M., and M.T. contributed to the experiments ; H.W., T.I., and K.T. contributed to the discussion ; K.T. prepared the tables and figures ; K.T. wrote the manuscript.

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Supplemet Table1. Patient background

Group	No.	Sex	Age	Height (cm)	Weight (kg)	BMI (kg m ⁻²)	Medication (/day)	Patient education	
Normal	1	M	51	165	60	22.0	None		
	2	M	54	174	82	27.1	None		
	3	M	26	168	62.4	22.1	None		
	4	M	50	168	72	25.5	None		
	5	F	45	165	68	25.0	None		
	6	F	31	155	47	19.6	None		
IBS	1	M	32	161	74	28.5	None		
	2	M	56	177	67	21.4	None		
	3	M	36	180	73	22.5	None	Physical activity and food ntake recommendation	
	4	M	43	165	73	26.8	None		
	5	F	27	155	56	23.3	None		
	6	M	31	173	95	31.7	Polycarbophil Calcium 3.0 g		
	7	M	60	173	73.4	24.5	Ramosetron Hydrochloride 10 µg Polycarbophil Calcium 3 g Bifidobacterium 36 mg Loperamide Hydrochloride 1 mg		
UC	1	F	45	161	67.7	26.1	Mesalazine 4800 mg Clostridium butyricum 60 mg		
	2	M	66	164	63	23.4	Salazosulfapyridine 1000 mg		
	3	F	41	165	61	22.4	Mesalazine 4000 mg		
	4	F	37	160	62	24.2	Salazosulfapyridine 3000 mg		
	5	M	51	173	73	24.4	Mesalazine 4000 mg Clostridium butyricum 60 mg		
	6	M	38	169	61	21.4	Mesalazine 4000 mg Clostridium butyricum 60 mg		
	7	F	65	148	42	19.2	Mesalazine 2000 mg Clostridium butyricum 40 mg Magnesium Oxide 500 mg		
CD	1	M	23	170	64	22.1	Mesalazine 2000 mg Ustekinumab 90 mg (every 12 wks)		
	2	M	23	175	67	21.9	Mesalazine 2000 mg Adalimumab 40 mg (every 2 wks)		
	3	M	41	163	70.3	26.5	Mesalazine 2000 mg Clostridium butyricum 40 mg Infliximab 200 mg (every 8 wks)		
	4	F	30	157	55	22.3	Mesalazine 3000 mg Ustekinumab 90 mg (every 8-12 wks)		
	5	M	23	176	57	18.4	Mesalazine 3000 mg Clostridium butyricum 120 mg Infliximab 290 mg (every 8 wks)		
	6	M	34	167	100.5	36.0	Mesalazine 3000 mg Clostridium butyricum 120 mg Infliximab 500 mg (every 8 wks)		
	7	M	33	174	78	25.8	Mesalazine 1500 mg Infliximab 400 mg (every 8 wks)		

IBS, irritable bowel syndrome ; UC, ulcerative colitis ; CD, Crohn's disease ; M, male ; F, female