

Open

Prune Juice Containing Sorbitol, Pectin, and Polyphenol Ameliorates Subjective Complaints and Hard Feces While Normalizing Stool in Chronic Constipation: A Randomized Placebo-Controlled Trial

Taishi Koyama, MS^{1*}, Naoyoshi Nagata, MD, PhD^{2*}, Kengo Nishiura, BS³, Naoki Miura, MD⁴, Takashi Kawai, MD, PhD² and Hiroataka Yamamoto, PhD¹

INTRODUCTION: The aim of this study was to determine the effectiveness of prune juice on chronic constipation.

METHODS: We conducted a double-blind, randomized, placebo-controlled trial in Japanese subjects with chronic constipation.

RESULTS: Prune intake significantly decreased hard and lumpy stools while increasing normal stool and not increasing loose and watery stools. Prune intake also ameliorated subjective complaints of constipation and hard stools, without alteration of flatulence, diarrhea, loose stools, or urgent need for defecation. There were no adverse events or laboratory abnormalities of liver or renal function after prune intake.

DISCUSSION: Prune juice exerted an effective and safe natural food therapy for chronic constipation.

Am J Gastroenterol 2022;117:1714–1717. <https://doi.org/10.14309/ajg.000000000001931>

INTRODUCTION

There are a wide variety of laxatives available for chronic constipation treatment, but they have several problems, including side effects and insufficient efficacy (1,2). Instead of drug treatment, there has been increasing recognition of natural food treatment, which is beneficial in its safety and prevalence (3). Among natural foods, prune potentially exerts an ameliorating effect on constipation (4,5), but little data are available on the effectiveness in chronic constipation subjects or on side effects such as abdominal discomfort or diarrhea symptoms. We aimed to evaluate the effects of prune juice consumption on stool consistency and subjective complaints of constipation symptoms in Japanese subjects with chronic constipation.

METHODS

This study was conducted in accordance with the Declaration of Helsinki with the approval of the institutional review boards of the Miura Clinic (approval number: R2001) and Tokyo Medical University (approval number: T2021-0243). Written informed consent was obtained from all subjects before their enrollment into this study.

This study included subjects aged 20–75 years who presented symptoms of treatment-naïve chronic constipation. The criterion for chronic constipation was defined according to Rome IV as fewer than 3 bowel movements per week and/or hard stool defined by the Bristol Stool Form Scale (BSFS) 1 or 2, for the past 3 months,

with symptom onset at least 6 months earlier (6). Subjects were randomly assigned to the prune juice group or placebo group and consumed 54 g of each test food in a day for 8 weeks. The placebo is designed to match the flavor, color, and taste of prune juice (see Table 1, Supplementary Digital Content, <http://links.lww.com/AJG/C620>). Stool consistency by BSFS (7) and subjective complaints by the Gastrointestinal Symptom Rating Scale (GSRS) (8) were assessed for constipation improvement. Stool consistency was recorded at each bowel movement and analyzed as the rate of each score in every week throughout the study period. GSRS was measured at baseline, 4 weeks, and 8 weeks after starting intake. Subjects reported any adverse events (AEs) during the study period. Laboratory parameters were assessed by blood and urine tests at baseline and in the postintake period. The severity of AEs or laboratory abnormalities was evaluated according to the definition by the Common Terminology Criteria for Adverse Events, version 5.0 (9) (ClinicalTrials.gov number, University hospital Medical Information Network Identify Document: 000041384). Detailed methods are provided in Methods (see Supplementary Digital Content, <http://links.lww.com/AJG/C621>).

RESULTS

A total of 84 subjects were enrolled and included in the intention-to-treat analysis (see Figure 1, Supplementary Digital

¹Institute for Health Science, MIKI Corporation, Hyogo, Japan; ²Department of Gastroenterological Endoscopy, Tokyo Medical University, Japan; ³Department of Rehabilitation, Fujita Health University Hospital, Aichi, Japan; ⁴Miura Clinic, Medical Corporation Kanonkai, Osaka, Japan. **Correspondence:** Naoyoshi Nagata, MD, PhD. E-mail: nnagata_ncgm@yahoo.co.jp. Hiroataka Yamamoto, PhD. E-mail: hyamamoto@miki prune.co.jp.

*Taishi Koyama and Naoyoshi Nagata contributed equally to this work as first author.

Received April 22, 2022; accepted July 6, 2022; published online August 12, 2022

Table 1. Baseline characteristics, adverse events, and laboratory abnormalities

	Placebo (n = 42)	Prune juice (n = 41 ^a or 42)	P value
Baseline characteristics			
Age (yr)	50.5 ± 10.5	50.8 ± 11.1	0.904
Sex, female, n (%)	31 (73.8%)	32 (76.2%)	0.801
Height (cm)	159.5 ± 7.3	160.8 ± 8.2	0.472
Weight (kg)	55.7 ± 8.3	55.0 ± 9.3	0.540
BMI (kg/m ²)	21.8 ± 2.5	21.2 ± 2.5	0.241
Current smoker, n (%)	3 (7.1%)	3 (7.1%)	1.000
Alcohol drinker, n (%)	19 (45.2%)	15 (35.7%)	0.374
Food frequency and rice ^b	5.40 ± 0.96	5.07 ± 1.24	0.245
Food frequency and breads ^b	4.14 ± 1.14	4.10 ± 1.25	0.980
Food frequency and vegetables ^b	4.48 ± 1.57	3.88 ± 1.76	0.105
Food frequency and fruits ^b	3.00 ± 1.36	2.90 ± 1.25	0.904
Food frequency and meats ^b	3.95 ± 1.01	3.83 ± 1.08	0.589
Food frequency, cheese, and yogurt ^b	2.90 ± 1.25	2.74 ± 1.25	0.476
Food frequency and natto ^b	1.90 ± 0.93	2.29 ± 1.02	0.091
Food frequency, soy sauce, and miso ^b	3.98 ± 1.33	3.95 ± 1.31	0.786
Food frequency and pickles ^b	1.98 ± 0.84	2.38 ± 1.21	0.135
Adverse events ^c			
Nausea, ≥grade 3	0 (0.0%)	0 (0.0%)	—
Headache, ≥grade 3	0 (0.0%)	0 (0.0%)	—
Dizziness, ≥grade 3	0 (0.0%)	0 (0.0%)	—
Laboratory abnormalities ^d			
Increased AST, ≥grade 3	0 (0.0%)	0 (0.0%)	—
Increased ALT, ≥grade 3	0 (0.0%)	0 (0.0%)	—
Increased ALP, ≥grade 3	0 (0.0%)	0 (0.0%)	—
Increased γ-GTP, ≥grade 3	0 (0.0%)	0 (0.0%)	—
Increased creatinine, ≥grade 3	0 (0.0%)	0 (0.0%)	—
Proteinuria, ≥grade 3	0 (0.0%)	0 (0.0%)	—
Glucosuria, ≥grade 3	0 (0.0%)	0 (0.0%)	—

Data are expressed as n (%) or mean ± SD. The severity of the adverse events or laboratory abnormalities was graded as grade 1 (mild), grade 2 (moderate), grade 3 (severe), or grade 4 (life-threatening consequences) according to the definition by the CTCAE, version 5.0.

ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; CTCAE, Common Terminology Criteria for Adverse Events; γ-GTP, γ-glutamyl transpeptidase.

^aOne subject withdrew from the postintake laboratory test.

^bFood frequencies were assessed using a 7-point Likert scale (1, never or rarely; 2, 1 to 3 times/month; 3, 1 to 3 times/week; 4, four to six times/week; 5, once/day; 6, twice/day; and 7, 3 or more times/day) for typical eating patterns in the previous month.

^cAdverse events were reported at lower grades. The number of cases with mild/moderate symptoms (grade 1/2) is as follows: nausea (1/0, 0/0), headache (2/0, 2/0), and dizziness (1/0, 0/0) for placebo and prune juice groups, respectively.

^dThe number of cases with mild/moderate symptoms (grade 1/2) is as follows: increased AST (1/0, 1/0), increased ALT (4/0, 2/0), increased ALP (1/0, 3/0), increased γ-GTP (1/0, 0/0), increased creatinine (0/0, 2/0), proteinuria (2/0, 0/0), and glucosuria (0/0, 0/0) for placebo and prune juice groups, respectively.

Content, <http://links.lww.com/AJG/C619>). There were no significant differences in baseline characteristics (Table 1) including age, sex, body mass index, dietary habits, BSFS score (Figure 1), and bowel symptoms (Table 2) between the groups. In the prune juice group, the rates of hard and lumpy stools (BSFS 1 or 2) were significantly decreased from baseline and were significantly lower than the placebo group after 3 weeks (Figure 1). The rates of normal stools (BSFS 3 or 4) were

significantly increased from baseline and were significantly higher than the placebo group after 3 weeks. The rates of loose and watery stools (BSFS 5, 6, or 7) were not significantly changed during the study period.

Next, we focused on alterations of subjective complaints using GSRS scores after prune juice intake. In the prune juice group, constipation, hard stools, incomplete evacuation, and flatulence scores significantly decreased at week 4 or 8 (Table 2). Prune juice

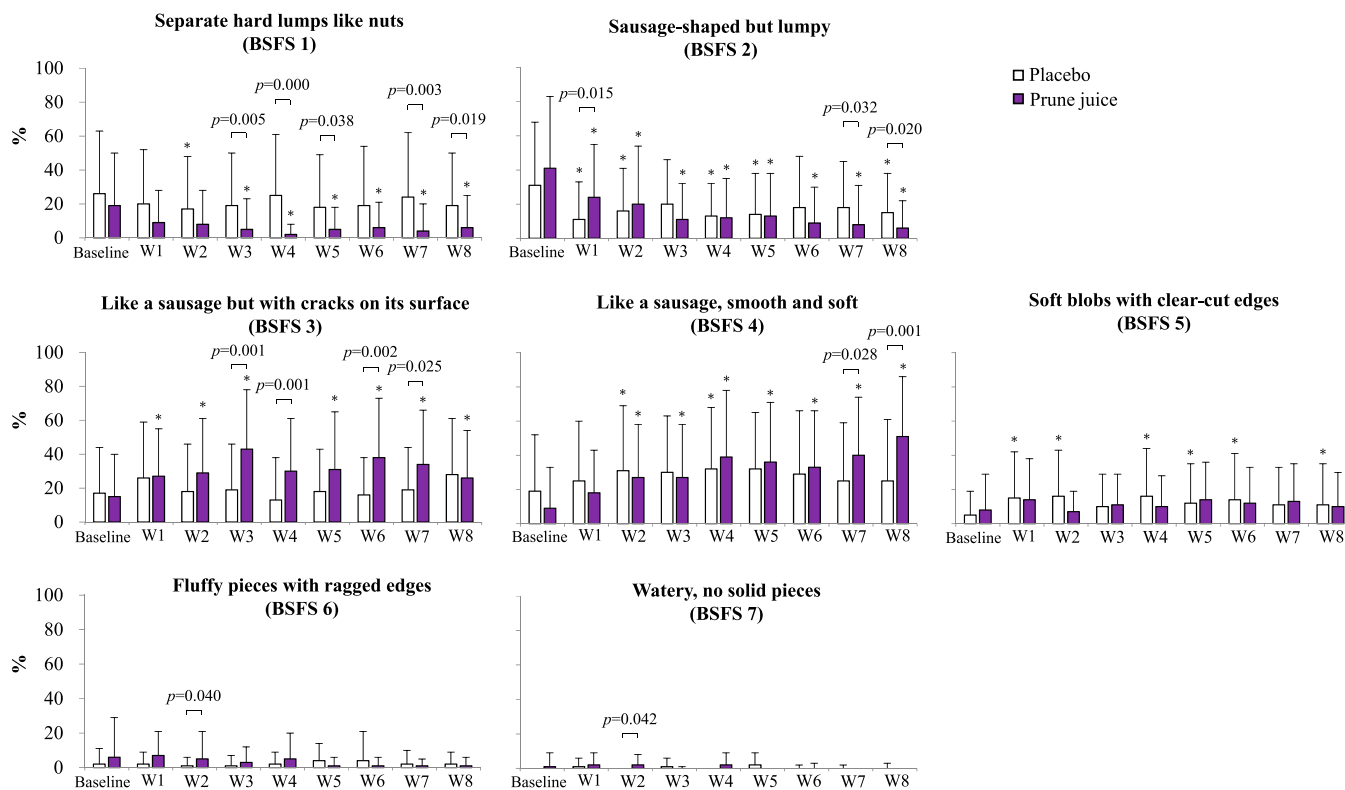


Figure 1. Rates of each BSFS score at baseline and after intake period. Subjects recorded BSFS scores at each bowel movement. Rates of each BSFS score compared with total bowel movements within 1 week were calculated at baseline and after an 8-week intake period (W1–W8). Data are expressed as mean value. Error bars represent SD. $n = 42$ in each group. P values in the graph field represent significant differences between the groups. * $P < 0.05$ compared with baseline. BSFS, Bristol Stool Form Scale.

intake showed significant differences in constipation and hard stools from the placebo group at week 8. Meanwhile, diarrhea, loose stools, and urgent need for defecation scores were not significantly changed from baseline. During the study period, there were no AEs or laboratory abnormalities of liver or renal function based on the Common Terminology Criteria for Adverse Events definition between baseline and postintake period in either group (Table 1).

DISCUSSION

Notably, BSFS 1 (hard stool) rates significantly decreased after 3 weeks, whereas BSFS 4 (normal stool) rates significantly increased after 7 weeks of prune juice intake compared with placebo (Figure 1). Although a previous study has also shown a significant increase in the mean BSFS after prune intake in chronic constipation (4,5), it has not focused on alteration of each BSFS score. Importantly, the persistence of BSFS 4 was reported to be significantly correlated with the quality of life (10). Previous studies focusing on constipation and prune intake have limited evaluation to study periods ≤ 4 weeks (4,5). Collectively, our study underlies that it is important to improve stool shape in ≤ 4 weeks, but that quality of life determination should take place after at least 8 weeks.

One issue for prune intake that should be raised is its tendency to cause diarrhea and flatulence (11,12). In our study, frequency of loose and watery stools (BSFS 5, 6, or 7) was not altered by prune juice intake (Figure 1). More importantly, we evaluated subjective complaints using GSRS (Table 2), not assessed in

previous studies, and found that prune juice substantially decreased constipation and hard stools without alteration of flatulence, diarrhea, or other bowel discomfort compared with placebo. Furthermore, the safety assessment showed that prune juice intake did not cause AEs or laboratory abnormalities of liver function or renal function (Table 1). These data suggest that prune juice could be used continuously and safely by those with chronic constipation.

The prune juice used in this study contained abundant sorbitol (see Table 1, Supplementary Digital Content, <http://links.lww.com/AJG/C620>), which has been reported to improve constipation (13). In addition, the prune juice contained dietary fiber, especially pectin, and polyphenols, both of which have been reported to improve constipation (14,15). Accordingly, it was supposed that the observed effects of ameliorating constipation by prune juice were mainly because of the combination of sorbitol, pectin, and polyphenol.

One limitation of our study is that we did not score the emergence of bloating, which was considered a frequent AE of prune juice (5). However, no subjects reported bloating, although subjects were asked about changes in physical condition during the study period.

In conclusion, our study demonstrated that prune juice ameliorates both stool forms and subjective complaints of constipation symptoms, without any abdominal discomfort, in patients with chronic constipation. Our data emphasize the effectiveness of prune juice intake for chronic constipation,

Table 2. Subjective evaluation of gastrointestinal symptom-related QOL by a GSRS questionnaire at baseline and changes from baseline during the intake period (week 4 and 8)

	Placebo (n = 42)	Prune juice (n = 42)	P value
Flatulence			
Baseline	2.93 ± 1.11	3.02 ± 1.24	0.801
Δ4w	-0.36 ± 1.21	-0.48 ± 1.35 ^a	0.480
Δ8w	-0.38 ± 1.13 ^a	-0.43 ± 1.36	0.982
Constipation			
Baseline	4.50 ± 0.99	4.74 ± 1.01	0.490
Δ4w	-1.24 ± 1.41 ^a	-1.62 ± 1.36 ^a	0.163
Δ8w	-1.43 ± 1.56 ^a	-2.24 ± 1.41 ^a	0.024
Diarrhea			
Baseline	1.55 ± 0.80	1.57 ± 0.83	0.826
Δ4w	0.14 ± 1.20	0.07 ± 1.09	0.914
Δ8w	0.05 ± 0.94	-0.05 ± 1.08	0.741
Loose stools			
Baseline	1.64 ± 0.91	1.48 ± 0.59	0.714
Δ4w	-0.02 ± 1.00	0.21 ± 0.90	0.352
Δ8w	0.02 ± 0.87	0.26 ± 0.91	0.412
Hard stools			
Baseline	4.33 ± 1.37	4.81 ± 1.13	0.172
Δ4w	-1.26 ± 1.58 ^a	-1.83 ± 1.32 ^a	0.082
Δ8w	-1.33 ± 1.71 ^a	-2.31 ± 1.30 ^a	0.009
Urgent need for defecation			
Baseline	2.38 ± 1.13	2.33 ± 1.32	0.643
Δ4w	0.05 ± 1.38	-0.10 ± 1.74	0.934
Δ8w	-0.26 ± 1.15	-0.21 ± 1.57	0.703
Incomplete evacuation			
Baseline	4.24 ± 1.49	4.36 ± 1.36	0.938
Δ4w	-1.12 ± 1.70 ^a	-1.48 ± 1.47 ^a	0.219
Δ8w	-1.45 ± 1.56 ^a	-1.81 ± 1.42 ^a	0.222

Data are expressed as mean ± SD. The P-values with significant difference are described in bold.
 GSRS, Gastrointestinal Symptoms Rating Scale; QOL, quality of life.
^aP < 0.05 compared with baseline.

supporting recommendations to select natural food treatment as an alternative or complement to drug use.

CONFLICTS OF INTEREST

Guarantor of the article: Hirotaka Yamamoto, PhD.

Specific author contributions: T. Koyama and H.Y. designed and planned the study. T. Koyama and N.M. collected the data. K.N. performed statistical analysis. T. Koyama and H.Y. prepared the original draft. N.N. and T. Kawai supported editing of the original draft and critically revised the manuscript. All authors approved the final draft.

Financial support: This study was partially funded by MIKI Corporation.

Potential competing interests: This study was partially funded by MIKI Corporation. N. Nagata and K. Nishiura received a grant from MIKI Corporation. MIKI Corporation has outsourced some of this research to Oneness Support on a fee-for-service basis. N. Miura received a payment from Oneness Support. T. Koyama and H. Yamamoto are employees of MIKI Corporation. The sponsor had no control over the interpretation, writing, publication, or decisions about this work. The other authors declare no conflicts of interest.

Ethics: This study was conducted in accordance with the Declaration of Helsinki. Human rights of the subjects were well protected, and the study was conducted with the approval of the institutional review boards of the Miura Clinic (approval number: R2001) and Tokyo Medical University (approval number: T2021-0243). Written informed consent was obtained from all subjects before their enrollment into the study.

Clinical Trial Registration: This study was registered at ClinicalTrials.gov (<https://www.umin.ac.jp/english/>, UMIN 000041384).

REFERENCES

- Rao SSC, Brenner DM. Efficacy and safety of over-the-counter therapies for chronic constipation: An updated systematic review. *Am J Gastroenterol* 2021;116:1156–81.
- Müller-Lissner S, Tack J, Feng Y, et al. Levels of satisfaction with current chronic constipation treatment options in Europe—an internet survey. *Aliment Pharmacol Ther* 2013;37:137–45.
- Currò D, Ianiro G, Pecere S, et al. Probiotics, fibre and herbal medicinal products for functional and inflammatory bowel disorders. *Br J Pharmacol* 2017;174:1426–49.
- Attaluri A, Donahoe R, Valestin J, et al. Randomised clinical trial: Dried plums (prunes) vs. psyllium for constipation. *Aliment Pharmacol Ther* 2011;33:822–8.
- Chey SW, Chey WD, Jackson K, et al. Exploratory comparative effectiveness trial of green kiwifruit, psyllium, or prunes in US patients with chronic constipation. *Am J Gastroenterol*. 2021;116:1304–12.
- Mearin F, Lacy BE, Chang L, et al. Bowel disorders. *Gastroenterology* 2016;150:1393–1407.
- O'Donnell LJ, Virjee J, Heaton KW. Detection of pseudodiarrhoea by simple clinical assessment of intestinal transit rate. *BMJ* 1990;300:439–40.
- Dimenäs E, Glise H, Hallerbäck B, et al. Well-being and gastrointestinal symptoms among patients referred to endoscopy owing to suspected duodenal ulcer. *Scand J Gastroenterol* 1995;30:1046–52.
- National Cancer Institute. Common Terminology Criteria for adverse events (CTCAE) version 5.0. https://ctep.cancer.gov/protocolDevelopment/electronic_applications/ctc.htm#ctc_50. Accessed April 17, 2022.
- Ohkubo H, Yoshihara T, Misawa N, et al. Relationship between stool form and quality of life in patients with chronic constipation: An internet questionnaire survey. *Digestion* 2021;102:147–54.
- Saibil FG. Factitious diarrhea. *Can Med Assoc J* 1974;111:1108–9.
- Piirainen L, Peuhkuri K, Bäckström K, et al. Prune juice has a mild laxative effect in adults with certain gastrointestinal symptoms. *Nutr Res* 2007;27:511–3.
- Lederle FA, Busch DL, Mattox KM, et al. Cost-effective treatment of constipation in the elderly: A randomized double-blind comparison of sorbitol and lactulose. *Am J Med* 1990;89:597–601.
- Durrington PN, Manning AP, Bolton CH, et al. Effect of pectin on serum lipids and lipoproteins, whole-gut transit-time, and stool weight. *Lancet* 1976;2:394–6.
- Na J-R, Lee KH, Kim E, et al. Laxative effects of a standardized extract of dendropanax morbiferus H. Léveillé leaves on experimental constipation in rats. *Medicina* 2021;57:1147.

This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.