Preventive Effect of Germinated Barley Foodstuff on Diarrhea Induced by Water-soluble Dietary Fiber in Rats

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We investigated the preventive effect of germinated barley foodstuff (GBF) added to the diet on diarrhea induced by the dietary water-soluble dietary fibers, polydextrose, hemicellulose, and poly-acrylic acid sodium salt, in Sprague-Dawley rats. The minimum content of GBF necessary for blocking diarrhea was 3% (by weight) of the diet.

Since GBF is mainly derived from the aleurone and scutellum of malted barley, we assessed the physiological effects of the aleurone and scutellum fractions derived from barley grains before and after germination. The addition of fractions containing only germinated barley, and not barley collected before germination, increased the fecal output and jejunal mucosal protein content. The effects of malted barley were very similar to those of GBF.

It was concluded that germination was necessary to bring about the physiological effects of GBF. Since non-lignified hemicellulose and Glu-rich protein were newly synthesized during germination, these might have contributed to the increased fecal output and jejunal mucosal protein content.

Key words: intestine; dietary fiber; germination; diarrhea; barley

Under experimental conditions, some dietary fibers have been found to reduce diarrhea. While dietary fiber generally improves defecation, there have been some reported cases of dietary fiber aggravating constipation or diarrhea because of its indigestibility and stimulation of the gastrointestinal tract. In our previous study, rats fed on the water-soluble dietary fiber, polydextrose, developed experimentally diarrhea.

Germinated barley foodstuff (GBF) increases the fecal output and jejunal mucosal protein content, and GBF is thought to thicken the intestinal mucosa. Therefore, GBF could be expected to improve defecation under normal conditions, as well to alleviate the diarrhea induced by an inclusion in the diet of water-soluble dietary fiber.

We consider that germination provides the major difference between GBF and other dietary fiber sources. There are few foodstuffs containing germinated seed other than malt or bean sprouts. In our previous study, we proposed that germination would be necessary to produce the physiological effects of GBF. During germination, the scutellum of barley has been reported to synthesize non-lignified hemicellulose, which ferments well is the lower gastrointestinal tract, and induces the production volatile fatty acids (VFA). These VFA are thought to increase the intestinal mucosal protein content or the growth of enterocytes.

We collected the aleurone and scutellum fractions of barley grain before and after germination by threshing, and we assessed their physiological effects on rats. If germination is indeed necessary for these physiological effects, these fractions of the barley grain collected before germination would not have any potency for increasing the fecal output and jejunal mucosal protein content. In this study, we examined the preventive effect of GBF on diarrhea and whether germination was necessary to manifest the increased fecal output and protein content in intestinal mucosa.

Materials and Methods

Materials. Based on our previous studies, we selected water-soluble dietary fibers that caused diarrhea. These were polydextrose (PD; purchased from Pfizer Co., Tokyo, Japan), poly-acrylic acid sodium salt (PAC; Aonvis MS, purchased from Nihon Junyaku Co., Tokyo), and water-soluble-hemicellulose (HC; Nihon Shokuhin Kakou Co., Tokyo). All the dietary components, except for corn oil (Ainamoto Co., Tokyo) and corn starch (Nacalai Tesque Co., Tokyo), were purchased from Oriental Yeast Co. (Tokyo). All reagents were purchased from Wako Pure Chemical Industries Co. (Osaka, Japan). GBF was obtained by Kishi's method. Barley grains before germination (raw barley; RB) and after germination (malted barley; MB) at Kirin Brewery Takasaki Factory (Gunma, Japan) were used.

Methods. Experiment 1. In this experiment, we evaluated the preventive effect of GBF on diarrhea in rats fed on the PD, PAC, and HC-containing diets. Male Sprague-Dawley rats weighing about 50 g each were purchased from Charles River Japan (Yokohama, Japan). They were individually housed in metabolic cages in a room kept at 22 ± 1°C, with a 12-h light and dark cycle (light from 8:00 a.m. to 8:00 p.m.). The rats were fed ad libitum with a commercial diet (EC2, Nihon Clea, Tokyo) for 7 days during the acclimatization period, and were then randomly allocated to the 3 groups respectively given PD, PAC, and HC. These 3 groups were divided into 2 sub-groups respectively given cellulose (CE)- and GBF-containing diets. There were thus 6 groups, each fed on PD with CE (PD-CE) or GBF (PD-GBF), PAC with CE (PAC-CE) or GBF (PAC-GBF), and HC with CE (HC-CE), or GBF (HC-GBF). The protein and neutral detergent fiber

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The technique of polishing rice for Japanese sake with rice whitening machine

Protein

The measured and diets measured the (NDF) contents of all diets were adjusted to the same level. After acclimatization, each group was fed with the experimental diet for 14 days, the rats being allowed free access to their respective diets and to drinking water. The composition of each experimental diets is shown in Table I. During the experimental period, the food intake and body weight were measured every 3 days. Photographs of the rats fed with the respective diets were taken on day 14. During this experiment, the PD-CE, PAC-CE, and HC-CE groups had severe diarrhea, and we could not collect their feces. On day 14, the rats were anesthetized with urethane, and the jejunum was excised. The protein content in the jejunal mucosa of each rat was measured by the method used in our previous study.13

Experiment 2. In this experiment, we investigated the relationship between percentage of GBF in the diet and the prevention of diarrhea induced by feeding PAC. After acclimatization, the rats were assigned to the following groups of 5 rats each: PAC-CE: 10% GBF and PAC (PAC-10% GBF); 5% GBF and PAC (PAC-5% GBF); 3% GBF and PAC (PAC-3% GBF); and 1% GBF and PAC (PAC-1% GBF). The protein and NDF contents of all the diets were adjusted to the same level. The composition of these diets is shown in Table II. The other experimental conditions were the same as those described for Experiment 1.

Experiment 3. In this experiment, we examined the relationship between barley germination and its physiological effects. Isolation of the aleurone and scutellum fractions of RB and MB was carried out by modifying the technique of polishing rice for Japanese sake with a rice whitening machine for brewery use (TDB-2A, Satake Co., Hiroshima, Japan).14 Twenty kg of RB or MB was weighed and placed in the TDB-2A machine. We milled these grains gradually and then collected and weighed the residual seeds. The aleurone and scutellum fractions of RB and of MB were isolated on the basis of the weight range (from 88% to 85% of the initial weight). The weight range from 100% to 88% of these samples is defined as the husk fraction, and the residual from these was recognized as the endosperm. In these fractions, we confirmed the specific aleurone layer by scanning electron microscopy (data not shown). The compositions of the aleurone and scutellum fractions of RB and MB are shown in Table III. After acclimatization, the rats were assigned to groups fed with CE, GBF, the aleurone and scutellum fractions of GB, and the same fractions of MB. The compositions of the diets are shown in Table IV. The protein and NDF contents of all the diets were adjusted to the same level. The rats were fed with these diets for 14 days. On days 11 to 13, we collected and counted fresh feces from all groups, the feces then being lyophilized and weighed. On day 14, the jejunum was excised, and the protein content of the jejunal mucosa from each rat was determined.

Table I. Composition of the Experimental Diets (Experiment 1)

<table>
<thead>
<tr>
<th></th>
<th>PD-CE</th>
<th>PD-GBF</th>
<th>PAC-CE</th>
<th>PAC-GBF</th>
<th>HC-CE</th>
<th>HC-GBF</th>
</tr>
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<tbody>
<tr>
<td>Casein</td>
<td>146</td>
<td>100</td>
<td>146</td>
<td>100</td>
<td>146</td>
<td>100</td>
</tr>
<tr>
<td>Vitamin mixture</td>
<td>10.0</td>
<td>10.0</td>
<td>10.0</td>
<td>10.0</td>
<td>10.0</td>
<td>10.0</td>
</tr>
<tr>
<td>Mineral mixture</td>
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<td>35.0</td>
<td>35.0</td>
<td>35.0</td>
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<td>35.0</td>
</tr>
<tr>
<td>Choline chloride</td>
<td>2.0</td>
<td>2.0</td>
<td>2.0</td>
<td>2.0</td>
<td>2.0</td>
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<td>60.0</td>
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<td>20.0</td>
<td>60.0</td>
<td>60.0</td>
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<tr>
<td>PAC</td>
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<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>HC</td>
<td>30.0</td>
<td></td>
<td>30.0</td>
<td></td>
<td>30.0</td>
<td></td>
</tr>
<tr>
<td>Cellulose</td>
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<td>50.0</td>
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<tr>
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<td>643</td>
<td>707</td>
<td>683</td>
<td>667</td>
<td>643</td>
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<tr>
<td>Corn starch</td>
<td>667</td>
<td>643</td>
<td>707</td>
<td>683</td>
<td>667</td>
<td>643</td>
</tr>
</tbody>
</table>

a The vitamin mixture was prepared according to the AIN 91 vitamin mixture protocol.16
b The mineral mixture was prepared according to the AIN 93G mineral mixture protocol.16
c PD, polydextrose
d PAC, polyacryl acid sodium salt
e HC, hemicellulose (water soluble)
f GBF, germinated barley foodstuff
g PD-CE, mixed PD and CE diet
h PD-GBF, mixed PD and GBF diet
i PAC-CE, mixed PAC and CE diet
j PAC-GBF, mixed PAC and GBF diet
k HC-CE, mixed and CE diet
l HC-GBF, mixed HC and GBF diet

Table II. Composition of the Experimental Diets (Experiment 2)

<table>
<thead>
<tr>
<th></th>
<th>PAC-CE</th>
<th>PAC-10% GBF</th>
<th>PAC-5% GBF</th>
<th>PAC-3% GBF</th>
<th>PAC-1% GBF</th>
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<td>123</td>
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<tr>
<td>Choline chloride</td>
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<td>PAC</td>
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</tr>
<tr>
<td>Cellulose</td>
<td>30</td>
<td>15</td>
<td>21</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td>GBF</td>
<td>60</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
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<tr>
<td>Corn oil</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>Corn starch</td>
<td>707</td>
<td>683</td>
<td>695</td>
<td>700</td>
<td>705</td>
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</tbody>
</table>

abe See the legend to Table I.
c PAC, polyacryl acid sodium salt
d PAC-CE, 3% cellulose and 2% PAC diet
e PAC-10% GBF, 10% GBF and PAC diet
f PAC-5% GBF, 5% GBF and PAC diet
g PAC-3% GBF, 3% GBF and PAC diet
h PAC-1% GBF, 1% GBF and PAC diet
i PAC-1% GBF, 1% GBF and PAC diet

Protein and neutral detergent fiber of all diet groups were adjusted to the same level.

Analytical methods. The protein content (N × 6.25) of GBF, the aleurone and scutellum fractions of RB, and the same fractions of GB were measured by the Kjeldahl method. The NDF contents of the samples were measured by the method of Van Soest and Wine,15 while the methods for excising the jejunum and assaying the protein content of its mucosa were described in our previous study.31 Briefly, the jejunum was defined as 15–30 cm of the small intestine from the pylorus, its mucosa was obtained by scraping and the protein content was measured by using a commercial eye-binding kit. The contents of DNA and RNA of the jejunal mucosa were determined by Schneider's method.29

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Table III. Chemical Composition of Raw Barley and Malted Barley

<table>
<thead>
<tr>
<th></th>
<th>Raw barley (RB)*</th>
<th>Malted barley (MB)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>(g/kg of sample)</td>
<td></td>
<td></td>
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<tr>
<td>Water</td>
<td>6.5</td>
<td>8.0</td>
</tr>
<tr>
<td>Protein</td>
<td>18.0</td>
<td>11.5</td>
</tr>
<tr>
<td>Lipid</td>
<td>6.6</td>
<td>5.9</td>
</tr>
<tr>
<td>Dietary fiber</td>
<td>31.0</td>
<td>30.7</td>
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<tr>
<td>Ash</td>
<td>5.8</td>
<td>5.5</td>
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<tr>
<td>Other carbohydrates</td>
<td>32.1</td>
<td>38.4</td>
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</table>

Composition of dietary fiber

<table>
<thead>
<tr>
<th></th>
<th>RB (%)</th>
<th>MB (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cellulose</td>
<td>36.7</td>
<td>21.6</td>
</tr>
<tr>
<td>Hemicellulose</td>
<td>57.1</td>
<td>73.6</td>
</tr>
<tr>
<td>Lignin</td>
<td>6.2</td>
<td>4.7</td>
</tr>
</tbody>
</table>

* RB, the aleurone and scutellum fraction of raw barley.
* MB, the aleurone and scutellum fraction of malted barley.

Table IV. Composition of the Experimental Diets (Experiment 3)

<table>
<thead>
<tr>
<th></th>
<th>CE*</th>
<th>GBE*</th>
<th>RB*</th>
<th>MB*</th>
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<tbody>
<tr>
<td>(g/kg of diet)</td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>Casein</td>
<td>146</td>
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<td>128</td>
<td>135</td>
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<tr>
<td>Vitamin mixture</td>
<td>10</td>
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<td>10</td>
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<td>Mineral mixture</td>
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<td>Choline chloride</td>
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</tr>
<tr>
<td>Cellulose</td>
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<tr>
<td>GBF</td>
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<tr>
<td>RB</td>
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<td>MB</td>
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<tr>
<td>Corn oil</td>
<td>50</td>
<td>50</td>
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<tr>
<td>Corn starch</td>
<td>727</td>
<td>703</td>
<td>675</td>
<td>669</td>
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</table>

Table V. Body Weight Gain, Food Intake, Mucosal Protein Content, and Number of Rats with Diarrhea (Experiment 1)

<table>
<thead>
<tr>
<th>Group*</th>
<th>Body weight gain (g/14 days)</th>
<th>Food intake (g/day)</th>
<th>Mucosal protein content (mg/cm of jejenum)</th>
<th>Diarrhea</th>
</tr>
</thead>
<tbody>
<tr>
<td>PD-CE</td>
<td>104 ± 4.9</td>
<td>21.1 ± 1.4</td>
<td>4.35 ± 0.05</td>
<td>5/5</td>
</tr>
<tr>
<td>PD-GBF</td>
<td>119 ± 9.4</td>
<td>22.9 ± 1.2</td>
<td>5.00 ± 0.25*</td>
<td>0/5*</td>
</tr>
<tr>
<td>PAC-CE</td>
<td>94.3 ± 2.3</td>
<td>21.7 ± 0.4</td>
<td>3.66 ± 0.11</td>
<td>5/5</td>
</tr>
<tr>
<td>PAC-GBF</td>
<td>108 ± 2.7*</td>
<td>22.4 ± 0.6</td>
<td>4.91 ± 0.35*</td>
<td>0/5*</td>
</tr>
<tr>
<td>HC-CE</td>
<td>101 ± 3.2</td>
<td>22.4 ± 0.5</td>
<td>4.16 ± 0.11</td>
<td>5/5</td>
</tr>
<tr>
<td>HC-GBF</td>
<td>111 ± 9.5</td>
<td>23.4 ± 1.4</td>
<td>4.65 ± 0.15*</td>
<td>0/5*</td>
</tr>
</tbody>
</table>

* Abbreviations are the same as those shown in the legend to Table I.
* The overall mean for initial body weight was 101.7 ± 0.9 g.
* Food intake represents the mean for the final 3 days.
* This value is the number of rats with diarrhea, and means showing an asterisk within the same column are significantly different in the CE and GBF groups within the same water-soluble fiber group (p < 0.05).

Although the food intake by the CE and GBF sub-groups was almost the same for each pair of the three water-soluble dietary fiber groups, the body weight gain of all three GBF-fed groups was slightly higher than that of the corresponding CE group. Only with the PAC-fed group was there a significant difference in body weight gain between the CE- and GBF-fed rats.

The jejunal mucosal protein content in each GBF group was significantly higher than that in the corresponding CE group. Each water-soluble dietary fiber caused diarrhea, but diarrhea was prevented in the GBF-fed rats. We could not collect the feces from any rats in the CE groups, because the diarrhea was so severe.

Experiment 2

The body weight gain, food intake, jejunal mucosal protein content, and the number of rats with diarrhea in each group are shown in Table VI. There was no significant difference among the groups in the body weight gain or food intake. The jejunal mucosal protein content was the highest in the PAC-10% GBF group, and it differed significantly from that in the PAC-CE group. A weak relationship between the GBF- ingestion level and the jejunal mucosal protein content was found; the jejunal mucosal protein content in PAC-5% GBF group was higher than that in the PAC-CE group, and lower than that in the PAC-10% GBF group. The number of rats with diarrhea was dependent on the amount of GBF in the diet: a dietary content exceeding 3% of GBF prevented the diarrhea caused by PAC. The degree of inflammation around the anus in those rats fed on the PAC diet was also reduced by including GBF in the diet.

Experiment 3

The protein content of RB was higher than that of MB, but the dietary fiber content was almost the same. While RB was high in lignin, and relatively low in hemicellulose, MB was the reverse.

As shown in Table VII, the body weight gain and food...
intake were comparable across the groups. The number of feces, and the fecal dry weight in the GBF and MB groups were significantly higher than those in the CE group. There was no significant difference between the GBF and MB group in the number of feces and fecal dry weight. The jejunal mucosal protein content in the GBF group and the MB group was significantly higher than that in the CE or the RB group. As shown in Table VIII, the DNA and RNA content of the jejunum in the GBF group was significantly higher than that in the CE group.

**Discussion**

It has been reported that water-soluble dietary fiber does not generally increase the fecal output,7 and in some circumstances, it has been reported to cause diarrhea.2,3,7 In particular, PD is known to cause severe diarrhea in healthy volunteers.2,8 It has been assumed that this diarrhea was caused by the increased osmotic pressure, inhibition of electrolyte absorption, or a change in the microflora in the gastrointestinal tract.22,23

Dietary GBF increased not only the mucosal protein content, but also the DNA and RNA contents. This indicates that the number of enterocytes in the GBF-fed rats was increased. Furthermore, as it has been reported that one of the main components of feces is dropped enterocytes,24 so that the increase in the number of enterocytes by dietary GBF would be related to the increase in fecal output. However, the increased number of enterocytes in our experiments is thought to have been different from that in diseased hyperplasia, because no
abnormal symptoms have been found with the long-term GBF feeding to some animals.16 Although GBF is defined as a type of dietary fiber, it has the distinctive characteristic of suppressing diarrhea and lessening injury to the mucosa.5-7 Dietary GBF also resulted in the normal excretion of feces without any decrease in the mucosal protein content in an induced diarrhea model.

The inclusion of at least 3% GBF in the diet was found to be necessary to prevent diarrhea. When GBF was given at 1%, it did not completely prevent diarrhea. As dietary fiber affects excretion due to its bulk and density,5,6 digestion of the volume of GBF that is transported to the lower intestine would be necessary to manifest the effect of GBF in blocking diarrhea. A detailed dose-response study of the appropriate ingestion level of GBF is needed. It is clear that GBF itself did not cause diarrhea, and that GBF prevented the diarrhea produced by other water-soluble dietary fibers. The risk of diarrhea by a massive quantity of ingested GBF should be very low.

In addition to the diarrhea caused by certain water-soluble dietary fibers, severe diarrhea can be caused by some drug administrations as described next. The methotrexate-induced diarrhea model12,13 and the dextran sulfate-induced colitis model have been reported to result in severe damage to the intestinal mucosa,25,27 and in these models, a deficiency in nutrients and electrolytes would arise. That is to say, diarrhea might be intimately related to the condition of the intestinal mucosa. As GBF increases the mucosal enterocyte population and restores defecation to normal levels in rats fed on water-soluble dietary fiber, GBF might improve defecation in these disease models as well. We intend to study this possibility in future.

GBF is derived from germinated seed and can be isolated from the husk fraction of Brewer’s spent grain. We tested the aleurone and scutellum fractions of RB and MB to clarify the effect of germination on the manifestation of the increased fecal output and intestinal mucosal protein content. During the germination process, the hemicellulose content in the aleurone and scutellum fractions increased, while the lignin content decreased.19 These results suggest that synthesis of non-lignified hemicellulose occurred during germination. Non-lignified hemicellulose is considered to be efficiently utilized in the lower gastrointestinal tract, leading to the production of VFA, which is thought to increase the number of enterocytes.28,29

The protein content of the aleurone and scutellum fractions decreased during germination, and the protein has been reported to be partly converted to some hydrolytic enzymes in the embryo. Although the protein content was less after germination, the proportion of Gln to the total nitrogen content has been reported to be increased by germination.10 This increment of Gln seems to contribute to the increased number of enterocytes.30,31 To improve the mucosal condition and defecation, it is necessary to increase the content of not only non-lignified hemicellulose but also of Gln.

In this study, we examined the effects of GBF on the jejunal mucosa and on defecation in a model of diarrhea induced by water-soluble dietary fiber. Germination is thought to be very important to manifest the physiological effects of GBF. As dietary GBF and MB caused an increase in the mucosal protein content and improved the defecation.
in rats, they might also aid defecation and prevent mal-
nutrition due to malabsorption by the mucosa in patients
with enterico-collitis and other diseases. We are planning to
examine these effects of GBF and MB.

In conclusion, GBF effectively blocked the diarrhea
caused by water-soluble dietary fiber, and MB increased the
jejunal mucosal protein content and fecal output. Germa-
nation resulting in an increased Gln content and non-lignified
hemicellulose content, appears to have played an important
role in manifesting these effects of GBF and MB.

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Teramoto (Satake Co., Hiroshima, Japan) for preparing the aleurone
and scutellum fractions from barley and malted barley. We also thank
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Hokkaido University School of Veterinary Medicine) and Naomu Ishiwaki
(Kirin Brewery Co.) for their helpful advice.

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