Effects of Fructooligosaccharides on the Absorption of Magnesium in the Magnesium-Deficient Rat Model

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Summary Magnesium (Mg) is an essential dietary element that plays important roles, acting as a cofactor of many enzymes. Rats fed a Mg-deficient diet have been reported to exhibit auricular and facial peripheral hyperemia and hemorrhage. Moreover, increased intake of calcium (Ca) or phosphorus (P) has been reported to impair apparent absorption of Mg. We tried to induce such typical inflammation in Mg-deficient rats by feeding low-Mg, high-Ca, and high-P diets. Increasing concentrations of Ca or P in the experimental diets significantly decreased the apparent absorption of Mg. And all rats fed the low-Mg (0.25 mg/g diet), high-Ca (10.4 mg/g diet), and high-P (12.0 mg/g diet) diet exhibited auricular and facial peripheral hyperemia and hemorrhage. Then, we used the low-Mg, high-Ca, and high-P diet to investigate the effects of the fructooligosaccharides (FO) on absorption of Mg and skin inflammation. In the rats fed FO-containing (1 or 5%) diet, apparent absorption of Mg was significantly increased as compared with that of the control (FO 0%) group. In the rats fed a 5% FO-containing diet and sufficient Mg (0.50 mg/g), auricular and facial peripheral hyperemia and hemorrhage were significantly reduced. We concluded that FO increased the Mg absorption in rats fed a low-Mg, high-Ca, and high-P diet. Moreover, FO reduced inflammation in Mg-deficient rats, such as peripheral hyperemia and hemorrhage.

Key Words fructooligosaccharides, calcium, magnesium, phosphorus, rat, absorption, deficient, auricular, hyperemia, hemorrhage

Magnesium (Mg) is an essential dietary element that plays important roles, acting as a cofactor of many enzymatic reactions, including glucose use; the synthesis of fat, protein, and nucleic acids; the metabolism of adenosine tri-phosphate; muscle contraction; and some membrane transport systems (1, 2).

Rats fed a Mg-deficient diet have been reported to exhibit auricular and facial peripheral hyperemia and hemorrhage (3–7). Such typical skin inflammation in
Mg-deficient rats is caused by increased secretion of histamine from mast cells (6, 7). These symptoms of Mg-deficiency were observed in rats fed a diet containing almost no Mg. Meanwhile, the level of Mg-deficiency responsible for such inflammation is unknown. Increased intake of calcium (Ca) or phosphorus (P) has been reported to impair apparent absorption of Mg (8, 9). Mg is absorbed from both the small intestine (10,11) and the large intestine (12) including the cecum (13). Indigestible saccharides appear to affect Mg absorption from the large intestine (14,15). Recently, we found that fructooligosaccharides (a mixture of 1-kestose, nystose, and 1F-β-fructofuranosyl nystose), which stimulate growth of bifidobacteria in the intestine, increase the absorption of Ca, P and, especially, of Mg (16). The same effects were observed with inulin (17) and other indigestible oligosaccharides (18,19).

In the present study, we tried to elucidate the dietary composition by which typical Mg-deficient symptoms such as auricular and facial peripheral hyperemia and hemorrhage occur. Then, we investigated the effects of the fructooligosaccharide mixture on the apparent absorption of Mg and on the incidence of skin inflammation.

MATERIALS AND METHODS

Diet and animals. Five-week-old male Sprague-Dawley rats (Clea Japan, Tokyo) were housed in individual stainless-steel metabolic cages in a temperature- and humidity-controlled room (25°C and 55% relative humidity). Six rats were used in each experimental subgroup. All groups received diets that contained 50.8% sucrose (w/w) and 41.0% (w/w) constant components (25.0% casein, 10.0% corn oil, AIN-76 vitamin mixture, 5.0% cellulose, and 3.5% Ca-, Mg-, P-free AIN-76 mineral mixture (w/w)). In the first experiment (Exp. 1), rats were fed different concentrations of Ca (5.2 or 10.4mg/g diet) and P (4.0, 8.0, or 12.0 mg/g diet) and a constant Mg concentration (0.25mg/g diet) for 14 days. In the second experiment (Exp. 2), rats were fed constant concentrations of Ca (10.4mg/g diet) and P (12.0mg/g diet) plus two concentrations of Mg (0.25 and 0.50mg/g diet) and three concentrations of fructooligosaccharides (0, 1, or 5%, w/w) for 25 days. The composition of the diets is shown in Table 1. Calculated concentrations of minerals added agreed well with analyzed values (Table 1). On the final day of each experiment, we examined auricular peripheral and facial hyperemia and hemorrhage in detail.

In both experiments, the rats were anesthetized with diethyl ether on the final day of experiment. Blood was obtained by orbital puncture.

The extent of auricular and facial hyperemia and hemorrhage was graded as follows: −, rats with no inflammation; ±, rats with only hyperemia; +, rats with less than 10 sites of hemorrhage; ++, rats with more than 10 sites of hemorrhage.

Mineral balance studies. In Exp. 1, 10 days after the start of the experiment,
Table 1. Composition of experimental diets.

| Ingredient (g/kg) | Exp. 1 | EXP. 2 |
|------------------|--------|--------|
| Constant components¹ | NCNP | NCMP | NCHP | HCNP | HCMP | HCHP | Cont. | +Mg | FO 1% | FO 5% |
| Casein | 250g | | | | | | | | | |
| Corn oil | 100g | | | | | | | | | |
| Vitamin premix (AIM-76) | 10g | | | | | | | | | |
| Cellulose | 50g | | | | | | | | | |
| Ca-, Mg-, P-free mineral premix | 35g | | | | | | | | | |
| NaCl | 2,590 | | | | | | | | | |
| K₃C₆H₅O₇·H₂O | 7,700 | | | | | | | | | |
| K₂SO₄ | 1,820 | | | | | | | | | |
| MnCO₃ | 123 | | | | | | | | | |
| Fe-citrate | 210 | | | | | | | | | |
| ZnCO₃ | 56 | | | | | | | | | |
| CuCO₃ | 10.5 | | | | | | | | | |
| Na₂SeO₃·5H₂O | 0.35 | | | | | | | | | |
| KIO₃ | 0.35 | | | | | | | | | |
| Cr(SO₄)₂·12H₂O | 19.3 | | | | | | | | | |
| Sucrose | 22,470 | | | | | | | | | |
| Fructooligosaccharides² | | | | | | | | | | |

Chemical analysis (mg/kg)

| Ingredient | Exp. 1 | Exp. 2 |
|------------|--------|--------|
| Calcium | 5,800 | 11,500 |
| Magnesium | 210 | 205 |
| Phosphorus | 4,950 | 11,900 |

¹Constant components: casein 250g, corn oil 100g, vitamin premix (AIM-76) 10g, cellulose 50g, Ca-, Mg-, P-free mineral premix 35g consisted of the following (mg): NaCl, 2,590; K₃C₆H₅O₇·H₂O, 7,700; K₂SO₄, 1,820; MnCO₃, 123; Fe-citrate, 210; ZnCO₃, 56; CuCO₃, 10.5; Na₂SeO₃·5H₂O, 0.35; KIO₃, 0.35; Cr(SO₄)₂·12H₂O, 19.3; sucrose, 22,470. ²Fructooligosaccharides (Meioligo-P: oligosaccharides, 95% w/w).
rats were subjected to a mineral balance study for 5 days. In Exp. 2, 7 and 21 days after the start of the experiment, rats were subjected to a mineral balance study for 5 days. All feces and urine were collected during each 5-day period. The apparent absorption of minerals and retention of minerals were calculated from the following formulae:

\[
\text{Apparent absorption} = \frac{(\text{intake} - \text{fecal excretion})}{(\text{intake})} \times 100(\%)
\]

\[
\text{retention} = \frac{(\text{intake} - \text{fecal excretion} - \text{urinary excretion})}{(\text{intake})} \times 100(\%)
\]

**Determinations of calcium, magnesium, and phosphorus.** The amounts of calcium, magnesium, and phosphorus in diets, feces, and urine were determined with an inductive coupled plasma emission spectrometer (ICPS-5000; Shimadzu). Foods and feces were first dried and then micropulverized. Micropulverized samples (100 mg) were ashed at 600°C for 24 h in the presence of 1 ml of nitric acid. The ashed samples, dissolved in 4 ml of 2 N HCl, were diluted appropriately with distilled water for atomization. Urine was diluted appropriately with distilled water and subjected to atomization directly.

Serum levels of Mg, Ca, and P were analyzed with commercial kits (magnesium B-test, calcium C-test, phospha C-test, Wako Pure Chem. Ind., Tokyo, Japan).

**Chemicals.** Fructooligosaccharides (concentrations of oligosaccharides were above 95%) were obtained from Meiji Seika Kaisha, Ltd. (Tokyo). Other dietary components apart from minerals were purchased from Oriental Yeast Co. (Tokyo). Minerals and all other reagents were of analytical grade and were purchased from Wako Pure Chem. Ind.

**Statistics.** Tukey’s test or the \(\chi^2\)-test were used to compare group means. The level of significance was taken as at \(p < 0.05\).

**RESULTS**

**Exp. 1**

The body weight and food consumption are shown in Table 2. The final body

Table 2. Body weights and food intake of the rats fed experimental diets for 14 days (Exp. 1).

| Group\(^{1}\) | Initial weight (g) | Final weight (g) | Food intake (g) |
|--------------|-------------------|-----------------|-----------------|
| NCNP         | 124±4 ns          | 232±9\(^{ab}\)  | 243±15 ns       |
| NCMP         | 124±3             | 242±14\(^{a}\)  | 260±22          |
| NCHP         | 124±3             | 227±9\(^{ab}\)  | 234±15          |
| HCNP         | 124±3             | 222±17\(^{ab}\) | 240±30          |
| HCP          | 122±6             | 232±8\(^{ab}\)  | 252±13          |
| HCHP         | 122±5             | 216±12\(^{b}\)  | 231±15          |

M±SD (\(n=6\)), ns = not significant; values with different superscript letters are significantly different (\(p < 0.05\)). \(^{1}\)See legend to Table 1.

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Table 3. Mineral balances and serum concentrations of Ca, Mg, and P (Exp. 1).

| Group  | Intake (mg/day) | Fecal excretion (mg/day) | Urinary excretion (mg/day) | Absorption \(^2\) (mg/day) | Absorption ratio \(^3\) (%) | Retention \(^4\) (mg/day) | Retention ratio \(^5\) (%) | Serum concentration (mmol/liter) |
|--------|----------------|--------------------------|---------------------------|-----------------------------|-----------------------------|--------------------------|-----------------------------|--------------------------------|
| Ca     |                |                          |                           |                             |                             |                          |                             |                                |
| NCNP   | 112 ± 6 \(^6\) | 36.5 ± 7.7 \(^7\)       | 0.42 ± 0.13 \(^{abc}\)    | 75.9 ± 10.1 ns              | 67.4 ± 7.2 \(^6\)           | 75.5 ± 10.1 \(^6\)       | 67.1 ± 7.3 \(^6\)           | 2.26 ± 0.15 ns                 |
| NCMP   | 113 ± 14 \(^4\) | 35.0 ± 5.4 \(^4\)       | 0.38 ± 0.14 \(^{abc}\)    | 78.5 ± 12.6 \(^4\)         | 69.0 ± 4.4 \(^4\)           | 78.1 ± 12.5 \(^4\)       | 68.6 ± 4.4 \(^4\)           | 2.36 ± 0.38 \(^4\)             |
| NCHP   | 101 ± 7 \(^7\) | 32.3 ± 2.2 \(^a\)       | 0.31 ± 0.05 \(^a\)        | 68.2 ± 6.4 \(^a\)          | 67.8 ± 2.0 \(^a\)           | 67.9 ± 6.4 \(^a\)        | 67.5 ± 2.0 \(^a\)           | 2.17 ± 0.33 \(^a\)             |
| HCNP   | 206 ± 27 \(^b\) | 125.6 ± 18.5 \(^b\)    | 0.84 ± 0.36 \(^b\)        | 80.7 ± 10.1 \(^b\)         | 39.2 ± 2.2 \(^b\)           | 79.9 ± 9.9 \(^b\)        | 38.8 ± 2.2 \(^b\)           | 2.14 ± 0.37 \(^b\)             |
| HCMN   | 211 ± 12 \(^b\) | 125.7 ± 11.9 \(^b\)    | 0.75 ± 0.58 \(^b\)        | 85.1 ± 12.6 \(^b\)         | 40.3 ± 5.1 \(^b\)           | 84.4 ± 12.5 \(^b\)       | 40.0 ± 5.1 \(^b\)           | 2.20 ± 0.27 \(^b\)             |
| HCHP   | 194 ± 17 \(^b\) | 128.5 ± 13.3 \(^b\)    | 0.52 ± 0.22 \(^b\)        | 65.4 ± 7.0 \(^b\)          | 33.8 ± 2.7 \(^b\)           | 64.9 ± 7.0 \(^b\)        | 33.5 ± 2.8 \(^b\)           | 2.28 ± 0.24 \(^b\)             |
| Mg     |                |                          |                           |                             |                             |                          |                             |                                |
| NCNP   | 4.02 ± 0.23 \(^a\) | 0.66 ± 0.13 \(^a\) | 1.11 ± 0.62 \(^a\)       | 3.36 ± 0.19 \(^a\)         | 83.6 ± 2.8 \(^a\)           | 2.24 ± 0.66 \(^a\)       | 56.0 ± 16.1 \(^a\)          | 0.81 ± 0.31 \(^a\)             |
| NCMP   | 4.06 ± 0.51 \(^a\) | 1.17 ± 0.33 \(^abc\)    | 1.13 ± 0.10 \(^a\)       | 2.89 ± 0.47 \(^a\)         | 71.2 ± 6.6 \(^a\)           | 1.76 ± 0.42 \(^a\)       | 43.0 ± 6.6 \(^a\)           | 0.66 ± 0.11 \(^a\)             |
| NCHP   | 3.60 ± 0.26 \(^a\) | 1.47 ± 0.28 \(^c\)      | 0.52 ± 0.12 \(^b\)       | 2.13 ± 0.21 \(^b\)         | 59.3 ± 5.8 \(^c\)           | 1.61 ± 0.17 \(^abc\)     | 44.7 ± 3.8 \(^ab\)           | 0.71 ± 0.07 \(^ab\)            |
| HCNP   | 3.81 ± 0.50 \(^a\) | 1.02 ± 0.20 \(^ab\)     | 1.19 ± 0.20 \(^a\)       | 2.79 ± 0.48 \(^a\)         | 73.0 ± 5.2 \(^a\)           | 1.60 ± 0.41 \(^a\)       | 41.3 ± 7.2 \(^abc\)          | 0.53 ± 0.08 \(^a\)             |
| HCMN   | 3.89 ± 0.21 \(^a\) | 1.70 ± 0.18 \(^c\)      | 0.78 ± 0.27 \(^ab\)      | 2.20 ± 0.33 \(^ab\)        | 56.2 ± 6.3 \(^c\)           | 1.41 ± 0.31 \(^bc\)      | 36.2 ± 7.6 \(^c\)           | 0.61 ± 0.14 \(^ab\)            |
| HCHP   | 3.58 ± 0.31 \(^a\) | 2.24 ± 0.31 \(^d\)     | 0.38 ± 0.06 \(^a\)       | 1.34 ± 0.34 \(^c\)         | 37.2 ± 8.5 \(^d\)           | 0.96 ± 0.30 \(^c\)       | 26.6 ± 7.4 \(^d\)           | 0.52 ± 0.07 \(^d\)             |
| P      |                |                          |                           |                             |                             |                          |                             |                                |
| NCNP   | 96 ± 6 \(^a\) | 5.1 ± 2.2 \(^a\)       | 62 ± 9 \(^a\)            | 91 ± 5 \(^a\)              | 94.7 ± 2.1 \(^a\)           | 29.4 ± 5.6 \(^a\)       | 30.7 ± 7.0 \(^bc\)          | 2.16 ± 0.37 \(^a\)             |
| NCMP   | 160 ± 20 \(^c\) | 11.3 ± 3.4 \(^bc\)     | 113 ± 19 \(^c\)          | 149 ± 18 \(^c\)            | 93.0 ± 1.6 \(^c\)           | 35.7 ± 4.9 \(^c\)       | 22.7 ± 4.8 \(^ab\)          | 2.04 ± 0.33 \(^c\)             |
| NCHP   | 183 ± 13 \(^bc\) | 16.0 ± 4.1 \(^b\)      | 111 ± 14 \(^c\)          | 167 ± 11 \(^c\)            | 91.3 ± 1.7 \(^b\)           | 55.9 ± 16.5 \(^bc\)     | 30.2 ± 7.6 \(^e\)           | 1.61 ± 0.68 \(^ab\)            |
| HCNP   | 91 ± 12 \(^a\) | 14.9 ± 2.8 \(^b\)      | 39 ± 6 \(^a\)            | 77 ± 11 \(^a\)             | 83.7 ± 2.6 \(^b\)           | 37.8 ± 9.9 \(^ab\)      | 40.8 ± 7.6 \(^b\)           | 1.15 ± 0.19 \(^b\)             |
| HCMN   | 154 ± 8 \(^b\) | 31.6 ± 5.2 \(^b\)     | 59 ± 8 \(^b\)            | 122 ± 7 \(^b\)             | 79.4 ± 2.9 \(^b\)           | 62.8 ± 11.3 \(^c\)      | 41.0 ± 7.1 \(^a\)           | 2.06 ± 0.63 \(^b\)             |
| HCHP   | 183 ± 16 \(^b\) | 42.3 ± 4.9 \(^d\)     | 107 ± 13 \(^c\)          | 140 ± 15 \(^bc\)           | 76.8 ± 2.9 \(^d\)           | 33.5 ± 14.4 \(^a\)      | 18.2 ± 7.1 \(^a\)           | 1.76 ± 0.32 \(^ab\)            |

M±SD (n=6), ns = not significant; values with different superscript letters significantly different (p<0.05). \(^1\) See legend to Table 1. \(^2\) Intake — fecal excretion. \(^3\) (Absorption/intake) × 100. \(^4\) Intake — fecal excretion — urinary excretion. \(^5\) (Retention/intake) × 100.
weight and food intake of rats fed high-Ca (10.4mg/g diet) and high-P (12.0mg/g diet) diets were lower than these of rats fed other diets.

The balances and serum concentrations of Ca, Mg, and P are shown in Table 3. Fecal excretion of Ca and P were increased with increases in the intake of each mineral. Both increasing dietary Ca and increasing dietary P increased fecal Mg excretion and decreased apparent Mg absorption.

Serum Mg concentrations decreased with decreases in Mg-retention values. All rats fed a high-Ca (10.4mg/g diet) and high-P (12.0mg/g diet) diet and a half of the rats (three rats) fed high-Ca (10.4mg/g diet) and medium-P (8.0mg/g diet) diet exhibited auricular and facial peripheral hyperemia and hemorrhage.

**Exp. 2**

The body weight and food consumption are shown in Table 4. The final body weight and food intake of rats fed the control diet (Ca, 10.4mg/g diet; P, 12.0mg/g diet; Mg, 0.25mg/g diet; and FO, 0%) were lower than the final body weight and food intake of rats fed other diets.

Increasing the intake of FO decreased fecal excretion of Mg and increased Mg absorption and its retention during both periods examined. However, mean serum concentration of Mg in the rats fed the 5% FO-containing diet was similar to that of rats fed the control diet.

The extent of hyperemia and hemorrhage is shown in Table 6. All rats fed sufficient Mg and 5 rats fed a 5% FO-containing diet had no hyperemia or hemorrhage. The extent of hyperemia and hemorrhage in these two groups was significantly lower than that in the control group.

**DISCUSSION**

Brink et al. reported that increased intake of Ca or P impairs the apparent absorption of Mg in rats (9). We tried to elucidate the mineral composition of a diet that would cause Mg-deficient rats to exhibit auricular and facial peripheral hyperemia and hemorrhage by feeding low-Mg diets with different amount of Ca
### Table 5. Mineral balances and serum concentrations of Ca, Mg, and P (Exp. 2).

| Group | Intake (mg/day) | Fecal excretion (mg/day) | Urinary excretion (mg/day) | Absorption ($^2$) (mg/day) | Absorption ratio ($^3$) (%) | Retention (mg/day) | Retention ratio ($^4$) (%) | Serum concentration (mmol/liter) |
|-------|-----------------|--------------------------|---------------------------|-----------------------------|----------------------------|-------------------|--------------------------|---------------------------------|
|       |                 |                          |                           |                             |                            |                   |                          |                                 |
| **Ca (7–11 days)** |                 |                          |                           |                             |                            |                   |                          |                                 |
| Cont. | 193±11$^a$      | 99±7 ns                 | 0.47±0.24$^a$             | 94±9$^a$                    | 48.5±2.8 ns               | 93±8$^a$         | 40.1±3.2 ns             |                                 |
| + Mg  | 218±13$^b$      | 109±16                  | 0.71±0.56$^a$             | 109±11$^b$                  | 50.2±5.2                  | 108±10$^b$       | 38.9±6.0                |                                 |
| FO 1% | 207±10$^ab$     | 102±7                   | 0.48±0.17$^a$             | 104±8$^ab$                  | 50.5±2.7                  | 104±7$^b$        | 43.3±3.0                |                                 |
| FO 5% | 208±9$^ab$      | 97±9                    | 1.63±0.45$^a$             | 112±9$^b$                   | 53.6±3.7                  | 110±9$^b$        | 41.5±2.7                |                                 |
| (21–25 days) |                 |                          |                           |                             |                            |                   |                          |                                 |
| Cont. | 224±25$^a$      | 137±18$^b$              | 0.61±0.25$^a$             | 87±17$^a$                   | 38.9±6.0 ns              | 87±17 ns         | 38.7±6.1 ns             | 2.55±0.18$^b$                  |
| + Mg  | 248±5$^b$       | 149±6$^b$               | 0.64±0.14$^a$             | 100±9$^ab$                  | 40.1±3.2                 | 99±9             | 39.9±3.2                | 2.68±0.13$^a$                  |
| FO 1% | 221±24$^a$      | 125±16$^b$              | 0.67±0.39$^a$             | 95±12$^b$                   | 43.3±3.0                 | 95±13            | 42.9±3.0                | 2.65±0.13$^b$                  |
| FO 5% | 261±20$^b$      | 153±16$^b$              | 1.65±0.84$^a$             | 108±9$^b$                   | 41.5±2.7                 | 106±9            | 40.8±2.8                | 2.39±0.22$^a$                  |
| **Mg (7–11 days)** |                 |                          |                           |                             |                            |                   |                          |                                 |
| Cont. | 3.56±0.21$^a$   | 1.62±0.15$^a$           | 0.44±0.07$^a$             | 1.94±0.23$^a$               | 54.4±4.5$^a$             | 1.50±0.18$^a$    | 42.1±3.2$^b$            |                                 |
| + Mg  | 7.48±0.44$^a$   | 3.35±0.60$^b$           | 1.34±0.29$^b$             | 4.12±0.52$^c$               | 55.2±6.8$^a$             | 2.79±0.31$^c$    | 37.3±4.4$^b$            |                                 |
| FO 1% | 3.82±0.18$^a$   | 1.44±0.05$^a$           | 0.59±0.14$^a$             | 2.38±0.20$^ab$              | 62.3±2.4$^a$             | 1.78±0.11$^ab$    | 46.7±1.9$^b$            |                                 |
| FO 5% | 3.85±0.17$^a$   | 1.08±0.26$^a$           | 0.73±0.13$^a$             | 2.76±0.25$^b$               | 71.8±6.3$^b$             | 2.02±0.21$^b$     | 52.7±4.4$^b$            |                                 |
| **P (7–11 days)** |                 |                          |                           |                             |                            |                   |                          |                                 |
| Cont. | 182±10$^a$      | 36.1±5.3 ns             | 49.2±7.3 ns               | 145±8$^a$                   | 80.1±2.2 ns              | 96±6 ns          | 53.0±3.3 ns             |                                 |
| + Mg  | 205±12$^b$      | 43.2±7.4                | 64.9±23.5                 | 162±6$^b$                   | 79.0±2.4                 | 97±14            | 47.6±7.8                |                                 |
| FO 1% | 195±9$^ab$      | 35.3±4.3                | 61.4±14.4                 | 159±10$^{ab}$               | 81.8±2.3                 | 98±11            | 50.4±6.0                |                                 |
| FO 5% | 196±9$^a$       | 34.1±12.4               | 51.5±17.1                 | 153±10$^{ab}$               | 78.1±5.6                 | 102±8            | 51.9±5.1                |                                 |
| **(21–25 days)** |                 |                          |                           |                             |                            |                   |                          |                                 |
| Cont. | 211±23$^a$      | 53.9±7.6$^a$            | 88±23 ns                  | 157±24 ns                   | 74.2±4.5$^b$             | 69±23 ns         | 32.8±11.1 ns            | 1.96±0.19$^a$                  |
| + Mg  | 234±5$^b$       | 61.6±5.8$^b$            | 109±32                    | 172±9                       | 73.7±2.8$^b$             | 63±30            | 27.1±13.2               | 3.38±0.71$^b$                  |
| FO 1% | 208±23$^a$      | 45.2±5.5$^a$            | 79±15                     | 163±21                      | 78.2±2.3$^b$             | 83±7             | 40.5±1.8                | 2.64±0.82$^b$                  |
| FO 5% | 245±19$^b$      | 76.3±13.3$^b$           | 104±33                    | 169±15                      | 69.0±4.3$^b$             | 81±38            | 26.6±10.3               | 2.38±0.25$^b$                  |

M±SD (n=6), ns = not significant; values with different superscript letters are significantly different (p<0.05). $^1$ See legend to Table 1. $^2$ Intake—fecal excretion. $^3$ (Absorption value/intake)×100. $^4$ Intake—fecal excretion—urinary excretion. $^5$ (Retention/intake)×100.
Table 6. Auricular and facial hyperemia and hemorrhage in rats fed experimental diets (Exp. 2).

| Group     | n  | - | ± | +  | ++ |
|-----------|----|---|---|----|----|
| Cont.     | 6  | 1 | 1 | 2  | 2  |
| +Mg       | 6  | 6 | 0 | 0  | 0  |
| FO 1%     | 6  | 4 | 2 | 0  | 0  |
| FO 5%     | 6  | 5 | 0 | 1  | 0  |

Group names with different superscript letters are significantly different (p<0.05). - , no inflammation. ± , only auricular hyperemia. + , fewer than 10 sites of auricular and facial hemorrhage. ++ , more than 10 sites of auricular and facial hemorrhage. ¹See legend to Table 1.

and P. In the present experiment, we observed the same inhibitory effects of Ca and P on the Mg absorption as done by Brink et al. The increases in both dietary Ca and P concentrations decrease Mg absorption. All rats fed a low-Mg (0.25mg/g diet), high-Ca (10.4 mg/g diet), and high-P (12.0 mg/g diet) diet exhibited auricular and facial peripheral hyperemia and hemorrhage. Mg was absorbed at the amount of about 1.3 mg/day in these rats and serum Mg concentrations were lower in these rats than in the other groups. The incidence of skin problems was suppressed by feeding a Mg-sufficient diet. Therefore, the hyperemia or hemorrhage of rats in this experiment resembled typical Mg-deficient.

Under a dietary mineral condition of low-Mg, high-Ca, and high-P, fructooligosaccharides increased Mg absorption dose-dependently. In addition fructooligosaccharides reduced the occurrence of auricular and facial peripheral hyperemia and hemorrhage.

The rats fed the diet containing 5% of fructooligosaccharides absorbed Mg at about 3.0 mg/day (from day 21 to day 25 of the experiment). This rate of Mg absorption was similar to that of rats fed a Mg-sufficient diet.

Thus, we thought that improving effect of fructooligosaccharides on inflammation of Mg-deficient rats was due to increased absorption of Mg. Ishiguro et al. suggested that decreased serum concentrations of Mg increase histamine secretion from mast cells (6). However, the serum Mg concentrations of rats fed the diet containing 5% of fructooligosaccharides were similar to those of rats fed a control diet. So, in the rats fed the diet containing 5% of fructooligosaccharides, Mg absorption was not enough to raise the serum Mg concentrations. Thus the serum level of Mg is not the main factor in auricular and facial peripheral hyperemia and hemorrhage in rats. In both experiments, the rats that absorbed less than about 2 mg Mg/day exhibited auricular and facial peripheral hyperemia and hemorrhage.

Mg was absorbed from both the small intestine and the large intestine, including the cecum (10–12). Brink et al. concluded that increased intake of Ca and P decreased Mg absorption by the formation of an insoluble Ca-Mg-P complex in the intestinal lumen (9). Schulz et al. reported that levels of Mg²⁺ ions were
increased by decreases in the pH in the intestinal lumen (19). Our previous study showed that there was a significant correlation between the apparent absorption of Mg and the concentration of lactate in the cecum (16).

Scharrer et al. suggested that butyrate affects Mg absorption from the colon (13). We suggest that there are two reasons for the enhancement of the Mg absorption by fructooligosaccharides. The first reason is that a reduction in the pH in the intestine dissolves the insoluble Ca-Mg-P complex and raises the Mg solubility. The second reason is that short-chain fatty acids, such as the products of fermentation of fructooligosaccharides, in the cecum, promote Mg absorption from the colon directly.

Many reports suggest that Mg-deficiency increases risk of several diseases (myocardial infarction (20), diabetes (21), nephrocalcinosis (22), etc.). Intake of fructooligosaccharides might be useful in attempts to decrease the risk of these diseases via increased absorption of Mg.

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