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# Dietary fructose *v.* glucose in rats raises urinary excretion, true absorption and ileal solubility of magnesium but decreases magnesium retention

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**Apparent Mg absorption, that is Mg intake minus faecal excretion, was found to be greater in rats fed on diets containing fructose instead of glucose. This effect of fructose was accompanied by enhanced urinary excretion and diminished retention of Mg. True Mg absorption was then determined with the use of oral and intraperitoneal administration of tracer doses of $^{28}$Mg. True Mg absorption was significantly greater in rats fed on fructose. There was no significant effect of fructose *v.* glucose on faecal excretion of endogenous Mg. It was hypothesized that fructose enhances the solubility of Mg in the ileal lumen and thereby facilitates its absorption. The distribution of Mg between the solid and liquid phases of the ileum was determined in rats fed on either glucose or fructose. Fructose reduced the amount of Mg in the solid phase but raised both the amount and the concentration of Mg in the liquid phase. We conclude that the dietary-fructose-induced stimulation of Mg absorption in rats is caused by a raised solubility of ileal Mg, but the mechanism by which fructose exerts this effect and why it was not associated with a decrease in faecal excretion of endogenous Mg remain unknown. Dietary fructose *v.* glucose did not systematically affect the apparent absorption of Ca and P.**

**Fructose: Magnesium: Absorption: Solubility: Rat**

The amount of sucrose in the human diet, and thus also that of fructose, has increased dramatically during the last decades (Woteki *et al.* 1982). Since fructose *v.* glucose has been shown to raise apparent Mg absorption in humans (Holbrook *et al.* 1989), the increased intake of fructose could enhance Mg status which might be advantageous in relation to prevention of osteoporosis, hypertension, coronary heart disease and cancer (Shills, 1988). However, apparent Mg absorption is not always a valid index of Mg availability from the diet. Apparent Mg absorption is calculated as intake minus faecal excretion and thus includes faecal excretion of endogenous Mg. For instance, replacement of soya-bean protein by casein in the diet of rats has been shown to raise apparent Mg absorption but this was due to a decrease in faecal excretion of endogenous Mg (Brink *et al.* 1992*b*). The mechanism underlying the enhancing effect of fructose on apparent Mg absorption is unknown (Brink & Beynen, 1992), and theoretically it could be due to a decreased loss of endogenous Mg. On the other hand, fructose could raise true Mg absorption. The amount of Mg absorbed depends on the concentration of soluble Mg in the ileal lumen (Brink *et al.* 1992*a*). If and when fructose improves true Mg absorption, it can be hypothesized that this is caused by raising the solubility of Mg in the intestine. *In vitro* experiments have indicated that fructose may form with Mg ions a stable, soluble chelate (Charley *et al.* 1963).

In the present studies with rats, two questions were addressed. First, does fructose *v.*

glucose raise true fractional Mg absorption? We determined true Mg absorption with the use of the radiotracer $^{28}Mg$ which was administered orally or intraperitoneally. From the two retention curves of the administered isotope, true Mg absorption was calculated using the method of Heth & Hoekstra (1965). Faecal excretion of endogenous Mg was calculated as the difference between true and apparent absorption. The second question was whether fructose influences the solubility of Mg in the intestine. We therefore examined the distribution of Mg between the solid and liquid phases of the ileal contents.

## MATERIALS AND METHODS

The experimental protocols were approved by the animal experiments committee of the Department of Laboratory Animal Science, Utrecht University.

### *Animals and housing*

Two separate experiments were carried out; the interval between them was 4 weeks. Outbred, male Wistar rats (Hsd/Cpb:WU; Harlan, Zeist, The Netherlands) aged 6 (Expt 1) or 3 (Expt 2) weeks were used. On arrival the rats were housed in groups of four animals in wire-topped, polycarbonate cages (375 × 225 × 150 mm) with a layer of sawdust as bedding. After 2 (Expt 1) or 6 (Expt 2) d the animals were housed individually in metabolism cages (Tecniplast Gazzada, Buguggiata, Italy). The cages were placed in a room with controlled temperature (20–22°), relative humidity (40–65%) and light cycle (light, 06.00–18.00 hours). After the pre-experimental period (day 0) the rats were divided into two groups of either nine (Expt 1) or twelve (Expt 2) rats each so that body-weight distributions were similar. Each group was assigned randomly to one of the two experimental diets.

### *Diets*

On arrival the rats had *ad lib.* access to a commercial, pelleted diet (RMH-B®; Hope Farms, Woerden, The Netherlands) and tap water. After 2 (Expt 1) or 4 (Expt 2) d the rats were transferred to the glucose diet (Table 1) and demineralized water for another 8 d. Then (day 0), half of the rats were switched to the fructose diet. The composition of the diets is shown in Table 1. The diets contained either glucose (Morsweet 01934; Cerestar, Haubourdin, France) or fructose (Fruchtzucker Art. no. 0781; Südzucker AG, Mannheim/Ochsenfurt, Germany) as the sole source of carbohydrate. Apart from the carbohydrate source the diets were formulated according to the nutrient requirements of rats (National Research Council, 1978). Separate batches of diet were used for each experiment. The purified diets, which were in powdered form, were stored at 4° until feeding. Feed consumption and body weight were recorded weekly.

In Expt 1, food and demineralized water were freely available. For Expt 2 it was considered important to standardize the nutritional state of the rats because ileal digesta were to be collected. Thus, the animals were fed on a restricted basis. Each rat received an amount of food equivalent to 80% of *ad lib.* intake as based on earlier experiences. The food was provided in two meals of identical size, at 09.00 and 17.00 hours. The rats had free access to demineralized water. A period of 7 d (days −7 to 0) was used to accustom the animals to the feeding regimen.

### *Radiotracer study*

For this study the older rats were used because true absorption of Mg in each rat had to be determined over an interval of 14 d. It was expected that the efficiency of Mg absorption would drift with aging to a lesser extent in older rats. $^{28}Mg$ administrations (Expt 1) were performed on days 14 and 23. On day 14, after overnight fasting, five animals from each

Table 1. *Composition of the experimental diets*

| Diet... | Glucose | | Fructose | |
|---|---|---|---|---|
| Ingredients (g/kg) | | | | |
| Glucose | 709·4 | | — | |
| Fructose | — | | 709·4 | |
| Constant components* | 290·6 | | 290·6 | |
| Chemical analysis (mmol/kg) | Expt 1 | Expt 2 | Expt 1 | Expt 2 |
| Calcium | 95 | 115 | 110 | 115 |
| Magnesium | 14 | 11 | 15 | 12 |
| Phosphorus | 113 | 139 | 132 | 139 |

* The constant components consisted of (g/kg diet): casein 151, maize oil 25, coconut fat 25, cellulose 30, $CaCO_3$ 12·4, $NaH_2PO_4.2H_2O$ 15·1, $MgCO_3$ 1·4, KCl 1·0, $KHCO_3$ 7·7, mineral premix 10, vitamin premix 12. The mineral premix consisted of the following (mg): $MnO_2$ 79, $FeSO_4.7H_2O$ 174, $ZnSO_4.H_2O$ 33, $NiSO_4.6H_2O$ 13, NaF 2, $CrCl_3.6H_2O$ 1·5, $SnCl_2.2H_2O$ 1·9, $NH_4VO_3$ 0·2, KI 0·2, $Na_2SeO_3.5H_2O$ 0·3, $CuSO_4.5H_2O$ 15·7, maize meal 9679·2. The vitamin premix consisted of the following (mg): thiamin 4, riboflavin 3, nicotinamide 20, DL-calcium panthothenic acid 17·8, pyridoxine 6, cyanocobalamin 50, choline chloride 2000, pteroylmonoglutamic acid 1, biotin 2, menadione 0·05, DL-alpha tocopheryl acetate 60, retinyl acetate and retinyl palmitate 8 (1200 retinol equivalents), cholecalciferol 0·025, maize meal 9828·125.

dietary group received $[^{28}Mg]MgCl_2$ (Interfaculty Reactor Institute, University of Technology, Delft, The Netherlands) with an extrinsically labelled meal. The remaining four animals of each group were injected with the radiotracer intraperitoneally. To equalize handling and treatment of each rat, the rats receiving the radiotracer orally were injected intraperitoneally with distilled water and the rats that were injected with $^{28}Mg$ were given a meal without the radiotracer. On day 23 the route of administration of radiotracer for each animal was alternated. On the days of radiotracer administration, treatment order of the rats was randomized.

The radioactive meals were prepared by adding 100 $\mu$l 163·2 mM $[^{28}Mg]MgCl_2$ (1·2 GBq/mol) in distilled water to 2 g experiment diet. For intraperitoneal administration the 100 $\mu$l of radiotracer solution was injected. The meals with or without radiotracer were presented to the rats after 16 h without access to food. The meals were consumed within 5 min. Subsequently the intraperitoneal injection was given. Radioactivity in individual rats was counted in a specially designed whole-animal gamma scintillation detector (Barneveld & Van den Hamer, 1984) within 5 min after administration of $^{28}Mg$. Thereafter all rats received their normal diets. For another 4 d the animals were counted for radioactivity every 8 h. All animals were also measured on day 22, 1 d before the second administration of the radiotracer; whole-body radioactivity was found not to differ from background measurements. The efficiency of the whole-body counter for detection of $^{28}Mg$ was 65%, and its stability was monitored by counting a $^{65}Zn$ source.

### *Collection of ileal digesta*

On day 14 (Expt 2), 2·5 h after their morning meal, the rats were anaesthetized by exposure to diethyl ether. Blood was obtained by orbital puncture and the rats were immediately killed by cervical dislocation. The entire small intestine, between stomach and caecum, was removed. The contents in the distal half of the intestine were collected in pre-weighed centrifuge tubes by gently squeezing the intestine between finger and thumb. The ileum was chosen for measurement of Mg solubility because this intestinal segment is most prominent in Mg absorption (Hardwick *et al.* 1991). The intestinal contents were immediately

centrifuged (10 min, 10000 *g*), and supernatant and pellet were separated. The weights of pellet and supernatant were determined. The pH of the supernatant was measured directly (Russell combination pH electrode, Type RS-53; Auchtermuchty, Fife).

### *Collection of faeces and urine*

From day 14–18 and day 23–27 (Expt 1) and day 10–13 (Expt 2), urine and faeces of each rat were collected quantitatively. The cages and tubes for collection of faeces and urine had been washed with phosphate-free detergent and rinsed thoroughly with 0·1 M-HCl and demineralized water. To block bacterial and mould growth, 100 $\mu$l of a 308 mM-$NaN_3$ solution was added daily to the urine collecting tubes.

### *Chemical analyses*

Faeces and ileal pellets were freeze-dried overnight, homogenized and weighed. A sample of 150 mg was ashed at 500° for 17 h and dissolved in 6 M-HCl. Feed samples (750 mg) were processed in the same way. To 50 $\mu$l ileal supernatant, 450 $\mu$l 5% (w/v) trichloroacetic acid (TCA) was added and the TCA-soluble fraction was obtained by centrifugation (2 min, 10000 *g*). Of the urine, 5 ml was acidified with 1 ml 6 M-HCl and centrifuged (10 min, 1200*g*). The supernatant and the remaining nonacidified urine were frozen at −20° until further analysis. Plasma was collected from the heparinized blood samples by centrifugation.

Ca and Mg were determined in feed samples, plasma, urine, faeces and ileal contents in the presence of 41 mM-$LaCl_3$ with a Varian atomic absorption spectrophotometer type AA-475C (Varian Techtron, Springvale, Australia). Phosphate was determined with the use of a commercial test combination (Phosphate, MA-KIT 10 ROCHE; Roche Diagnostics, Basel, Switzerland) and a COBAS-BIO auto-analyser (Hoffmann–La Roche BV, Mijdrecht, The Netherlands). For complete recovery of phosphate from the ashed samples, analysis was performed at least 1 week after dissolution. Urinary creatinine concentrations were determined with the use of a commercial test combination (Creatinine, MA-KIT 10 ROCHE; Roche Diagnostics) and the auto-analyser.

### *Calculations*

The distribution of minerals between the solid and liquid phases of ileal contents was calculated. The pellet obtained after centrifugation of the ileal contents comprises the solid phase contaminated with liquid phase. The weight of the solid phase was obtained after freeze-drying the pellet. The weight of the liquid phase was calculated as the sum of the weight of liquid phase in the pellet (= total pellet weight minus solid phase) and that of supernatant. The concentration of minerals in the supernatant was assumed to be identical to that in the liquid phase. The amount of minerals in the solid phase was calculated as that in the total pellet minus that in the liquid phase of the pellet. Multiplying mineral concentration (mM) in the supernatant by the weight of the liquid phase gave the amount of minerals in the liquid phase.

Apparent absorption of minerals was calculated as mineral intake minus faecal excretion and expressed as a percentage of intake. Retention of minerals was calculated as mineral intake minus faecal-plus-urinary excretion.

True Mg absorption was calculated according to Heth & Hoekstra (1965). Counting measurements were corrected for background and radioisotope decay, and then expressed as a percentage of the administered dose. Plots of the logarithm of percentage radioactivity retention after intraperitoneal and oral $^{28}$Mg administration *v.* time were constructed. The zero-time intercepts were determined by extrapolating the linear parts of the curves. Percentage true absorption was calculated by dividing the intercept of the retention curve for oral $^{28}$Mg by that of the retention curve for intraperitoneal $^{28}$Mg and multiplying by

Table 2. *Growth performance and excreta production of rats fed on diets containing glucose or fructose as the sole carbohydrate source*‡

(Mean values with their standard errors for nine (Expt 1) or twelve (Expt 2) rats per dietary group)

| | Expt 1 | | | | Expt 2 | | | |
|---|---|---|---|---|---|---|---|---|
| | Glucose | | Fructose | | Glucose | | Fructose | |
| | Mean | SE | Mean | SE | Mean | SE | Mean | SE |
| Body wt | | | | | | | | |
| Initial (g) | 224 | 3·2 | 224 | 2·8 | 102 | 1·1 | 102 | 1·2 |
| Final‡ (g) | 289 | 5·3 | 288 | 2·7 | 149 | 1·2 | 149 | 1·4 |
| Feed intake§ (g/d) | 16·7 | 0·2 | 17·2 | 0·2 | 10 | | 10 | |
| Faeces | | | | | | | | |
| Production (g/d) | 1·56 | 0·05 | 1·67 | 0·08 | 0·49 | 0·03 | 0·50 | 0·03 |
| Dry matter (g/kg) | 542 | 21 | 526 | 14 | 791 | 17 | 775 | 12 |
| Urine | | | | | | | | |
| Production (ml/d) | NP¶ | | NP¶ | | 6·3 | 1·3 | 4·6 | 0·8 |
| pH | 8·7 | 0·2 | 7·8 | 0·4 | 8·5 | 0·1 | 7·5* | 0·1 |

NP, not presented.
Mean value was significantly different from that of the glucose group: * $P < 0·05$.
† For details of diets and procedures, see Table 1 and pp. 568–570.
‡ Expt 1, day 28; Expt 2, day 14.
§ In Expt 2 the animals were fed on a restricted basis and thus SE values are not given.
¶ Not presented because urine collection was incomplete due to whole-body counting.

100. This calculation was executed for each animal. True Mg absorption in mg was calculated by multiplying Mg intake by percentage true Mg absorption.

Faecal excretion of endogenous Mg was calculated as true absorption in mg minus apparent absorption of Mg in mg.

### *Statistical analyses*

The equations for the radioactivity retention curves were fitted using the least squares method. Within the dietary groups of Expt 1, the results of radiotracer administration on day 14 *v.* day 23, including the slopes of the retention curves for the same administration route, were not significantly different (Student's *t* test), and thus the data were pooled. The same held for the results of the two balance periods in Expt 1. Differences between group means were evaluated with Student's *t* test when the data were normally distributed and with Wilcoxon's rank sum test when the data were not normally distributed. Data within groups were checked for normality with the Kolmogorov–Smirnov test. The variances of the treatment groups were tested for heterogeneity using Fisher's *F* test. In cases of homogeneity the pooled variance estimates were used, and in cases of heterogeneity we used the separate variance estimates in the Student's *t* test. The level of significance was preset at $P < 0·05$.

## RESULTS

### *Body weight and excreta production*

Within each experiment, final body weight and faeces production did not differ significantly between the dietary groups (Table 2). In Expt 2, urine production by the glucose and fructose groups was similar. The older rats in Expt 1 produced faeces with a higher water

Table 3. *Apparent absorption and urinary excretion of Mg, Ca and P in rats fed on diets containing glucose or fructose as the sole carbohydrate source*†

(Mean values with their standard errors for nine (Expt 1) or twelve (Expt 2) rats per dietary group)

| | Expt 1‡ | | | | Expt 2§ | | | |
|---|---|---|---|---|---|---|---|---|
| | Glucose | | Fructose | | Glucose | | Fructose | |
| | Mean | SE | Mean | SE | Mean | SE | Mean | SE |
| Magnesium | | | | | | | | |
| Intake¶ (mmol/d) | 0·21 | 0·01 | 0·24* | 0·01 | 0·12 | | 0·12 | |
| Absorption (%) | 36·4 | 4·5 | 57·4* | 1·8 | 76·0 | 1·7 | 82·0* | 1·4 |
| Urine (μmol/μmol creatinine (Expt 1) or μmol/d (Expt 2)) | 0·47 | 0·09 | 0·80* | 0·12 | 17·7 | 2·3 | 39·1* | 2·3 |
| Calcium | | | | | | | | |
| Intake¶ (mmol/d) | 1·53 | 0·04 | 1·71* | 0·04 | 1·15 | | 1·15 | |
| Absorption (%) | 25·2 | 5·7 | 34·7 | 3·1 | 64·1 | 1·2 | 62·5 | 2·6 |
| Urine (μmol/μmol creatinine (Expt 1) or μmol/d (Expt 2)) | 0·09 | 0·03 | 0·09 | 0·01 | 5·5 | 0·6 | 8·5* | 1·2 |
| Phosphorus | | | | | | | | |
| Intake¶ (mmol/d) | 1·83 | 0·04 | 2·05* | 0·05 | 1·39 | | 1·39 | |
| Absorption (%) | 58·7 | 3·2 | 71·3* | 1·7 | 83·8 | 0·9 | 84·9 | 1·3 |
| Urine (μmol/μmol creatinine (Expt 1) or μmol/d (Expt 2)) | 10·7 | 1·3 | 14·4 | 1·9 | 352 | 17 | 400 | 14 |

Mean value was significantly different from that of the glucose group: * $P < 0·05$.

† For details of diets and procedures, see Table 1 and pp. 568–570.

‡ Average values for days 14–18 and 23–27.

§ Days 10–13.

¶ In Expt 2 the animals were fed on a restricted basis and thus SE values are not given.

content than the younger rats in Expt 2. Fructose feeding instead of glucose feeding lowered urinary pH.

### *Apparent absorption of minerals*

In Expt 1, Mg, Ca and P intakes were significantly higher in the fructose group. This is explained by the greater group mean food intake and higher dietary mineral concentrations for the fructose group in Expt 1. In Expt 2, in which the rats were given a restricted amount of food, there were no group differences in mineral intake. In the two experiments the fructose diet significantly raised apparent Mg absorption, which was associated with increased urinary excretion of Mg (Table 3). Urinary Mg values in Expt 1 are expressed relative to urinary creatinine because urine collection was incomplete as a result of whole-body counting. Apparent absorption of Ca was not affected by fructose *v.* glucose in the diet. In Expt 2, Ca excretion in urine was raised by fructose. In Expt 1, but not in Expt 2, the apparent absorption of P was significantly enhanced in the fructose group. In Expt 1, mineral absorption efficiencies were markedly lower than in Expt 2.

### *Plasma minerals*

In Expt 2, plasma mineral concentrations were measured. Fructose *v.* glucose caused significantly increased plasma P concentrations (2·32 (SE 0·05) *v.* 2·05 (SE 0·05) mM, *n* 12) but did not alter Ca and Mg concentrations (1·83 (SE 0·02) *v.* 1·82 (SE 0·02) mM and 0·55 (SE 0·02) *v.* 0·59 (SE 0·02) mM respectively).

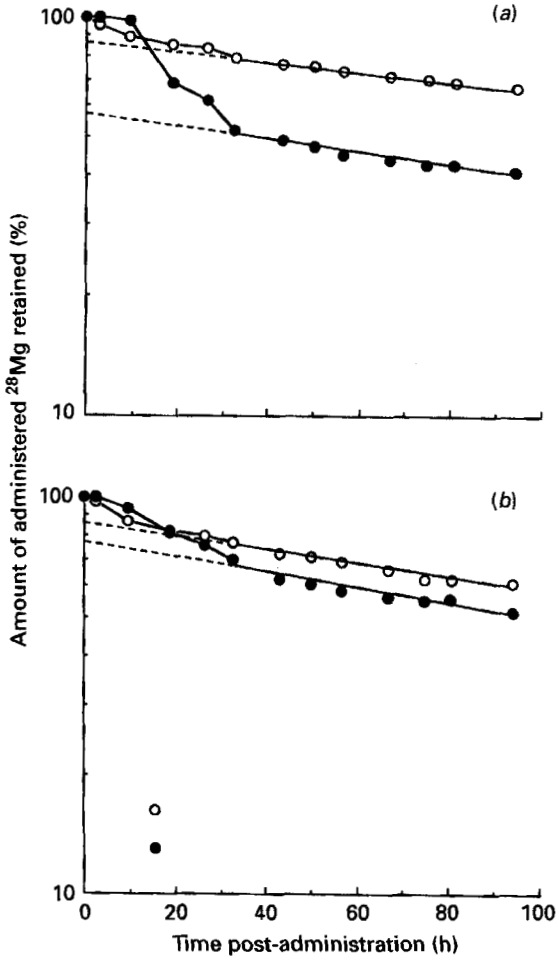


Fig. 1. Retention curves for radioactivity in rats fed on diets containing either glucose (*a*) or fructose (*b*) after oral (●) and intraperitoneal (○) administration of $^{28}$Mg. Data are presented as means for nine rats per dietary group. Linear regression equations for each curve were established for the seven timepoints beyond 33 h post-administration. Glucose diet, intraperitoneal: $\log y = -1{\cdot}15 \times 10^{-3}$ (SE $5{\cdot}7 \times 10^{-5}$)$x + 1{\cdot}93$ (SE $5{\cdot}3 \times 10^{-3}$); oral: $\log y = -1{\cdot}58 \times 10^{-3}$ (SE $8{\cdot}5 \times 10^{-5}$)$x + 1{\cdot}76$ (SE $1{\cdot}6 \times 10^{-2}$). Fructose diet, intraperitoneal: $\log y = -1{\cdot}61 \times 10^{-3}$ (SE $1{\cdot}1 \times 10^{-4}$)$x + 1{\cdot}93$ (SE $7{\cdot}3 \times 10^{-3}$); oral: $\log y = -1{\cdot}86 \times 10^{-3}$ (SE $1{\cdot}0 \times 10^{-4}$)$x + 1{\cdot}88$ (SE $1{\cdot}3 \times 10^{-2}$).

### *True Mg absorption*

For both dietary treatments in Expt 1 the semi-logarithmic retention curves for orally and intraperitoneally administered $^{28}$Mg are presented in Fig. 1. In rats fed on fructose, true Mg absorption was significantly higher than in rats fed on glucose (Table 4). There was no statistically significant carbohydrate effect on the excretion of endogenous Mg.

### *Minerals in ileal digesta*

In Expt 2, rats fed on fructose had a significantly larger liquid-phase volume in their ileal contents than rats fed on glucose (Table 5). Fructose feeding significantly raised the pH of the liquid phase. In rats fed on the fructose diet the amount of Mg in the solid phase was significantly reduced, but that in the liquid phase was raised. The concentration of Mg in the liquid phase was significantly elevated in rats fed on fructose (Table 5). After feeding

Table 4. *Expt 1. Influence of fructose* v. *glucose on true Mg absorption and loss of endogenous Mg in the rat*†‡

(Mean values with their standard errors for nine rats per dietary group)

| | Glucose | | Fructose | |
|---|---|---|---|---|
| | Mean | SE | Mean | SE |
| True absorption (%) | 67·1 | 2·4 | 89·0* | 2·2 |
| Endogenous loss (μmol/d) | 65·8 | 9·6 | 74·1 | 5·5 |

Mean value was significantly different from that of the glucose group: * $P < 0.05$.

† For details of diets and procedures, see Table 1 and pp. 568–571.

‡ True Mg absorption was calculated on the basis of $^{28}Mg$ retention after radiotracer administration on days 14 and 23. Loss of endogenous Mg was calculated from true and apparent absorption, the latter being the average value for days 14–18 and 23–27.

Table 5. *Expt 2. Distribution of minerals between the liquid and solid phases of the ileal lumen in rats fed on diets containing glucose or fructose as the sole carbohydrate source*†

(Mean values with their standard errors for twelve rats per dietary group)

| | Glucose | | Fructose | |
|---|---|---|---|---|
| | Mean | SE | Mean | SE |
| Intestinal content‡ | | | | |
| Solid phase wt (g) | 0·078 | 0·009 | 0·066 | 0·005 |
| Liquid phase wt (g) | 0·314 | 0·030 | 0·414* | 0·017 |
| pH of liquid phase | 7·56 | 0·06 | 7·83* | 0·05 |
| Magnesium | | | | |
| Amount in solid phase (μmol) | 10·4 | 0·7 | 2·5* | 0·5 |
| Amount in liquid phase (μmol) | 2·3 | 0·1 | 4·0* | 0·3 |
| Concentration in liquid phase (mM) | 7·7 | 0·5 | 10·0* | 0·8 |
| Calcium | | | | |
| Amount in solid phase (μmol) | 87·8 | 7·3 | 58·4* | 9·2 |
| Amount in liquid phase (μmol) | 4·5 | 1·2 | 8·2* | 0·6 |
| Concentration in liquid phase (mM) | 13·0 | 2·5 | 20·3* | 1·7 |
| Phosphorus | | | | |
| Amount in solid phase (μmol) | 60·4 | 4·0 | 23·2* | 4·6 |
| Amount in liquid phase (μmol) | 2·6 | 0·5 | 0·6* | 0·1 |
| Concentration in liquid phase (mM) | 8·1 | 1·6 | 1·8* | 0·3 |

Mean value was significantly different from that of the glucose group: * $P < 0.05$.

† For details of diets and procedures, see Table 1 and pp. 568–570.

‡ Ileal digesta was collected on day 14 of the experiment.

the fructose diet, the concentration of Ca in the liquid phase was raised significantly, but that of P was reduced. The total amount of Mg, Ca and P in ileal digesta was lowered in rats given fructose.

## DISCUSSION

In the two experiments, dietary fructose *v.* glucose stimulated the apparent absorption of Mg. This fructose effect is in accordance with other experiments in rats (Brink & Beynen, 1992) and humans (Holbrook *et al.* 1989). The efficiency of Mg absorption was higher in

Expt 2 than in Expt 1, which may either relate to the younger age of the rats used in Expt 2 or to the fact that these rats were given a restricted amount of diet. In Expt 1, older, slowly growing rats were used whereas in Expt 2 the rats grew more rapidly. Nevertheless, the stimulatory effect of fructose on apparent Mg absorption was seen in both experiments. The major objective of this study was to find out whether fructose stimulates true Mg absorption and why it would do so.

As in earlier work (Brink *et al.* 1992*b*), true Mg absorption was measured with the use of oral and intraperitoneal administration of tracer doses of $^{28}$Mg. The initial loss of total body activity after oral administration of $^{28}$Mg is caused by passage of the radiotracer through the intestine and its excretion in faeces. Compared with glucose in the diet, fructose markedly reduced the initial loss of label (Fig. 1). This indicates, as was indeed found after calculation (Table 4), that true Mg absorption was enhanced by fructose. Thus, the observed stimulatory effect of fructose on apparent absorption of Mg reflects true absorption rather than depressed loss of endogenous Mg. In fact, faecal excretion of endogenous Mg was not affected by fructose in the diet.

Up to concentrations of 20 mM there is a direct relationship between soluble ileal Mg and apparent Mg absorption in rats (Brink *et al.* 1992*a*). Thus, we hypothesized that fructose enhances the ileal solubility of Mg which in turn may elevate the amount of Mg that can cross the intestinal epithelium. Indeed, we found that fructose *v.* glucose significantly raised the concentration of Mg in the liquid phase of the ileum. It is not known why dietary fructose raises the amount of soluble Mg in the intestine. Fructose *v.* glucose produced a significantly higher ileal pH, but this would lower ileal Mg solubility (Heijnen *et al.* 1993). Possibly, in the intestine fructose can form with Mg ions a stable, soluble chelate as has been demonstrated under *in vitro* conditions (Charley *et al.* 1963). Fructose *v.* glucose markedly lowered the total amount of Mg in the ileal contents. The basis for this observation is unknown.

The form and site of entry of endogenous Mg into the intestinal tract are unknown. This makes it difficult to speculate on the effect, if any, of dietary fructose on the metabolism of endogenous Mg. Nevertheless, it could be expected that dietary fructose not only raises the intestinal solubility of exogenous Mg, but also solubilizes Mg from endogenous sources and thus stimulates reabsorption of endogenous Mg. However, the fructose-induced stimulation of true Mg absorption was not associated with a decrease in faecal excretion of endogenous Mg, suggesting that endogenous and exogenous Mg are not mixed indistinguishably in the intestine and thus behave differently. Perhaps this relates to the notion that dietary and endogenous Mg enter the digestive tract at different times and do not interact with ingested fructose in the same way. Another possibility could be that fructose enhances the excretion of endogenous Mg while at the same time stimulating endogenous Mg absorption, but this is not likely.

The observed rise in ileal Mg solubility in rats fed on fructose may not be causatively related to the increase in Mg absorption. Fructose feeding raised the volume of the ileal liquid phase, which may be caused by an osmolar action of fructose. This effect of fructose could result in distension of the intestine, causing opening of intercellular junctions and permitting a greater flow. As a consequence, Mg absorption by the paracellular route (Hardwick *et al.* 1991) would be enhanced. However, such a mechanism should also raise the reabsorption of endogenous Mg. Thus, the alternative explanation for the fructose-induced stimulation of Mg absorption also appears at variance with the unchanged faecal excretion of endogenous Mg.

The stimulation of true Mg absorption in rats fed on fructose was accompanied by enhanced urinary excretion of Mg. Dietary fructose *v.* glucose produced a decreased urinary pH, which confirms studies showing that fructose promotes acidosis (Bergström *et*

*al.* 1968; Sahebjami & Scalettar, 1971). The fructose-induced lowering of urinary pH may decrease tubular reabsorption of Mg (McDougal & Koch, 1989) and may thus have contributed to the observed rise in urinary excretion of Mg in rats fed on fructose. Theoretically, it is possible that the stimulation of Mg absorption caused by fructose feeding is secondary to the enhanced loss of Mg in urine, but for such a mechanism there is no metabolic basis (Hardwick *et al.* 1991). Furthermore, acidifying the urine of rats by the feeding of $NH_4Cl$ caused stimulation of urinary excretion of Mg but did not affect apparent Mg absorption (Toothill, 1963; Kaup & Greger, 1990). In Expt 2, retention of Mg was significantly lower after feeding fructose instead of glucose (53·3 (SE 2·1) *v.* 68·9 (SE 2·4) $\mu$mol/d, *n* 12). Thus, the enhanced urinary excretion of Mg in rats fed on fructose was not fully compensated for by the stimulation of Mg absorption. This could imply that the net effect of fructose on Mg bioavailability is a decrease.

The concentration of soluble ileal Ca was also increased by the fructose diet. Apparent Ca absorption was not affected by fructose feeding, which agrees with earlier work in rats (Vaughan & Filer, 1960). Since there is hormonally controlled, active transport of Ca across the intestinal epithelium (Wilkinson, 1976), ileal solubility of Ca may not be a limiting factor for Ca absorption. Apparent absorption of P was stimulated by fructose feeding in Expt 1, but not in Expt 2. However, in Expt 2 the concentration of P in the liquid phase of the ileal content was significantly lowered. Possibly, there is no relation between soluble P concentration in the ileum and its apparent absorption. Alternatively, under the present conditions transport of P across the intestinal epithelium was saturated so that changes in P solubility could not influence absorption.

We conclude that the stimulation of apparent Mg absorption in rats fed on fructose instead of glucose, reflects improvement of true Mg absorption, which is caused by an increase in solubility of ileal Mg. The basis for the fructose-induced rise in the amount of soluble Mg in the intestine and the reason why fructose feeding did not produce a fall of faecal excretion of endogenous Mg remain unknown. Fructose *v.* glucose feeding enhanced urinary excretion of Mg to a greater extent than Mg absorption so that it lowered the retention of Mg.

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