diol (I), cannabinol (II), and tetrahydrocannabinol (II), demonstrated that the marijuana absorption curve was primarily contributed by a combination of these three substances (Table III) rather than by any single cannabinoid or cannabinoid pair. The fact that these constituents occur only in marijuana confers high specificity and diagnostic value on the spectrophotometric analysis.

Test Comparison—Table IV compares the proposed field test with those reported in the literature in terms of reagent requirements, steps involved, and reported interferences.

CONCLUSIONS

The proposed field test was rapid, simple, sensitive and selective. It required only one liquid reagent, which served as the extracting-eluting solvent. Color development and sample extraction were accomplished simultaneously. Colors appeared almost immediately and were easy to interpret against the white background of the microcolumn. The use of a dry absorbent such as alumina offered several advantages since it acted as a diluent for the color reagent and as a medium for the color reaction, and, more importantly, provided a means for differentiating marijuana from other plant materials such as nutmeg and its mace, rhubarb, and *C. sagrada*, whose colored products remained tightly adsorbed to the microcolumn and were not eluted by petroleum ether–methanol mixtures.

The dry microcolumn formulation of Fast Blue B resulted in a reagent that remained stable to ambient conditions such as light and air for periods over 6 months. Since both ends of the glass tube enclosing the microcolumn could be sealed with collodion, adverse effects from moisture, air, and contaminated atmospheres were avoided. The inclusion of differential and confirmatory steps improved the test from a simply presumptive one to a tool with diagnostic capability. None of the plant samples tested by this procedure was confused with marijuana.

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Metabolic Performance and GI Function in Magnesium-Deficient Rats

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Abstract □ A quantitative evaluation of the mass balance and GI motor effects of dietary magnesium deficiency in the adult male Sprague–Dawley rat is described. Seventy-seven animals were used. Both sham control and experimental groups were maintained on a commercial stock laboratory diet *ad libitum* for 30 days, after which the experimental rats were switched for 30 days to the magnesium-deficient diet *ad libitum*, containing a magnesium concentration of 16.2 ppm. Ten rats were used to determine the acetylcholine responsiveness of duodenal muscle segments *in vitro*. In all cases, the segments from the deficient rats were hyperresponsive to a fixed acetylcholine dose. Forty-six rats were used to determine the average intestinal transit rate, which increased significantly in 30-day magnesium-deficient rats. A final series employed 21 rats who were housed in individual metabolic cages. After 5 days on the deficient diet, the average daily fecal pellet counts and fecal weights were significantly reduced. It is concluded that chronic magnesium deficiency is associated with altered GI motor function in the adult male rat.

Keyphrases □ Magnesium deficiency—GI motility, metabolism, rats □ GI tract—magnesium deficiency, motility, metabolism, rats □ Nutritional disorders—magnesium deficiency, GI motility, metabolism, rats

With few exceptions, most of the existing literature concerning the effects of chronic magnesium deficiency in the rat considers the GI tract only as a defective intake route: magnesium deficiency resulting from malabsorption, failure of magnesium conservation in the gut, and loss of fluid and ions *via* the intestines.

Curiously, the effect of magnesium deficiency on the functioning of the GI tract itself was not considered until the motor effects from exposure of the small intestines of rats (1) and humans (2–4) to ionizing radiation were significantly associated with hypomagnesemia. The data also indicated that prophylactic administration of soluble magnesium salts prior to exposure had a mitigating effect in both cases. These observations led to the proposal that the GI symptomatology defined by the acute intestinal radiation syndrome in the rat was the result of acute hypomagnesemia (5, 6).

Another interesting relationship is that between magnesium deficiency and the GI secretory apparatus. The effect of magnesium on gastric structure and function has received some attention, but reported results have been inconsistent. Recent observations (7) showed that dietary magnesium deficiency in rats alters the ratio of chief to parietal cells. Additional evidence (8) indicated that rats treated with parathyroid hormone for 2 weeks exhibited a reduced basal gastric acid secretory rate associated with nonspecific gastric mucosal damage. Veilleux (9) demonstrated that mast cells increase in the duodenum and kidney of magnesium-deficient rats. Unfortunately, these latter studies were not extended to the gastric mucosa. The foregoing results and the finding that the inhibition of calcium-induced acid secretion by magnesium may be caused by blockade of a calcium effect directly on the parietal cell (10) preclude any simple explanation of the effect of magnesium on gastric secretion.

Practically speaking, sufficient attention has not been directed to the effect of magnesium on the GI system. Therefore, the purpose of this study was to determine whether the GI motor functions of rats maintained on a magnesium-deficient diet were different from similar functions in control animals.

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Table I—Composition of the Magnesium-Deficient Diet

Ingredient	Amount, g/kg
Casein	250
Corn oil	50
Cellulose fiber	50
Magnesium-free salt	49.23
Vitamin mixture[a]	20
DL-Methionine	2.99
Dextrose	572.94
Choline chloride	4.84

[a] Standard fortification mix. Produced by Bioserv Inc., Frenchtown, N.J.

EXPERIMENTAL

Animals—The Sprague–Dawley rat was chosen as the experimental animal because a large portion of the relevant literature employed this breed (7, 9, 10). To obviate variations due to body size and estrus stage, only adult male rats weighing 125–150 g were used. The rats were acclimatized in the laboratory for 7 or more days before use. They were kept two per cage in an air-conditioned room under constant temperature (22°) and light cycles and were fed pelleted stock laboratory diet and water *ad libitum*. Some rats were housed in colony cages accommodating six animals. When necessary, coprophagy was minimized by employing cages with wire mesh false bottoms.

Magnesium-Deficient Diet—The basal magnesium-deficient diet[1] (Table I) was assayed[2] to contain ~16.2 ppm of magnesium. The magnesium content of the stock diet was reported by the manufacturer to be 2400 ppm.

Gross Metabolic Behavior—The first series of experiments was designed to determine whether magnesium-deficient rats would show any significant differences in gross metabolic behavior. Twenty-one adult rats were divided into two groups: an experimental group of 11 rats fed the magnesium-deficient diet and a control group of 10 rats fed the stock laboratory diet. With a week of preliminary conditioning, both groups became adjusted to a small individual cage, to a water bottle, and to a pelleted ration.

Both groups were then placed in individual plastic metabolism cages[3] where they consumed individual rations of pelleted stock diet and tap water *ad libitum*. An additional 30 days was allowed for the rats to adjust to the metabolism cages. The experimental group was then switched to the magnesium-deficient diet.

All animals, identified by coded ears, were weighed daily. The unconsumed water and food and urine and feces were collected daily. Water was supplied *ad libitum*, and water intake was measured by recording the water bottle contents. Food intake was more difficult to determine because of spillage. Feeders with narrow openings that permitted only the snout to enter reduced spillage. Food spillage could be further minimized by not filling the attached food containers to maximum capacity.

The usual food supply was 40 g of pelletized chow and 100 ml of water. Both quantities were sufficient for >2 days. Daily food and water intake

Figure 1—*Gross appearance of magnesium-deficient rat.*

[1] Bioserv Inc., Frenchtown, N.J.
[2] Technological Resources, Camden, N.J.
[3] Econo cage 110 with chrome extenders and conventional urinary-fecal separators, Maryland Plastics, New York, N.Y.

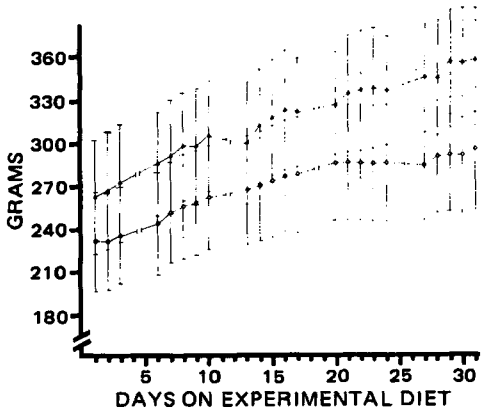

Figure 2—*Time courses of mean body weights from sham control* (▲) *and magnesium-deficient* (○) *rats.*

were determined by differences in the weights and volumes that were supplied the previous day. The collected feces from each animal were counted, weighed, and dried in an oven at 55° over 24 hr. The dry fecal weight was defined as net solid output. The loss in weight of the dry feces represented the fecal moisture weight. Net fluid output was obtained by adding the difference between wet and dry fecal weight in grams to the urine volume excreted in milliliters.

Corrected values for solid and fluid intake were made by subtracting a fixed percentage of the weight in grams of food consumed and directly adding this value to the volume of water consumed in milliliters. For such computations, the manufacturer of the magnesium-deficient diet specified the water content as being 6% by weight. The stock diet water content was 10.5% by weight. Utilization of these percentages and the requirement that weights in grams of water be numerically equal to volumes in milliliters at room temperature contributed to less absolute error than that produced by the inherent variability of the raw data collected.

***In Vitro* and *In Vivo* Intestinal Motor Activities**—The second series of experiments determined whether magnesium deficiency was associated with a change in overall small intestinal peristaltic activity in the rat. Two procedures were used. The classical contractile force measurement of isolated intestinal muscle segments in a tissue bath was used as a screening procedure. This measurement indicates muscular activity at a localized bowel region. The propulsive motility technique, which measures actual transit of intestinal contents over a given period, was used to assess overall small bowel activity.

The *in vitro* experiments were performed on 10 rats after 4 weeks on the diets. Each animal was fasted overnight. The animals were sacrificed by decapitation, followed quickly by the removal of 2–3-cm segments of the duodenum, jejunum, ileum, and descending colon. The responses of small and large intestinal segments to test drugs were recorded isometrically[4]. The particular segments were mounted in parallel in an isolated organ-tissue bath[5] with Tyrodes solution of the following composition (percent): NaCl, 0.8; KCl, 0.02; $CaCl_2$, 0.02; $MgCl_2$, 0.01; $NaHCO_3$, 0.1; NaH_2PO_4, 0.005; and glucose, 0.1. The solution was gassed with 95% oxygen and 5% carbon dioxide and maintained at 38 ± 1°. The pH of the solution varied between 7.4 and 7.6.

Comparison between the reactivity of two uneverted bowel segments was made simultaneously in parallel sets, with the respective segments mounted aborally from top to bottom in the bath chamber. The free proximal portion of the bowel segment was attached to a strain-gauge transducer, with the distal end fixed to the bottom of the bath. The bowel segment was attached by thread so that it was completely submerged in the Tyrodes solution, yet closed at each end so that the lumen was not bathed by the bath solution. No undue tension was applied to the segments during the mounting procedure.

System response amplitude was the measured variable and was always calibrated initially to the same value by means of an initial lever displacement, which was effected by hanging the same calibrating weight on each transducer system in turn. To avoid any differences due to the lever systems–transducers–polygraph channels, the two tested segments were alternated in successive experiments with the corresponding isometric lever force transducer and polygraph channel. The contraction height of the bowel segments after addition of fixed acetylcholine doses

[4] Grass polygraph, Grass Instrument Co., Quincy, Mass.
[5] Phipps and Bird, Richmond, Va.

Table II—Sham Control Regression Equations of Metabolic Performance as a Function of Time [a]

Variable	n	b	$\hat{Y}$	S_b	$S^2_{y \cdot x}$
Food intake					
Days 1–28	14	−0.046	11.42	0.0378	1.3821
Days 29–58	17	−0.084	11.34	0.0240	0.7822
Net water intake					
Days 1–28	14	−0.201	22.70	0.0633	3.8801
Days 29–58	17	−0.114	18.48	0.0404	2.2178
Number of fecal pellets					
Days 1–28	14	−0.836	42.12	0.0875	7.4153
Days 29–58	17	−0.307	27.74	0.0335	1.5212
Fecal wet weight					
Days 1–28	14	−0.021	6.613	0.0225	0.4013
Days 29–58	17	−0.095	8.613	0.0134	0.2460
Fecal dry weight					
Days 1–28	14	+0.033	2.44	0.0180	0.3134
Days 29–58	16	−0.046	4.35	0.0112	0.1599
Net fluid output					
Days 1–28	14	−0.053	11.69	0.0437	1.8437
Days 29–58	16	−0.1041	12.23	0.0129	0.2119

[a] n = number of observations, b = sample regression coefficient, $\hat{Y}$ = zero intercept, S_b = sample standard deviation, and $S^2_{y \cdot x}$ = mean square deviation from regression.

was taken as a measure of the segment's responsiveness. After the segment had contracted in response to acetylcholine, the medium was rinsed once or twice and replaced with fresh Tyrodes. After such procedures, the preparation was allowed to equilibrate for a few minutes before further stimulant was added.

All contraction measurements refer to maximum contraction amplitude observed on the polygram within a few seconds of drug addition to the bath. Acetylcholine was prepared immediately before use by dilution with the same physiological solution used in the bath and was added directly into the bath.

Intestinal transit measurement was made by the procedure of Macht as cited by VanLiere *et al.* (11). Briefly, 1 ml of a standard test meal, consisting of 10% charcoal suspended in an aqueous solution of 10% gum acacia, was fed by intragastric tube to 19, 48-hr fasted magnesium-deficient rats and 27 comparably fasted sham controls. The experimental rats, which had been fed the deficient diet for 30 days, were killed by decapitation in groups of 10 and 9 at 15 and 30 min, respectively, following intubation. The sham control groups for the 15- and 30-min intervals consisted of 13 and 14 rats, respectively.

Following sacrifice, the stomach and intestines were removed. The total small intestine length from pylorus to cecum was measured. The net distance that the charcoal had traversed from the pylorus was measured at the same time. Transit was defined as the distance traversed divided by the total intestine length.

Histopathology—Complete necropsies were done on sacrificed animals. The entire visceral contents were inspected visually to determine the presence of such obvious pathology as focal or generalized lesions and hemorrhage. The following organs and tissues were subjected to microscopic examination: stomach, representative segments of the small and large intestines, liver, heart, kidneys, and skeletal muscle from the thigh. Tissue samples were fixed in formaldehyde solution and embedded in paraffin. Sections were cut at 6 μm and stained with hematoxylin–eosin for routine histopathologic examination. All microscopic examinations were on a blind basis.

Reduction of Data and Interpretation of Results—All recorded values for the metabolic performance studies were normalized to 100 g of body weight to reduce the variations caused by differences in weights. The daily mean of the individual normalized values for each variable studied was plotted for the sham control and experimental groups, and least-squares linear regression lines were fitted through the points. Then, a pooled variances t test of the difference between regression coefficients was performed. This test only allows a determination of the significance of differences between average rates of change of metabolic performance; but if the difference between the rates is significant, it can be assumed that the metabolic performances of the two groups with respect to the variable being studied are not the same.

An F test to check for homogeneity of variance between the two least-squares lines to be compared was performed utilizing the mean square deviation from regression ($S^2_{y \cdot x}$) for each group. The appropriate degrees of freedom associated with each $S^2_{y \cdot x}$ are $n - 2$. If variance homogeneity could be assumed, the following pooled variances t test was used to compare the two regression coefficients:

$$t = \frac{b_1 - b_2}{\sqrt{S^2_{y \cdot x_{pooled}} \left(\frac{1}{S_{y \cdot x_1}} + \frac{1}{S_{y \cdot x_2}} \right)}} \quad \text{(Eq. 1)}$$

with $(n_1 + n_2 - 4)$ degrees of freedom, and where:

$$S^2_{y \cdot x_{pooled}} = \frac{S_{y \cdot x_{pooled}}}{n_1 + n_2 - 4} \quad \text{(Eq. 2)}$$

and:

$$S_{y \cdot x_{pooled}} = S_{y \cdot x_1} + S_{y \cdot x_2} \quad \text{(Eq. 3)}$$

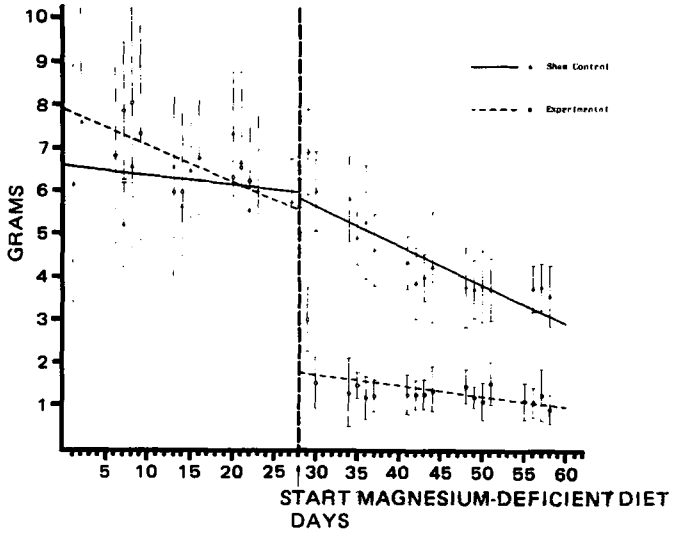

Figure 3—*Time courses of mean fecal wet weights from sham control and magnesium-deficient rats.*

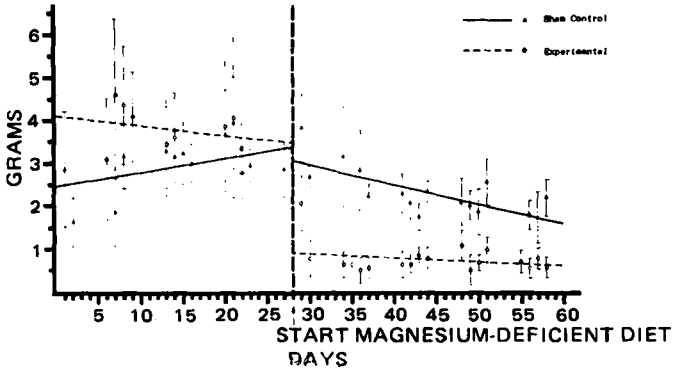

Figure 4—*Time courses of mean fecal dry weights from sham control and magnesium-deficient rats.*

Table III—Magnesium-Deficient Regression Equations of Metabolic Performance as a Function of Time [a]

Variable	n	b	$\hat{Y}$	S_b	$S^2_{y \cdot x}$
Food intake					
Days 1–28	10	−0.165	14.38	0.0983	4.2088
Days 29–58	18	−0.058	9.29	0.0165	0.4064
Net water intake					
Days 1–28	10	−0.209	24.24	0.2692	31.5779
Days 29–58	18	−0.116	16.89	0.0398	2.3490
Number of fecal pellets					
Days 1–28	10	−1.262	53.09	0.2167	20.4579
Days 29–58	18	−0.094[b]	11.59	0.0305	1.3833
Fecal wet weight					
Days 1–28	9	−0.081	7.89	0.0355	0.4042
Days 29–58	18	−0.025[b]	2.47	0.0099	0.1453
Fecal dry weight					
Days 1–28	9	−0.018	4.07	0.0290	0.2696
Days 29–58	18	−0.013[b]	1.32	0.0092	0.1260
Net fluid output					
Days 1–28	9	−0.0743	12.74	0.0511	0.8366
Days 29–58	18	−0.0989	10.844	0.0275	1.1212

[a] n = number of observations, b = sample regression coefficient, $\hat{Y}$ = zero intercept, S_b = sample standard deviation, and $S^2_{y \cdot x}$ = mean square deviation from regression. [b] Statistically significant difference when compared to corresponding values in Table II ($p \leq 0.05$).

Table IV—Effect of a 30-Day Magnesium-Deficient Diet on Small Intestinal Transit Performance and Related Data in 48-hr Fasted Rats [a]

Parameter	Sham Control Group		Experimental Group	
	15 min	30 min	15 min	30 min
Body weight, g	173.69 ± 18.42 (13)	174.32 ± 13.26 (14)	184.30 ± 26.45 (10)	197.56 ± 22.95[b] (9)
Length of small intestine, cm	119.15 ± 11.55	124.07 ± 5.68	116.80 ± 6.66	119.33 ± 4.00[b]
Normalized small intestinal length, cm/100 g of body weight	68.81 ± 4.97	71.53 ± 5.92	64.44 ± 9.25	61.19 ± 7.96[b]
Length of small intestine traversed, cm	54.92 ± 13.62	81.64 ± 12.18	83.00 ± 15.39[b]	90.00 ± 12.48
Percentage of small intestine traversed	46.02 ± 10.02	65.80 ± 9.35	70.83 ± 11.20[b]	75.33 ± 9.40[b]

[a] The ± indicates 1 *SD*; parentheses contain number of animals. [b] Statistically significant difference when compared with the mean values of sham control rats ($p \leq 0.05$).

Pooling increases the degrees of freedom and sensitivity of the test and is possible if the ratios of the mean square deviation from regression are satisfactorily homogeneous. If the F test showed that the ratios of the mean square deviation from regression were not satisfactorily homogeneous, a modified Welch test to test the significance of difference between slopes was used. The following formula expresses this test:

$$t' = \frac{b_1 - b_2}{\sqrt{\frac{S^2_{y \cdot x_1}}{x_1^2} + \frac{S^2_{y \cdot x_2}}{x_2^2}}} \qquad \text{(Eq. 4)}$$

The approximate degrees of freedom for t' was calculated using the following formula:

$$df = \frac{\left(\frac{S^2_{y \cdot x_1}}{x_1^2} + \frac{S^2_{y \cdot x_2}}{x_2^2}\right)^2}{\left(\frac{1}{df_1}\right)\left(\frac{S^2_{y \cdot x_1}}{x_1^2}\right)^2 + \left(\frac{1}{df_2}\right)\left(\frac{S^2_{y \cdot x_2}}{x_2^2}\right)^2} \qquad \text{(Eq. 5)}$$

For propulsive motility, a simple Student t test was used to compare the significance of the mean differences. In all statistical tests, significance was tested at the 5% level.

RESULTS

The progressive magnesium deficiency syndrome was observed in the deficient animals: hyperemia of the skin, nose, ears, footpads, and tail appeared on the 5th day and progressed to weeping, crusting lesions (Fig. 1).

The magnesium-deficient rats were inactive but irritable when stimulated with a blast of air. At the end of the 2nd week, the appetite of the animals improved considerably, although irritability became increasingly prominent. The weight curves of the sham control and magnesium-deficient groups are given in Fig. 2. The deficient group rats lagged in the rate of weight increase compared to the sham control group until the 3rd week, when they ceased to gain weight.

Results of changes in food intake, net water intake, and fecal and urinary excretions are given as daily average values for the rats fed the magnesium-deficient diet. After 5 days, the average daily wet fecal weight (Fig. 3), dry fecal weight (Fig. 4), and fecal pellet count (Fig. 5) were significantly less for the magnesium-deficient animals. At no time could it be concluded that differences existed in daily average food intake (Fig. 6), net water intake (Fig. 7), or net fluid output (Fig. 8). The regression equations fitted to the data points in Figs. 2–7 are presented in Tables II and III.

In all cases, muscle strips from the small intestine of magnesium-deficient animals showed a greatly increased contraction strength in response to a test acetylcholine dose (Fig. 9). This response was present 4 weeks following initiation of the magnesium-deficient regimen. Although not depicted, muscle segments from the colons of magnesium-deficient

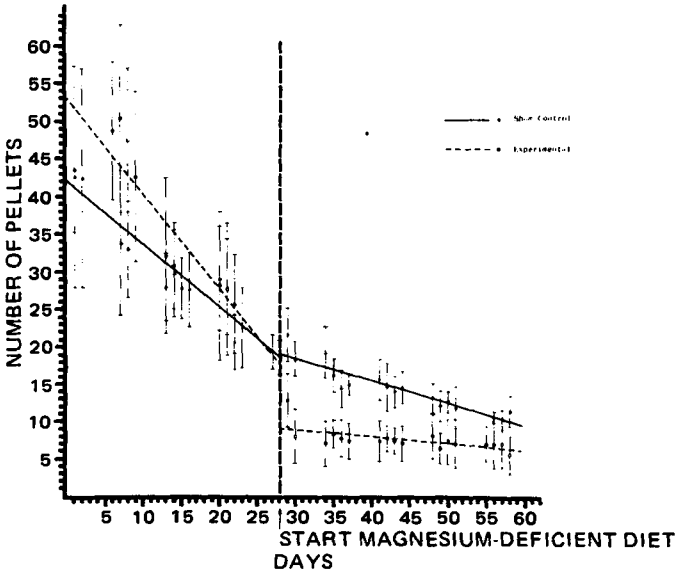

Figure 5—*Time courses of mean fecal pellet outputs from sham control and magnesium-deficient rats.*

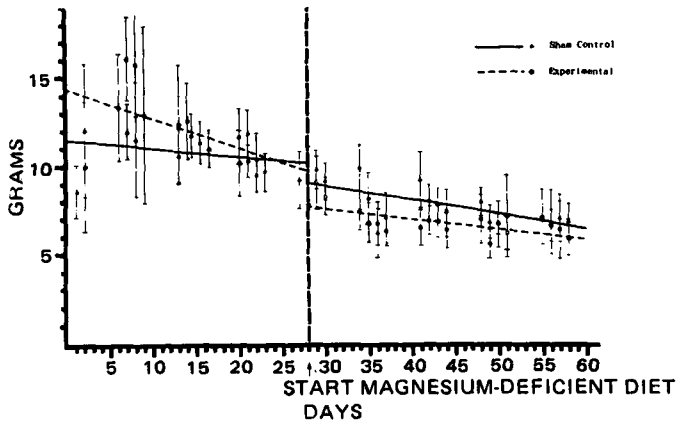

Figure 6—*Time courses of mean daily food intakes from sham control and magnesium-deficient rats.*

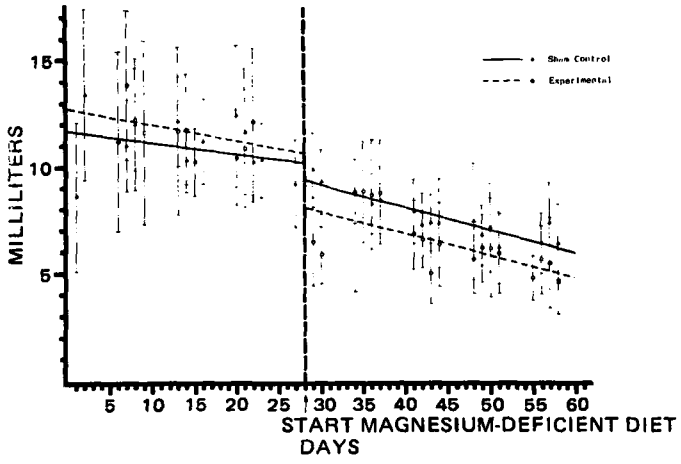

Figure 8—*Time courses of mean net fluid outputs from sham control and magnesium-deficient rats.*

animals either failed to show increased contractile force to acetylcholine or showed a decreased response. As seen in Table IV, statistically significant increases in the small intestinal transit rate were noted in the 4-week magnesium-deficient animals when contrasted to the sham controls. The mass transit data indicate that the effects noted in isolated duodenal muscle segments probably are generalized to other regions of the small intestine as well.

All animals carried for 30 days on the magnesium-deficient diet displayed significant morphological differences from the sham controls in the heart, liver, skeletal muscle, kidney, and gastric mucosa. In all magnesium-deficient rats of this group, there were focal degenerative and inflammatory changes in the myocardium. In the liver, areas of focal degeneration and increased vacuolization were noted. In the magnesium-deficient group, degenerative and inflammatory changes appeared in the voluntary muscles. The lesions consisted chiefly of a degenerative change and associated muscle bundle swelling, with an accompanying loss of sarcolemmal nuclei.

In the stomach, alterations were seen in the mucosa. These changes included occasional dilation and engorgement of small vessels and enlargement of gastric pits. Elsewhere, chief cells appeared reduced in number and compressed by swollen adjacent parietal cells. However, the most consistent abnormalities noted were in the kidneys. The kidneys of all magnesium-deficient rats showed large calcium deposits in the medullary tubule lumina, with a preponderance near the corticomedullary junction. These deposits were laminated, the affected tubules were dilated, and their epithelium was flattened.

DISCUSSION

The pathophysiological findings of magnesium deficiency in the rat were in good agreement with numerous previous studies (12–16). Hyperexcitability, cutaneous hyperemia, general fur loss, shaggy coat, ringed eye dermatitis, encrusted nostrils, and signs of early diarrhea were consistent findings. Histological findings also were in agreement with previously reported data to an extent that they confirmed that hypomagnesemia existed in the experimental rats (15).

However, certain metabolic effects were not found. For example, unlike the findings of Orent *et al.* (17), the average weight of the magnesium-deficient group never fell below the initial average weight of this parameter; and although the average rate of weight increase was less than that of the control group, the difference was not significant. Such inconsistencies may have been due to the use of different strains and ages of rats and to variations in the formulations of the deficient diets, particularly in earlier days when it was more difficult to make an accurately defined diet with simple magnesium deficiency alone.

Fecal wet weight and pellet count performance of the deficient group were reduced while the mean small intestinal transit fraction increased. These results are in agreement with *in vitro* studies which showed that isolated duodenal muscle segments were hyperreactive to a cholinergic stimulus, while no differences in acetylcholine reactivity were apparent in the colons of the deficient group. Upon necropsy, the colons of the magnesium-deficient rats were visually observed to be enlarged.

It is concluded that, in the rat, GI motor activity and, to some degree, excretory performance are affected by chronic magnesium deficiency. Frank liver damage suggests that the function of this organ may become impaired. Thus, the function of the digestive system is affected to such an extent that it cannot be regarded merely as a conduit for magnesium intake, excretion, and conservation.

The increased small intestinal transit rate in the deficient state suggests that a regeneratively destructive response may exist in this organ in response to magnesium deficiency: intake restriction results in impaired ability to absorb and/or conserve magnesium in the small bowel. The visual appearance of distended colons in deficient rats is consistent with the reduction in fecal water content in these animals; a condition of partial constipation would be consistent with efforts to conserve magnesium by increasing colonic residence time. This hypothesis is attractive in the particular case of the rat where, under normal circumstances, approximately 70% of the total magnesium absorption occurs in the cecum and ascending colon (18).

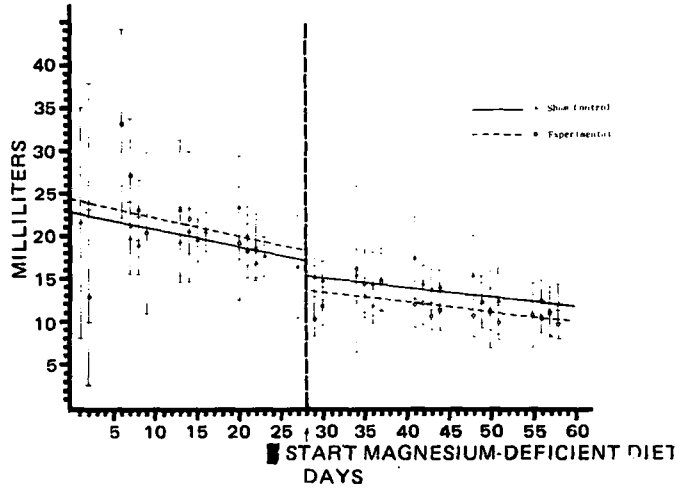

Figure 7—*Time courses of mean net water intakes from sham control and magnesium-deficient rats.*

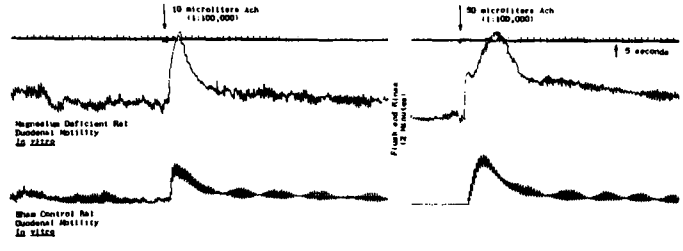

Figure 9—In vitro *motility responses of small intestinal muscle strips from sham control and magnesium-deficient rats.*

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Absorption and Penetration of Dinoprost (Prostaglandin $F_{2\alpha}$) and Dinoprost Methyl Ester into Perfused Mesenteric Circulation in Rats

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Abstract □ The absorption of dinoprost (prostaglandin $F_{2\alpha}$) and its methyl ester in rat jejunum was studied. A 22-cm segment of rat jejunum was cannulated at both ends and connected to an oscillating perfusion pump system. The mesenteric vasculature supplying this isolated segment also was cannulated and perfused with Kreb's bicarbonate buffer with dextran. Solutions of ^{3}H-dinoprost or its methyl ester were introduced into the lumen and oscillated through the segment. The disappearance of radioactivity from the lumen and the appearance of radioactivity in the vascular perfusate were monitored. The metabolite patterns in the vascular perfusate were analyzed by TLC. A lag between the time the drug disappeared from the lumen and the time it appeared in the mesenteric circulation was detected. This lag was longer for the methyl ester than for the free acid, even though the ester disappears from the lumen faster than does the free acid. Upon removal of dinoprost from the gut lumen, a gradual decrease in the amount of drug appearing in the mesenteric circulation could be detected. However, with the ester, a slight increase could be observed for ~0.5 hr, followed by a decrease. Metabolism by the gut wall appears to be greater for the ester than for the acid. The results suggest that, although the ester disappears from the lumen more quickly than does the acid, it actually penetrates to the blood at a slower rate and undergoes greater metabolism.

Keyphrases □ Dinoprost—absorption and penetration, mesenteric circulation, rats, metabolism □ Dinoprost—methyl ester, absorption and penetration, mesenteric circulation, rats, metabolism □ Pharmacokinetics—dinoprost and dinoprost methyl ester, mesenteric circulation, rats □ Prostaglandins—dinoprost, dinoprost methyl ester, absorption and penetration, mesenteric circulation, rats, metabolism

Prostaglandins have been viewed as potential panaceas almost since the moment of their discovery. Much research has been devoted to their endogenous and exogenous functions in various organs and tissues, and various roles have been assigned to this family of compounds. Because of their ubiquity and functional diversity, prostaglandins are appealing prospects as therapeutic agents for many conditions. However, before this potential can be realized, a practical administration route must be developed. The most desirable route would be oral. When dinoprost (prostaglandin $F_{2\alpha}$) or its methyl ester are administered orally, the major absorption site appears to be the small intestine since there is little absorption from the stomach[1]; although there can be some absorption by the large intestine, most of the compound disappears before reaching this area (1).

The present study was designed to gain insight into intestinal absorption of prostaglandins: their disappearance from the intestinal lumen, their appearance in the mesentric circulation, and the extent of their metabolism in the intestinal wall. Investigations into the rates of prostaglandin disappearance from the intestinal lumen (1, 2) have been based on studies of prostaglandin disappearance from the mucosal side of the intestine. From such studies, Ho and coworkers (3, 4) proposed that dinoprost absorption is diffusion dependent and that its metabolism may affect the absorption rate. In addition, previous work[2] showed that the lymphatic system does not play a role in the transport of orally administered prostaglandins.

This study looked at the serosal side of the intestine *via*

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