Strontium Uptake in Rats on Alginate-Supplemented Diet

Abstract. *Rats were fed a basic diet supplemented with sodium alginate and with tracer amounts of strontium-85 and calcium-45. Absorption of strontium was always inhibited by the alginate to a greater extent than absorption of calcium. Discrimination against strontium was greatest in alginate containing a high proportion of guluronic acid.*

Alginic acid is composed of one or more polyuronides containing guluronic and mannuronic acids in a proportion that depends on the botanical source of the alginate (*1*). When a standard laboratory diet is supplemented with sodium alginate, uptake of strontium in rats is reduced much more than uptake of calcium (*2*). Since it is generally supposed that alginates are not absorbed from the digestive tract, this observation is of considerable interest in the consideration of possible remedial measures to reduce Sr^{90} uptake in a human population exposed to large dietary amounts of Sr^{90}. This is a preliminary report on the relative uptake of dietary Sr and Ca in rats when alginates of various guluronic:mannuronic ratios were used to supplement basic laboratory diet.

Fifteen female albino rats, 8 weeks old and divided into five groups of three, were fed a basic diet containing 0.7 g percent Ca for 8 days. Distilled water containing 0.15 μc each of approximately carrier-free Ca^{45} and Sr^{85} was mixed to a paste-like consistency with the daily ration. The diet for four of the groups was identical with that for the fifth (the controls) except that it was supplemented with 10 percent sodium alginate as either Manucol SS/LD, Manucol SA/LD, or Manucol SA/LM, or with calcium alginate. Each rat was fed 16 g daily, kept in a separate metabolism cage, and given distilled water ad libitum. Separate bulked collections of urine were made from each rat throughout the 8-day experiment. When the rats were subsequently killed, the skeleton was separated from soft tissue and radioactivity assays were made for both tracers in whole skeleton and bulked urine.

Skeletal retention and urinary output of Ca^{45} for rats receiving the three Manucol supplements were probably not significantly less than for the controls (Table 1). For rats receiving the calcium alginate supplement, however, specific activity of the dietary Ca was reduced 1.7 times, since the calcium intake was raised from 0.7 to 1.2 g percent; this reduction would be expected to reduce absorption and, consequently, skeletal retention of Ca^{45}.

Skeletal retention and urinary excretion of Sr^{85} was least for rats given Manucol SS/LD, and absorption of the radioactive dose (assessed as urinary output plus skeletal retention) was some 4.5 times less for rats on this supplement than for the controls. This result encouraged us to repeat the experiment with two different levels of Manucol SS/LD.

The basic diet (0.91 g percent Ca, 3.4 mg percent Sr) was again powdered and mixed with two different levels of the dry Manucol SS/LD before the addition of Sr^{85} and Ca^{45} markers in distilled water. Three groups, each of 4 rats (8.5 weeks old), were fed for 24 days so that all groups had a constant dietary intake (16 g/day per rat). The two experimental groups received daily additives of 0.8 and 1.6 g of the alginate supplement. All animals were kept in metabolic cages and bulked urine was separately collected from each. When the rats were subsequently killed, blood was drawn by cardiac puncture and gut and carcass were separated from the skeleton. Radioactivity assays for Sr^{85} and Ca^{45} in urine, feces, carcass, skeleton, and plasma showed that the mean recovery of activity was between 95.9 and 99.3 percent of the total oral dose for both nuclides.

The results (Table 2) show that:

1) The experimental : control ratio of mean skeletal retention of Sr^{85} by rats on the 9-percent sodium alginate (Manucol SS/LD) supplement closely agreed with that for the same supplement in the first experiment (Table 1).

2) There was no evidence of "saturation" below 10-percent alginate supplementation.

3) The experimental : control ratio of mean skeletal retention of Ca^{45}, again greater than unity, indicated that suppression of uptake of Sr^{85} was not accompanied by a similar effect on Ca^{45}.

4) The concentration of Sr^{85} in plasma was about 3 times lower in rats on the higher alginate supplement than in the controls; there was no such change in the concentration in plasma of Ca^{45}. We conclude that the decreased skeletal retention was accompanied by decreased absorption of Sr^{85},

Table 1. Calcium-45 and strontium-85 (percentages of the total oral doses) in bulked urines and skeletons of 8-week-old rats fed the various supplements for 8 days.

Supplement	Rat (No.)	In urine (%)		In skeleton (%)		In urine + skeleton, means (%)	
		Ca^{45}	Sr^{85}	Ca^{45}	Sr^{85}	Ca^{45}	Sr^{85}
None	1	0.69	2.00	20.0	5.16	20.7	7.49
None	2	.59	1.95	21.1	5.64		
None	3	.69	2.06	19.1	5.66		
Manucol SS/LD	4	.41	0.44	29.3	1.37	27.5	1.68
Manucol SS/LD	5	.45	.45	25.7	1.19		
Manucol SS/LD	6	.34	.36	26.3	1.21		
Manucol SA/LD	7	.45	.75	27.4	2.97	22.3	3.13
Manucol SA/LD	8	.47	.74	18.1	2.00		
Manucol SA/LD	9	.48	.69	20.0	2.22		
Manucol SA/LM	10	.79	.94	25.2	2.79	23.9	3.48
Manucol SA/LM	11	1.10	1.07	23.0	2.47		
Manucol SA/LM	12	0.50	0.77	21.1	2.39		
Calcium alginate*	13	1.32	1.55	12.4	1.96	14.9	3.60
Calcium alginate*	14	1.17	1.48	13.6	2.15		
Calcium alginate*	15	0.83	1.10	15.5	2.54		

* Intake of Ca increased from 0.7 to 1.2 g per 100 g of diet.

Table 2. Mean percentages (of total oral dosage) of Ca^{45} and Sr^{85} in bulked urine, skeleton, and plasma of 8.5-week-old rats fed an alginate supplement for 24 days. Standard errors of means for four rats are in parentheses.

Supplement	In urine (%)		In skeleton (%)		In plasma (%/liter)		In urine + skeleton (%)	
	Ca^{45}	Sr^{85}	Ca^{45}	Sr^{85}	Ca^{45}	Sr^{85}	Ca^{45}	Sr^{85}
None	0.95 (0.01)	2.58 (0.04)	16.77 (1.04)	3.91 (0.18)	2.3	0.50	17.72	6.49
4.5% Manucol SS/LD	.68 (0.03)	0.92 (0.03)	19.64 (0.81)	1.45 (0.06)	2.8	.22	20.32	2.37
9.0% Manucol SS/LD	1.17 (0.05)	.74 (0.03)	17.87 (1.3)	1.01 (0.07)	2.3	.17	19.04	1.75

without corresponding decrease in absorption of Ca^{45}. This apparent difference in effect of sodium alginate on absorption of calcium and strontium probably does not reflect solely the relative ion-binding of alginate with Sr and Ca, since the observed difference in binding is quite small (*3*).

Ratios of guluronic acid to mannuronic acid, based on Manucol SS/LD at 1.0 (five determinations), were determined at: Manucol SA/LD, 0.36 (four determinations); Manucol SA/LM, 0.43 (four determinations); and calcium alginate, 0.45 (two determinations). We conclude that a sodium alginate with a high guluronic : mannuronic ratio more effectively reduces uptake of radioactive Sr from the diet.

Our results confirm that sodium alginate, unlike most other therapeutic agents used to reduce uptake of radioactive strontium, does not interfere with calcium absorption; they also show that even greater protection from such strontium is afforded by supplementing the diet with alginate containing a higher proportion of guluronic acid.

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Reference and Notes

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Intestinal Alkaline Phosphatase: Regulation by a Strain-Specific Factor in Mouse Milk

Abstract. *Two inbred strains of mice show a threefold difference in duodenal phosphatase activity at 11 days of age. When half-litters of the two strains are interchanged between the two mothers on the day of birth, enzyme activity in young of the low-activity strain is unaffected at 11 days by the source of milk, but is significantly reduced in high-activity young nursed by a low-activity mother.*

Some enzymes that have been studied in higher organisms appear to be constitutive in the sense that their formation is not "electively provoked by a substrate," the level of activity characteristic of a tissue or organ rather being genetically determined (*1*). Nevertheless, an increasing number of enzymes are known to be regulated by mechanisms that are not directly genetic. Tryptophane pyrrolase of rat liver is affected by substrate and by glucocorticoids (*2*), the effect of substrate being apparently to stabilize the enzyme (*3*). Adrenocortical hormones raise the levels of several enzymes, including alkaline phosphatase (*4*) and invertase (*5*) in the small intestine of the mouse and rat and gluconeogenic enzymes in the rat liver (*6*). Creatine represses development of arginine-glycine transaminidase in the liver of the chick embryo (*7*), and dietary constituents regulate threonine dehydrase activity in rat liver (*8*).

Alkaline phosphatase activity of the duodenum of the mouse has been extensively investigated (*9*). Preliminary studies with eight inbred strains revealed marked differences in intestinal phosphatase activity. The highest-activity strain (SWR/J; Jackson Laboratory) has activity almost three times that of the lowest-activity strain (LAS) (Swiss; maintained in this laboratory since 1949), and this difference has been consistently maintained through six generations during our investigation. Although a genetic basis is thus indicated, differences in amount or quality of milk produced by the two strains may influence phosphatase activity during nursing stages. We have found that high-activity-strain (HAS) milk does contribute to phenotypic expression of the HAS genotype. This is a heretofore unrecognized mode of enzyme regulation.

Because duodenal phosphatase begins to be affected by endogenous corticoids at about 13 days (*9*), we studied 11-day-old mice. When two litters were born on the same day, one to HAS (SWR/J) and one to LAS (local Swiss) parents, half of each litter was switched to the other mother on the day of birth; they were readily accepted by the foster mothers and gained weight as rapidly as their foster siblings. At 11 days the young of both litters were decapitated. An 8-mm piece of duodenum, just distal to the entrance of the common bile duct, was excised and homogenized in iced distilled water in a Ten Broeck grinder. The homogenate was assayed for protein content (*10*) and phosphatase activity against phenylphosphate (PhP) and beta-glycerophosphate (bGP) under optimal conditions for each substrate (*11*).

Mixtures of homogenates of HAS and LAS duodenum yielded average phosphatase values, indicating that the strain differences are not due to dissociable activators or inhibitors; this conclusion had been shown to hold for differences in phosphatase levels between infant and juvenile stages (*12*). It had also been shown that litter size (and consequent availability of milk) does not influence phosphatase activity (*13*); this fact we verified for both strains by reducing numbers in litters from ten to three at birth: there was no effect on enzyme level at 11 days, even though members of small litters weighed about 50 percent more than members of large litters.

When the infants of one strain were nursed by mothers of the other, however, striking differences appeared. Duodenal phosphatase was unaffected in LAS mice fostered by HAS mothers (Table 1). But in the opposite situation two changes occurred: (i) phosphatase activity was significantly lower in HAS young when they were raised by LAS mothers than when raised by their own mothers; (ii) activity on PhP was more severely affected than activity on bGP, so that the PhP : bGP ratio dropped. This ratio (which expresses the amount of P cleaved from PhP to that cleaved from bGP under optimal conditions for each substrate) is proportional to level of activity during the course of

Table 1. Duodenal alkaline phosphatase activity (micrograms of phosphate per milligram of protein per 30 minutes) in 11-day-old mice of both strains nursed by mothers of both high-activity (SWR/J) and low-activity (local Swiss) strains. Five litters of ten mice each were used in the exchanges of offspring between mothers. PhP, phenylphosphate; bGP, beta-glycerophosphate; LAS, low-activity strain; HAS, high-activity strain.

Mother	Phosphatase against:		PhP:bGP
	PhP	bGP	
	LAS offspring *		
LAS	546	700	0.78
HAS	561	698	0.80
	HAS offspring †		
HAS	1792	1723	1.04
LAS	1087	1197	0.91

*Difference between the two mothers not significant. † $P < .001$ for all three columns.