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The Effect of Sodium Alginate on the Absorption of Strontium and Calcium in Human Subjects

JOAN HARRISON, M.D., K. G. McNEILL, M.A., D.Phil.
and A. JANIGA, *Toronto*

The effect of sodium alginate on the gastrointestinal absorption of the tracers strontium-85 and calcium-47 was investigated in 19 human subjects. The tracers were administered orally with 100 mg. of a calcium carrier—calcium chloride. At the same time, sodium alginate was given in a commercial jelly. The seven-day per cent retentions of tracers were measured with a whole-body counter. After one month, the experiments were repeated without alginate so that each subject acted as his own control. Fifteen volunteers were given 1.5 g. of alginate, two were given 3.0 g. and two 0.3 g. 1.5 g. of alginate reduced the absorption of strontium by a factor of two with no significant effect on calcium absorption. The smaller dose of alginate (0.3 g.) appeared to have no effect on strontium or calcium absorption and the larger dose (3.0 g.) had no greater effect than the 1.5 g. dose.

L'effet de l'alginate sodique sur l'absorption gastro-intestinale des éléments marqués strontium-85 et calcium-47 a été étudié sur 19 êtres humains. Les radio-isotopes ont été administrés *per os* avec du chlorure de calcium, comme porteur de calcium. En même temps, on a donné l'alginate de sodium dans une gelée ordinaire du commerce. Les pourcentages de rétention des radio-isotopes après sept jours ont été mesurés au moyen d'un anthropogammamètre. Au bout d'un mois, on a renouvelé les expériences, cette fois sans l'alginate, de sorte que chaque sujet était son propre témoin. On a donné à 15 volontaires 1.5 g. d'alginate, à deux autres 3.0 g. et à deux autres encore 0.3 g. d'alginate. Une dose de 1.5 g. a permis de réduire l'absorption de strontium par un facteur de deux, sans modifier sensiblement l'absorption de calcium. La plus faible dose (0.3 g.) d'alginate n'a eu aucun effet sur l'absorption du strontium ou du calcium et la forte dose (3.0 g.) n'a pas exercé un effet plus marqué que la dose de 1.5 g.

IN recent years, the potential radiation hazard from strontium-90 has received considerable attention. This isotope has a relatively long radioactive half-life, and like the chemically similar element, calcium, it is absorbed from the gastrointestinal tract and retained in bone.[1]

Although the current risk from bomb fall-out is negligible, a therapeutic regimen for reducing either the body burden of strontium-90 or the uptake of this isotope would be of value, particularly in the event of a serious reactor accident. Attempts to remove strontium from bone have not proved successful.[2] Skoryna, Paul and Waldron-Edward[3-7] have shown, however, that in rats the gastrointestinal absorption of strontium is significantly reduced by the administration of sodium alginate and with a dose of alginate which reduced the strontium absorption by 50% there was very little effect on calcium absorption. In one human subject, Hesp and Ramsbottom[8] showed that sodium alginate reduced strontium absorption by a factor of 9. Sodium alginate and alginic acid in gram quantities do not appear to affect calcium absorption in humans.[9, 10]

The present study was carried out to investigate the effect of sodium alginate on the simultaneous absorption of both strontium and calcium in 15 human volunteers, using a double tracer of Sr^{85} and Ca^{47}.

METHOD

The radioisotopes Ca^{47} and Sr^{85} were supplied by Abbott Laboratories. The specific activity for Ca^{47} was more than 10 μc./mg. stable calcium and for Sr^{85} was more than 1 mc./mg. stable strontium. The double tracer was administered orally as an aqueous solution of $CaCl_2$ containing about 2 μc. Ca^{47}, 2 μc. Sr^{85} and 100 mg. of stable calcium.

The alginate was administered as an experimental jelly supplied by Salada Foods Ltd. Each portion contained 1.5 g. sodium alginate, 37.5 g. sugar, 1.6 g. citric acid, 0.73 g. sodium tripolyphosphate, 0.2 g. calcium carbonate, 0.05 g. magnesium carbonate, and water. The calcium was sufficient to exceed the binding capacity of the alginate. Each portion contained about a cupful of jelly. The sodium alginate was extracted from the giant Pacific Ocean kelp, *macrocystis pyrifera,* and is said to have a ratio of L-guluronic acid to D-mannuronic acid of approximately 3:7.

The experiment was carried out on 15 healthy volunteers from the University of Toronto and the Toronto General Hospital staff. The jelly was ingested three hours after the last meal and at least one-half hour before the next meal. The tracer solution was given immediately after the jelly was eaten. Seven days later, the whole-body retention of Ca^{47} and Sr^{85} was determined by a method described below.

After an interval of at least one month, the experiment was repeated in the same subjects, using the double tracer without the experimental jelly, so that each subject acted as his own control.

In addition to the main experiment, the effect of varying amounts of alginate jelly on tracer absorption was briefly investigated. Two subjects were given twice as much jelly (3.0 g. alginate) and two subjects given one-fifth the standard portion of jelly (0.3 g. alginate). Experiments were also carried out using sodium alginate contained in a capsule.

From the Departments of Medicine and Physics, University of Toronto.
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Address reprint requests to: Dr. Joan E. Harrison, Department of Physics, University of Toronto, Toronto 5, Ontario.

TABLE I.—WHOLE-BODY RETENTION OF Ca^{47} AND Sr^{85} AT SEVEN DAYS
(% dose)

	Subject	Ca^{47} Retention Alginate	Ca^{47} Retention Control	Sr^{85} retention Alginate	Sr^{85} retention Control	Sr/Ca retention ratio Alginate	Sr/Ca retention ratio Control
1.5 g. alginate	1	37.2	20.4	3.7	5.9	.10	.289
	2	14.0	20.4	1.7	4.3	.121	.210
	3	35.0	32.3	6.7	10.1	.191	.313
	4	21.0	36.6	2.8	10.8	.133	.295
	5	20.3	26.4	2.1	7.0	.103	.265
	6	27.2	35.7	4.3	9.3	.158	.260
	7	31.6	18.6	3.6	4.3	.114	.231
	8	10.7	13.8	1.4	2.8	.130	.203
	9	14.7	32.5	1.4	8.8	.095	.271
	10	16.7	16.7	4.6	5.1	.275	.305
	11	12.0	22.4	1.8	7.4	.150	.330
	12	21.0	17.0	3.6	5.3	.171	.312
	13	20.5	26.6	3.5	6.8	.171	.256
	14	9.6	31.4	1.1	8.1	.115	.258
	15	15.3	22.0	2.5	5.7	.163	.259
Mean		20.5	24.9	3.0	6.8	.146	.270
Standard deviation		± 8.7	± 7.4	±1.5	± 2.3	±.046	±.038
3 g. alginate	16	6.5	12.0	1.2	4.5	.185	.375
	17	11.1	16.0	1.6	5.0	.144	.313
0.3 g. alginate	18	25.0	24.5	5.3	6.4	.212	.261
	19	17.0	33.0	4.0	9.1	.235	.276

The whole-body retention measurements of Ca^{47} and Sr^{85} were made with the whole-body counter described previously.[11, 12] Briefly, the subjects were positioned in a standard chair geometry,[13] and the gamma rays were detected by a single 5-in. sodium iodide crystal which was connected to a 512 channel pulse-height analyser. The intensities of 1.25 MeV gamma rays from Ca^{47} and of 0.5 MeV gamma rays from Sr^{85} were measured. The correction for the Ca^{47} contribution to the Sr^{85} photopeak was determined previously in 10 subjects who received only Ca^{47} isotope. The contribution to the Ca^{47} and Sr^{85} photopeaks of the normal radioactivity in each subject due to K^{40} and Cs^{137} was determined by whole-body measurement before tracer administration and a correction was made for this background activity.

EXPERIMENTAL ERROR

The standard chair geometry is such that within ±5% the same body burden gives the same counting rate for persons of widely varying sizes provided the isotope is distributed throughout the body.[14] For a few days after oral administration this latter condition is not satisfied. The counting rate corresponding to the 100% body burden was therefore found by placing a source of strength equal to the administered dose in a position relative to the detector which previous experiments have shown to produce the same counting rate as tracer distributed in the body. The seven-day whole-body measurements were then expressed as per cent retention of the administered dose.

Experience has shown that retention values obtained in the same subject on repeated measurements are accurate to ±5%. In comparing the data obtained in different subjects, the error will be somewhat larger, owing to the effect of individual variation in size and shape on whole-body measurements.

RESULTS

The effect of the alginate jelly on the whole-body retention of calcium and strontium tracers is shown in Table I. The 1.5-g. dose of sodium alginate in jelly reduced the strontium retention from a mean control value of 6.8% to a mean of 3.0%. This difference is statistically significant with $p < 0.1$. In the same study, the mean retention of calcium was slightly reduced (from 24.9 to 20.5%), which is not significant ($p<0.2$).

From an analysis of the data, it is apparent that there is considerable variation in the normal absorption of Ca and Sr between individuals. Furthermore, the calcium retention data indicate considerable variation in the same individual on repeated tests. These variations are well outside experimental errors. Since alginate has little apparent effect on calcium absorption, the Sr/Ca retention ratio will demonstrate the effect of alginate on strontium absorption and, at the same time, smooth out some of the normal individual variations. As will be seen in Table I, the spread of values for the Sr/Ca ratios is considerably less than those for Ca and Sr. In 14 out of 15 subjects, the alginate jelly reduced the Sr/Ca ratio below the range of the control values (Fig. 1).

The effect of 3 g. and 0.3 g. doses of sodium alginate on Ca and Sr retention is also shown in the table. Since only two subjects were studied on each of these intake levels, no statistical evaluation can be made of the results. The data suggest that 0.3 g. alginate had little effect on the Sr/Ca ratio. The larger amount, 3.0 g. alginate, seems to have had no greater effect on the Sr/Ca ratio than the 1.5-g. dose.

DISCUSSION

Sodium alginate, 1.5 g., administered as a jelly reduced the gastrointestinal absorption of strontium

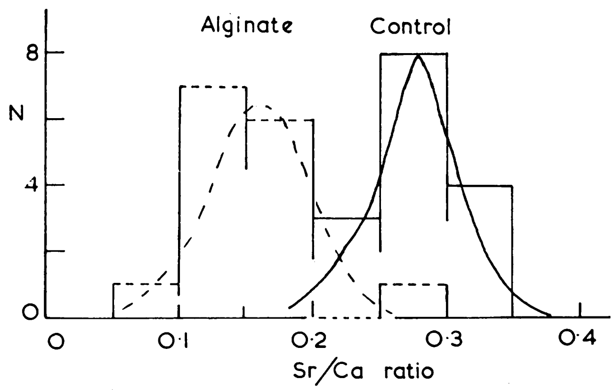

Fig. 1.—A histogram showing the effect of sodium alginate on the ratio of the seven-day retention of strontium to the retention of calcium in humans. N is the number of cases in which the Sr/Ca ratio was within the range indicated. The solid bars show the results for the control experiments and the dotted bars show the results obtained when alginate was taken. The curves are merely intended to guide the eye.

by a factor of 2 with little significant effect on calcium absorption. The Sr/Ca retention ratio was decreased from a mean of 0.27 to 0.146. These results support the observations made in rats.[5] It is, however, of interest that a comparable effect on calcium and strontium absorption in rats was obtained when 1.2 g. of sodium alginate was mixed with rat diet. In the rat this amount of alginate per unit body weight is more than 100 times the amount fed to humans in the present study.

In the human study reported by Hesp and Ramsbottom,[8] 10 g. of sodium alginate reduced strontium retention by a factor of 9. Although that study showed a much greater reduction in strontium retention than does the present report, the two studies show similar results for the actual amount of strontium absorbed when administered with alginate. In Hesp and Ramsbottom's experiment, the tracer was given without a carrier. As a result, the control value for tracer retention is expected to be much higher than in the present study in which the tracer was given with 100 mg. of calcium ion.

Although this experimental jelly proved a palatable and effective way of administering sodium alginate, it is recognized that other compounds in the jelly may have had some effect on the results. The absorption of calcium is reduced by phosphate, carbonate and magnesium as well as by increased concentration of calcium.[15] Although we saw little effect on calcium absorption, these compounds may well affect strontium absorption. In subsidiary experiments, we studied the administration of pure sodium alginate and its effects. The viscous solution of sodium alginate in water was found to be quite unpalatable. Also the ingestion of capsules of dry sodium alginate had no effect on the absorption of either calcium or strontium. This is attributed to the fact that a tough coating of alginic acid is formed around dry sodium alginate in dilute acid so that presumably the alginate is not available for metal binding. When we added a capsule of dry alginate to 0.1 N HCl at body temperature, the lump so formed did not break up with vigorous stirring for one hour. The aqueous solution of sodium alginate used in the human experiment by Hesp and Ramsbottom[8] is palatable owing to the low viscosity of the alginate that they used, and is presumably more readily available for metal binding than the dry material.

This study has shown that a small amount of alginate given in the form of a jelly can reduce significantly the absorption of strontium in human subjects. The results justify further investigation. In the event of accidental ingestion of serious amounts of radiostrontium, it would be important to know the amount and type of alginate that would exert a maximum therapeutic effect. Skoryna *et al.*[5, 6] have shown in rats increased non-absorbable strontium proportional to the increased dose of alginate. The brief investigation into the effect of different amounts of alginate, reported in the present paper, gave inconclusive results. In addition, the alginate derived from different sources is reported to vary in effectiveness and may be related to the different molecular structures with respect to the guluronic acid to mannuronic acid ratio.[7, 16, 17] Other factors which will vary the effectiveness of alginate include the time interval between strontium ingestion and alginate administration, and also the food content of the stomach.[4, 6]

SUMMARY

Sodium alginate, 1.5 g., given in the form of a commercial jelly reduced strontium absorption by a factor of two without significantly inhibiting calcium absorption.

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