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Received November 4, 1966. P.S.E.B.M., 1967, v124.

Effects of Sodium Alginate on Absorption and Deposition of Radioactive Cations in the Chick.*† (31792)

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A major problem involved in the use of cation-binding agents in removal of Sr is that Ca is removed concurrently and often to a greater degree. However, attempts have been made to use sodium alginate, a mucopolysaccharide from brown algae and Pacific kelp, as an agent for selective inhibition of the absorption of radiostrontium from the gut. Skoryna *et al*(1) found that sodium alginate reduced the uptake of Sr^{89} by 50-80% in the ligated intestine of rats without significantly affecting Ca^{45} absorption. Orogastric intubation and feeding the alginate were also reported to be effective in rats (2,3) and in humans(4). However, data are not available on dried kelp itself.

Materials and methods. To determine the effects of alginate on the preferential intestinal absorption of Sr^{89} and Ca^{45}, 20-day-old male chicks were distributed into 4 groups of 5 birds each, and fed a practical type ration supplemented with 0.5%, 1.0%, 2.0% sodium alginate, and 4.35% kelp (equivalent to 1.0% alginic acid), respectively. An additional group of 5 birds received a diet containing no alginate. All birds were given approximately 5 μc Ca^{45} orally 3 hours after they were placed on the experimental rations. Five other groups of 5 birds each were treated similarly, but were given approximately 5 μc Sr^{89} orally.

* Supported in part by Division of Radiological Health, USPHS Grant RH00354.

† Contribution of Texas Agric. Exp.. Station.

The feces from each group were collected daily for isotopic analysis and at the end of the 14-day experimental period all birds were killed and the right and left tibiotarsus taken for analysis of the appropriate isotope. Both isotopic analyses were performed by the method of Creger *et al*(5) and all data were calculated by the computer method of Creger *et al*(6).

Results and discussion. Table I shows the percent of the total dose recovered in the tibiotarsus and the excreta from birds receiving single oral doses of Sr^{89} and Ca^{45}, respectively, and fed diets containing various amounts of sodium alginate or an equivalent amount of dried Pacific kelp.

The smallest amount of Sr^{89} was recovered in the tibiotarsus of birds which received 0.0% and 0.5% dietary sodium alginate. However, when alginate was included in the diet at the 1% or 2% levels, the deposition of Sr^{89} increased. Correspondingly the greatest excretion of Sr^{89} was by birds receiving no alginate and the excretion decreased as the alginate content of the diet was increased. Both Sr^{89} deposition in bone and Sr^{89} excretion in the groups receiving 1% and 2% alginate were essentially the same.

The greatest amount of the total dose of Sr^{89} recovered from tibiotarsus was from birds receiving 4.35% dried kelp. The amount actually recovered in the bones of the group receiving the kelp was more than

TABLE I. Effect of Sodium Alginate and Kelp on the Absorption and Deposition of Sr^{89} and Ca^{45}.

Treatment	% Sr^{89} dose recovered		% Ca^{45} dose recovered	
	Tibiotarsus*	Excreta	Tibiotarsus*	Excreta
None	1.46	77.19	7.37	56.84
0.5% Na alginate	1.43	75.50	6.92	64.96
1.0% " "	1.59	74.78	5.97	61.10
2.0% " "	1.55	74.85	5.53	58.62
4.35% dried kelp†	2.88	68.26	4.27	48.76

* Mean values for the right and left tibiotarsus from 5 chicks in each group.
† Equivalent to 1% alginic acid.

1.5 times as high as the amount observed in the bones of the group fed an equivalent amount of alginate (1%). The Sr^{89} excretion was also lowest in the group receiving kelp. It is apparent from these data that dried kelp exerts more of a retentive effect on Sr^{89} than does sodium alginate alone.

While the skeletal deposition of Sr^{89} was increased by addition of sodium alginate into the diet, the reverse was found to be true for Ca^{45}. Birds receiving no dietary alginate incorporated more Ca^{45} into the tibiotarsus than did any of the groups which received the alginate. The amount of Ca^{45} incorporated into bone of the group fed dried kelp was the smallest of all treated groups.

In all groups less Sr^{89} than Ca^{45} was deposited in the tibiotarsus and more Sr^{89} was excreted than Ca^{45} which indicated a definite discrimination against Sr in favor of Ca in the chick as has been observed in other species(7-9).

Although the amount of Ca^{45} incorporated into the tibiotarsus decreased as the dietary alginate increased, the amount of Ca^{45} excreted was not increased, as was the Sr^{89}.

This can possibly be explained by the fact that little or no Sr^{89} is found in soft tissues after a post administration time of 14 days(10). This is not true for Ca as Ca is found in various concentrations in all tissue and in some tissue in fairly large quantities when compared to Sr. This is further confirmed by the fact that as the amount of Ca^{45} in the tibiotarsus increased and the amount of Ca^{45} in the feces decreased the ratio of Ca^{45} in the excreta to that in the tibiotarsus

$$\left(\frac{\%\ Ca^{45}\text{ dose recovered in excreta}}{\%\ Ca^{45}\text{ dose recovered in tibiotarsus}}\right)$$

decreased.

It is obvious from these data that the intestine of the chick reacts differently to chelating materials than does the intestine of mammals, since both sodium alginate and hydrobiotites have proven successful in suppressing Sr absorption in both rats and humans(1-4).

A possible reason for the discrepancies between these data and those obtained with rats may be that in the latter case the sodium alginate was given in aqueous solution. In this state the alginate expands considerably and forms a highly viscous solution; whereas, in the chick experiments described here the sodium alginate was given in dry form. Therefore, the alginate may require some activation such as dissolution before it is truly effective in suppressing Sr^{89}. This may not be possible in the gut of the chick which is much more acidic than the mammalian intestine.

Summary. Data from an investigation of the effects of sodium alginate on the intestinal absorption and skeletal deposition of orally administered Sr^{89} and Ca^{45} indicated that sodium alginate was not effective in selectively inhibiting the absorption of Sr^{89} while permitting Ca^{45} to proceed unhindered. The skeletal deposition of Sr^{89} was essentially unchanged, whereas, Ca^{45} deposition was reduced by increased amounts of dietary sodium alginate. An amount of dietary kelp equivalent to 1% sodium alginate decreased Ca^{45} deposition, but increased Sr^{89} deposition.

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Received November 14, 1966. P.S.E.B.M., 1967, v124.

A Comparison of Concurrent and Delayed Tests for Antitumor Activity of L-Asparaginase.* (31793)

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Two methods of testing have been used to measure the sensitivity of tumors to various L-asparaginase preparations(1-9). One of these which we may refer to as the concurrent test(1-6), measures the ability of the agent to repress the development of a tumor when a given number of tumor cells are inoculated. In this test the agent is administered within several hours after inoculation of the tumor. The second test (7-9), on the other hand, measures the ability of the agent to induce regression of an established tumor. This we may call the delayed test since the agent is not injected until the inoculated cells have developed into a measurable tumor. It might be assumed that if an agent can prevent the development of a tumor, it would also be efficient in bringing about regression of an established growth and, likewise, an agent which had no effect on tumor development would be inefficient in producing regression of an established transplant. These assumptions have been found to be incorrect in our work involving the effect of L-asparaginase from different sources on various tumors. The data reported here show that the result of one type of test cannot predict the outcome of the other. In fact, the two types of tests gave dissimilar results in each of 3 tumor systems tested.

Materials and methods. Guinea pig serum (GPS) was either obtained commercially or collected from Hartley guinea pigs by cardiac puncture under ether anesthesia. *Escherichia coli* L-asparaginase (EC-2) was purified according to the procedures described separately(10). Guinea pig serum L-asparaginase was administered as whole GPS but EC-2 was purified to some degree since the crude extract of *E. coli* is toxic. It was found, however, that the degree of purification of the enzyme did not alter the ability to detect its antilymphoma activity so long as the toxic materials were removed. Tumor cells were injected (EARAD1 into (C57BL/6 × A)F_1 mice (11), 6C3HED into C3H/HeJ mice(12), or P1798 into BALB/c mice(13)) subcutaneously in the flank of shaved female mice an hour before (concurrent test) or 7 days before (delayed test) the administration of L-asparaginase. The animals were treated

* Supported by NCI Grants CA 08765 and CA 08748 and funds from Cancer Chemotherapy National Service Center Contracts SA-43-ph-2445 and PH-43-65-619.

† Public Health Service Fellow—March 1965 to March 1967.