TABLE III. Distribution* of Hafnium^{181} Sodium Mandelate in Organs Expressed in % per g Corrected to a Standard Body Weight.

Organ	24 hr	48 hr	72 hr	96 hr	8 days	16 days
Liver	1.8	4.9	4.3	4.3	6.4	6.5
Spleen	5.5	9.4	19.2	23.8	17.4	6.3
Bone	0.8	0.8	1.2	0.9	1.5	0.6
Kidneys	1.5	0.8	0.4	0.8	1.3	0.9
Blood	0.5	0.1	†	†	†	†
Heart	0.3	0.3	0.3	0.1	0.2	0.2
Lungs	0.7	0.7	0.8	0.2	0.2	0.2
Pelt	0.2	0.1	†	†	†	†

* Each column represents avg determinations in 3 animals with exception of 8-day period, when 2 animals were studied.

† Negligible.

marked decline subsequently. Tissue autoradiograms confirm these findings and will be discussed in more detail later(11).

These data indicate that hafnium^{181} sodium mandelate has little specific localization in the body to recommend its consideration for radiation therapy of individual organs or tissues.

11. Boyd, G. E., Unpublished observations.

Conclusions. 1. The distribution and excretion of radioactive hafnium^{181} sodium mandelate after its intravenous administration was studied in 17 rats sacrificed at intervals of 1, 2, 3, 4, 8, and 16 days. 2. Seventy to 90% of the total activity was retained in the liver, spleen, the skeletal, muscular, and integumentary (pelt) systems. 3. Specific activities showed the spleen to be highest, followed by the liver, bone, and kidneys. 4. The adrenals, thyroid, pancreas, salivary glands, and testes showed a slight, but appreciable retention. 5. Hafnium^{181} in the blood was found chiefly (95%) in the plasma and remained in appreciable amounts to 4 days. 6. Seven per cent of the total dose was excreted in 16 days with more being eliminated in the urine than in the feces, the urine/feces ratio being 2.4.

The authors wish to express their appreciation for the generous technical assistance of Drs. W. C. Davis and Boyd Weaver, Plant Y-12, Oak Ridge, Tenn.

Received December 21, 1950. P.S.E.B.M., 1951, v76.

Failure of a Flavonoid to Reduce Radiation Mortality in Mice. (18463)

E. P. CRONKITE, W. H. CHAPMAN, AND F. W. CHAMBERS.

From the Naval Medical Research Institute, Bethesda, Md.

Various investigators have reported flavonoids to be beneficial in the treatment of animals after exposure of the whole body to potentially lethal amounts of radiation(1-3). Sokoloff *et al.*(3) have adequately discussed the beneficial reports. Other reports(4,5) have stressed the ineffectiveness of rutin. Further discussion of the rationale behind the use of these compounds is out of the scope of this paper which reports another failure.

Materials and methods. A flavonoid compound isolated from citrus fruit was used.* For injections the material was dissolved in saline (0.9%), pH adjusted to 7.0 and diluted so that 1 ml contained 6.6 mg of flavonoid. The flavonoid was started 5 days before ir-

1. Rekers, P. E., and Field, J. B., *J. Clin. Invest.*, 1949, v28, 746.

2. Clark, W. G., Uncapher, R. P., and Jordan, M. L., *Science*, 1948, v108, 629.

3. Sokoloff, B., Redd, J. B., and Dutcher, R., *Science*, 1950, v112, 122.

4. Cronkite, E. P., Eltzholtz, D. C., Sipe, C. R., Chapman, W. H., and Chambers, F. W., Jr., PROC. SOC. EXP. BIOL. AND MED., 1949, v70, 125.

5. Kohn, H. I., Robinett, P. W., and Cupp, M. N., Atomic Energy Commission Document 2176 (13p), 1948. Technical Information Division, Oak Ridge, Tenn.

* Supplied by Dr. Boris Sokoloff, Florida Southern College, Lakeland, Florida, and reported to contain Quercitin-like substance 4%, eriodictin 15%, chalcone hesperidin-glucose hesperidin 80%, and calcium phosphorus ash 0.38%.

TABLE I. Mortality Data of Flavonoid Treated and Control Irradiated Mice. (32 mice in each group).

Dose of x-ray	Days after x-ray →	No. of mice dying per day																	Total dying during period	% mort. in this exp.	% mort.* this strain mice
		3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	30			
1050 r	Treated		5	11	11	3	2	0											32	100	
	Untreated	1	2	4	2	3	5	2	2	5	6								32	100	99.6
950 r	Treated		3	4	10	8	5	1	1	0									32	100	
	Untreated		2	3	4	6	2	1	8	5	0	0	0	1					32	100	96
850 r	Treated		1	6	8	7	4	4	2	0									32	100	
	Untreated			1	3	1	4	4	4	6	3	3	0	0	1	0	0	0	30	94	88
750 r	Treated				3	5	3	6	8	0									25	78	
	Untreated		1	3	1	1	1	3	1	5	3	2	3	1	1	0	1		27	84	64
0	Treated																		0	0	
	Untreated																		0	0	

* Based on repeated mortality studies on total of over 5000 mice during period of June 1947 to June 1950.

radiation and continued until the mice died or for 15 days after irradiation. It was given 2 times per day subcutaneously. The total daily dose was 0.13 mg/g of mouse. White, Swiss, inbred, male mice weighing 20-26 grams were irradiated simultaneously with the radial beam of the 2.0 mev GE industrial x-ray machine(6). The radiation factors are: 2000 KVP, 1.5 ma, no added filter, 15.0 ($\pm$0.15r) r per minute in air at 2 meters, HVL 4.3 mm Pb. Mice were given the following doses of x-ray: 750, 850, 950, and 1050 r. Sixty-four mice were exposed at each dose. Thirty-two mice were treated and 32 were not treated with flavonoid. In addition, 30 mice were treated with the flavonoid, but were not irradiated.

Results. In Table I the results are tabulated. At the doses of radiation used the compound gave no protection. The control, non-irradiated, injected mice gained weight at the same rate as did the non-injected control mice. There was no evidence of any toxicity of the compound in mice at the dose used.

Discussion. The dose of flavonoid used was at least 4 times that per gram of animal used by Sokoloff *et al.*(3), in their experiments on rats that demonstrated an apparent protective action.

The doses of radiation used in these experiments varied from approximately an LD_{60} to almost an LD_{100} for this strain of mouse. In this dose range almost 100% of the mice dying after the 5th day have extensive purpuric hemorrhages throughout their organs. If, as reported by Field(1), Clark(2), and Sokoloff, *et al.*(3), the flavonoids protect against radiation by preventing hemorrhage through protection of the capillary bed, one might reasonably expect these compounds to protect mice at doses of radiation where hemorrhage is prevalent. The current experiments do not support this concept.

A summary of the data previously reported shows protection in dogs(1), rats(3), and guinea pigs(2), and no protection in rats(5) and mice(4). In some of the reports(1-3) it is not clear whether the treated and untreated mice were irradiated simultaneously or paired in some manner to assure that the control and treated groups are really comparable. Ample experience at this Institute with radiation lethality experiments has demonstrated the absolute necessity of simultaneous irradiation of paired control and treated animals.

It is our present opinion that these compounds have little, if any, protective effect against radiation. However, with the possibility of atomic war, the need of a non-

6. Chambers, F. W., Jr., Morgan, J. E., and Istock, E. T., Report 26, Project NM 006 012.08, 7 Dec. 1949, Naval Med. Research Inst., Bethesda, Md.

toxic compound that will be effective as a prophylactic and as a therapeutic agent is so great that further studies should be made with the flavonoid group of compounds on a wide spectrum of animals to make certain that no possibility of a beneficial effect is overlooked.

Conclusion. 1. A flavonoid (vit. "P") compound is of no value in the treatment of radiation injury in the LD_{60} to LD_{100} range in mice.

Received December 26, 1950. P.S.E.B.M., 1951, v76.

The Effect of Aureomycin on Digestion in Steers. (18464)

M. C. BELL, C. K. WHITEHAIR, AND W. D. GALLUP.
From the Departments of Animal Husbandry and of Agricultural Chemistry Research, Oklahoma Agricultural Experiment Station, Stillwater.

Experiments with several species of animals have demonstrated that aureomycin and other antibiotics have a pronounced effect on microorganisms in the gastrointestinal tract. The ruminant is primarily dependent upon an active microbial flora for efficient digestive processes. An experiment was undertaken, therefore, to determine the effect of aureomycin* on the digestion of feed by steers.

Experimental. Six Hereford steers weighing about 620 pounds were used in this digestion experiment. The steers were kept in metabolism stalls with provisions made for separate collection of feces and urine. They were fed a constant amount of ration during 10-day preliminary and 15-day collection periods. Digestibility of nutrients and nitrogen retention were calculated from the chemical analyses of feeds and excreta. Blood samples were taken periodically for the determination of blood urea. All other experimental technics were similar to those reported by Briggs and Gallup(1). The composition of the daily ration fed each steer during collection periods is given in Table I. The digestibility of these rations without the addition of aureomycin had been determined with these same steers in a previous series of digestion trials. In the previous experiment, each of the steers was fed the basal ration and the urea† ration during 10-day preliminary and 10-day collection periods. No feed refusals or digestive disturbances were observed during this entire period of approximately four months.

Prior to the present experiment it was necessary to obtain information on the approximate amount of aureomycin which would not interfere with continued feed consumption. A level of 0.6 g per day was found to produce a marked anorexia and a severe fetid diarrhea within 48 to 72 hours. This condition persisted for 4 to 5 days after aureomycin feeding was discontinued. The anorexia appeared to be due to a digestive disturbance and not to unpalatability of the ration. The feeding of 0.2 g per day did not appear initially to interfere with a constant daily feed intake. Aureomycin feeding was discontinued until the appetite and digestive processes appeared normal. A standard 10-day preliminary period was then conducted during which each steer was fed a constant amount of the assigned ration without aureomycin. Aureomycin (0.2 g) was then added to the rations of steers 1, 2, 3, and 6. Steers 4 and 5 were continued on the basal ration. Urine and feces collections were started immediately.

Results and discussion. The digestion coefficients, nitrogen retention, and blood urea levels determined in the previous experiment during which the steers were fed the rations without aureomycin are given in part A of

* The crystalline aureomycin hydrochloride was supplied by Dr. E. L. R. Stokstad, Lederle Laboratories Division, American Cyanamid Company, Pearl River, New York.

1. Briggs, H. M., and Gallup, W. D., *J. Ani. Sci.*, 1949, v8, 479.

† Urea in the form of "Two-Sixty-Two" feed compound was supplied by E. I. du Pont de Nemours and Company, Inc., Wilmington, Delaware.