Comments and Communications

The Formation of Malignant Tumors in Mice by Deuteron-bombarded Methylcholanthrene

As part of a more general program on the effects of ionizing radiations on the carcinogenic activity of various organic compounds, it has been found that deuteron bombardment of 20-methylcholanthrene produces a product which our preliminary data show is more active biologically than the original substance.

Solid 20-methylcholanthrene was bombarded with the Crocker Radiation Laboratory 20-Mev deuteron beam[1] for a total of 0.58 microampere hr. The melting point of the product was approximately 10° C below that of methylcholanthrene. No charring of the sample was observed. X-ray diffraction patterns indicate the presence of not more than 15% of unchanged methylcholanthrene in the irradiated sample. Chromatographic separations of the methylcholanthrene showed that some impurities were present in the sample. This impurity is being investigated for chemical and biological activity. From the irradiated sample three distinct fractions could be separated. The identifications of the fractions obtained are being carried out. As would be expected, the irradiated sample showed only short half-life radioactivity, which had completely decayed out prior to injection.

TABLE 1

		Dose (mg)	No. of mice used	No. of tumors developed	Avg. wt. of tumors (gm)
Irradiated material	Males	0.25	5	4	14.25
		0.125	5	5	7.1
		0.0625	5	2	2
	Females	0.25	5	3	14.6
		0.125	5	3	13.9
		0.0625	5	3	7.5
Unirradiated material Controls	Males	0.25	5	3	4.5
		0.0625	5	3	7.8
	Females	0.125	5	0	Died from toxic effect or other causes
Olive oil Controls	Males	0.00	5	0	Still living

Mice[2] of the C-57 strain were used in the experiment and injected subcutaneously with various amounts of methylcholanthrene or irradiated methylcholanthrene (unseparated), as indicated in Table 1.

[1] We wish to thank Dr. J. G. Hamilton, of the Crocker Radiation Laboratory at the University of California, for his interest in the project and also L. W. Tuttle and R. Haymond for making the bombardments.

[2] The animal experiments were financed by a grant-in-aid from the Sigma Xi Research Fund.

The results in Table 1 indicate that there were significant increases in the size of the tumors with the irradiated material when compared with methylcholanthrene.

The malignant tumors produced by the irradiated sample and methylcholanthrene were of the same type—that is, fibrosarcoma. In two animals, in addition to the sarcoma, early epidermoid carcinoma was present. The systemic toxic effect of methylcholanthrene was reduced by irradiation when higher concentrations (0.125–0.25 mg) were used.

Detailed reports on the histopathology will be given elsewhere.

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Deformylation of 3-Formoxy Steroids on Activated Alumina

In discussing our experiments on the conversion of 3-formoxy steroids to 3-hydroxy steroids by chromatography over activated alumina (Fisher), W. Dasler (*Science*, April 9, p. 369) suggested that this deformylation is a special case of a more general hydrolytic splitting undergone by 3-hydroxy-steroid esters under these conditions. However, deformylation can be made to proceed quantitatively, whereas other ester groups are hydrolyzed only to a very minor extent. In fact, chromatography is a frequent means of purifying 3-acyl steroids. Therefore, aside from any theoretical implications, the deformylation reaction becomes of interest as a preparative tool in steroid chemistry.

There are a number of examples which indicate that the reaction is probably general. Cholesterol can be obtained quantitatively from cholesteryl formate (our unpublished observation). Ethyl-3(β)-formoxy-Δ^5-thiolcholenate gives ethyl-3(β)-hydroxy-Δ^5-thiolcholenate (Levin, *et al.* *J. Amer. chem. Soc.*, 1948, **70**, 511), and methyl-3(α)-hydroxy-12(α)-formoxy cholanate is obtained from methyl-3(α),12(α)-diformoxycholanate (Spero, McIntosh, and Levin. *J. Amer. chem. Soc.*, 1948, **70**, 1907). Additional studies are under way.

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On the Use of Roughage in Rat Diets

The following comments are added to those recently made by Davis and Briggs (*Science*, March 19, p. 292) regarding the note of F. Hoelzel and A. J. Carlson (*Science*, December 19, 1947, pp. 616–617) in their discussion of the "not uncommon type of error in the design of diets which makes the results of their use questionable." In this discussion Hoelzel and Carlson state: "A similar error, made by Guerrant and Dutcher (*J. Nutrition*, 1934, 8, 397), led to the erroneous conclusion that cellulose had a vitamin B and G sparing effect.'' In this connection it is assumed that these authors were referring particularly to the following conclusion drawn by us (p. 418): ''Increasing amounts of fiber in the form of agar and Cell-U-Flour possessed a definite sparing effect on vitamins B and G utilization. The beneficial effect of fiber is thought to be due to the production of more favorable conditions for the growth of microorganisms in the digestive tract.''

A re-examination of the original data as well as those presented in Tables 1 and 2 (pp. 402, 403) and Figs. 5 and 6 (pp. 411, 413) seems to us to justify the above conclusion. (It is well to remember that at the time our experiments were carried out (1933) ''Vitamin B'' had not been subdivided into the numerous fractions known today.) To substantiate our contention, however, certain data taken from the original records (essentially as given in Table 2 of the above publication) are hereby presented:

Diet No.	Agar (%)	Cell-U-Flour (%)	Total food intake during depletion period (gm)	Growth during depletion period (gm)	Food intake per gm growth (gm)
337	0	0	73	4	18.25
338	2	.	76	7	10.86
339	4	.	77	10	7.70
340	6	.	86	13	6.62
341	8	.	79	17	4.65
342	10	.	75	16	4.69
345	..	2	65	7	9.29
346	..	4	67	13	5.15
347	..	6	69	13	5.31
348	..	8	74	19	3.89

These data show the average food intake and weight increase of the several groups of rats employed in this particular phase of our studies during that period (21-day depletion period) when no supplementary vitamin B or vitamin G was fed. Also, the relative amounts of the respective diets (including fiber, where the fiber replaced an equal weight of sucrose) ingested per gram gain in body weight are given. It is to be noted from these data that the rate of growth increased with an increase in the fiber content of the diet until 10% of the fiber (agar) was used. Since these diets had been proven to be deficient in the B-vitamins (Fig. 1), it seemed to us that the increased growth was due either to the sparing effect of the higher fiber diets on the body reserve of these vitamins or, more probably, to the increased intestinal synthesis of these vitamins in the presence of roughage. The authors favored the latter explanation.

When one considers the above data from the standpoint of the amounts of the respective diets ingested per gram increase in body weight, it is readily observed that the high fiber diets (8%) were more efficient in producing growth than was the basal diet (Diet 337) or the low fiber diets (Diets 338 and 345). This was previously shown by the relationship of caloric intake to growth (Table 2). This increased rate of growth per unit of food intake cannot be explained on the basis of the contention of Hoelzel and Carlson that ''the replacement of glucose by cellulose therefore reduced the carbohydrate content or increased the proportion of protein, fat, and other constituents of the utilizable part of the diet, and this may explain the results attributed to the cellulose.'' In fact, the replacement of 5–20% of sucrose by an equal weight of fat (Diet 319–323) failed to produce weight gains comparable to those obtained on diets in which 2–8% sucrose was replaced by a comparable weight of agar or Cell-U-Flour. Thus, the mere reduction in the proportion of the digestible carbohydrate content of the diet to the other digestible nutrients does not in itself explain the improved growth rates observed on the high fiber diets.

While the two sets of experiments were not carried out with the same objective in view or under comparable conditions, the writer has detected no conflict between the experimental findings reported by Mannering, Orsini, and Elvehjem (*J. Nutrition*, 1944, 28, 141) and those previously published by Guerrant and Dutcher (*J. Nutrition*, 1934, 8, 397).

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The Scientist and Social Issues

The excellent paper by Alfred B. Bonds, Jr., on ''Some Recommendations of the President's Commission on Higher Education'' (*Science*, April 16, pp. 379–383) contains a suggestion which leaves one with some misgivings. On page 381, this statement appears: ''In the physical and natural sciences, the Commission has put forward proposals aimed at equipping the prospective scientist with a broad understanding of the social issues related to his subject-matter field.'' One would hope this pronouncement does not in any way suggest that scientists be expected or urged to suppress or distort facts in such a way as to make them conform to a political or social ideology. The current effort in one of the totalitarian countries to shape scientists in this sort of mold will, one trusts, be forever frowned upon not only by scientists but by all thinking people elsewhere.

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