flabby, with air spaces between fleshy leaf sheaths. The proportional reduction in the amount of triphenylformazan produced in the treated samples was more pronounced after 50 days than it was on the twentieth day after treatment.

Table 2 gives the results found with onions grown in the dark and tested on the seventh day after maleic hydrazide treatment. In general the dehydrogenases were less active in the etiolated plants than in the plants that received full sunlight. These plants grew rapidly, and probably the waxy coating on the epidermis was not so thick as that on the plants grown in full sunlight. This condition may have favored the entrance of the chemical into the plant tissue. The 3,000 ppm sprays of maleic hydrazide frequently had less effect on the dehydrogenases than the sprays of 2,000 ppm. This might be attributed to local toxic effects severe enough to retard hydrazide translocation. Morphological differences were not apparent between the treated and control plants.

The results indicate that maleic hydrazide sprayed upon the foliage of plants affects respiration through the partial inactivation or inhibition of one or more of the dehydrogenases. The rapidity of the effects of the chemical apparently are governed by the rate of its absorption into the plant.

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The Effect of Desiccated Thyroid, Iodinated Casein, and Casein on a Rachitogenic Diet

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At Michigan State College a modified Steenbock rachitogenic ration is used for the assay of vitamin D milks. This ration is somewhat goitrogenic, as well as deficient in one of the essential amino acids—namely, lysine. Rats fed the Steenbock ration are found to have thyroid enlargements with hyperplasia. This is to be expected, since the diet on the average has a content of 15 γ iodine/g as determined by Levine, Remington, and von Kolnitz (*1*). The daily intake of iodine necessary to yield a concentration of 1% iodine in the thyroid (dry basis), which is essential to normal thyroid functioning, was found by the same workers (*2*) to be approximately 1γ/day. This same group found that the low-iodine goiter is produced when the iodine content in the gland is 0.03% or less (dry basis), and this corresponds probably to an iodine intake from known sources of 0.3 or 0.4γ/day. Therefore, inasmuch as lack of uniformity in the growth of animals might be due to variations in thyroid activity, it was considered likely that the use of desiccated thyroid or iodinated casein would influence the growth of rats fed the rachitogenic diet and result in more uniform growth. Because desiccated thyroid is expensive and its potency variable, iodinated casein, as prepared by Reineke (*3*), was also used, since it provided a comparatively inexpensive product of nonvariable high-thyroid activity.

With the knowledge of the amino acid requirements of the rat, Francis (*4*) tabulated the amount of the individual essential amino acids present in the Steenbock ration and found it to be deficient in lysine. The addition of 0.5% lysine effectively increased the growth rate in addition to reducing the incidence of respiratory infections. Therefore, a study was also made of the value of adding casein to increase the supply of lysine, one of the limiting amino acids.

Throughout the pre-rickets-producing period the rats were maintained on a diet that provided for normal development in all respects except that the supply of vitamin D was limited so that the rats would develop severe rickets in 21 days. For the rickets-producing period a rachitogenic ration consisting of table corn meal 72%, wheat gluten 20%, yeast 1%, and NaCl 1% was used, as well as the modifications indicated in Table 1.

TABLE 1

Ration No.	Modifications
I.....	Basal (the above ration)
II.....	1 kg basal + 5 gr desiccated thyroid*
III.....	1 kg basal + 10 " " "
IV.....	1 kg basal + 25 " " "
V.....	Basal + 1% iodinated casein
VI.....	Basal + 0.05% " "
VII.....	Basal + .025% " "
VIII.....	Basal + .0125% " "
IX.....	Basal + 0.025% iodinated casein – 5% casein
X.....	Basal + 5% casein

* ½ grain commercial desiccated thyroid tablets were used.

Young albino rats of the Michigan State College strain, weighing from 44 to 60 g and 21–25 days old, were assembled into groups of 2 or 3 and fed the rachitogenic diet or one of the above modifications for 21 days and water, *ad libitum*. They were then placed in separate cages 1 day prior to the beginning of the 10-day assay period, so as to adequately adjust themselves to their new surroundings. The animals received a supplement of homogenized vitamin D milk supplying 4 U.S.P. units of the vitamin. In each series some animals were included as negative controls. At the end of the assay period the animals were killed, and the distal ends of the radii and ulnae removed and cleansed of adhering tissue. The bones were then permitted to remain at least overnight in 95% ethanol; "line tests" were then run.

The criteria employed were growth during the experimental period, general appearance of the lines,

and width of the metaphyses, since these are the factors used in routine assay. The results are indicated in Table 2.

TABLE 2

Ration No.	No. Starting Animals	Av Initial Wt	Weekly Wts 1st	2nd	3rd	Av Wt Gained in 3 Weeks
I	30	48.7	55.9	66.1	74.1	25.4
II	16	49.2	55.4	67.4	81.6	32.4
III	16	47.8	56.4	65.2	72.5	24.7
IV	9	51.8	57.2	72.0	81.8	30
V	10	48.4	55.6	63.4	...	...
VI	13	48.0	53.1	62.6	68.2	20.2
VII	32	47.3	57.6	66.8	78.1	30.8
VIII	14	48.7	56.1	65.3	73.8	25.1
IX	16	51.8	58.7	74.8	88.9	37.1
X	16	47.2	53.1	71.2	79.4	32.2

The figures represent several similar series started at slightly different intervals.

(*a*) During the depletion period the following rats died: 1 each on rations III and VII; 10 on ration V; and 5 on ration VI. (*b*) During the assay period the following rats died: 1 each on rations II and VIII; 2 each on rations I, III, IX, and X; 3 on ration IV; and 4 each on rations VI and VII.

All rachitic metaphyses were of desirable width and character.

Line test results:

a) Rats on rations I and VIII produced medium to thin lines.

b) Rats on rations III, IV, and VI produced thin high lines.

c) Rats on rations II, VII, and IX produced uniform medium lines.

d) Rats on ration X produced lines varying from medium to diffuse.

From the data it is evident that rations III, IV, V, and VI are unsuitable for the standard 21-day period. This may be attributed to an excessive intake of desiccated thyroid or iodinated casein. The detrimental effects assert themselves usually within 2–4 weeks, as evidenced by the number of rats that died during the rickets-producing and assay periods and by the high thin line of calcification, which is usually the result of insufficient food consumption.

The addition of 5 grains of desiccated thyroid to the basal ration produced the best growth, as well as the most uniform lines, when compared with the rest of the respective series. Rations VII and I appear about equal in their ability to promote growth; however, the addition of 0.025% iodinated casein appears to aid definitely in calcification response. Each series of rats received Michigan State College homogenized vitamin D milk calculated to supply 4 U.S.P. units vitamin D. Some variation in the actual potency of vitamin D milks might, of course, be expected. A series containing rats fed 0.025% iodinated casein, 0.0125% iodinated casein, as well as plain basal, were fed milk of somewhat lower vitamin D content because the line test responses were generally smaller. Nevertheless, those receiving ration VII showed better responses.

The fact that rats on ration II seem to do better than rats on ration VII is quite interesting since apparently both represent optimum tolerable levels of desiccated thyroid and iodinated casein. The possibility exists that the thyroid extract may differ somewhat in its over-all physiological activity from that of the iodinated protein.

The results with ration VIII containing 0.0125% iodinated casein indicated that this amount of iodinated casein did not affect the animals with regard to rickets production and the line test.

In no case did the average gain in weight in 3 weeks of rats receiving either ration II or VII exceed the respective basal group by more than 7 g. This may be attributed to the fact that the basal ration is deficient in lysine as well as available phosphorus, thus limiting the effect of either the iodinated casein or desiccated thyroid as growth stimulators. When rations IX and X were employed, the growth rate was greatly increased over the corresponding basal fed group. Furthermore, the incidence of respiratory ailments was greatly reduced by the addition of casein to the ration, thereby providing greater economy in animal usage. The growth attained by the end of the first two weeks was sufficient to suggest that only a two-week period would be necessary for the preparation of rats for vitamin D assays. The results, therefore, compare favorably with those obtained with lysine. The line test results, using rations IX and X, further substantiate the effectiveness of iodinated casein in producing more uniform lines.

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Screening of Potential Cancer-inhibiting Agents[1]

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Fildes (*1*) in 1940 stated that modified essential metabolites should be sufficiently closely related to the essential metabolites on which they are based as to fit the same enzyme, but sufficiently different to be devoid of essential metabolic activity.

Since various investigators (*2*) had reported that the concentration of nucleic acids in tumor-bearing animals is greater than in normal animals, it was apparent that adenine and guanine inhibitors might be found which would retard tumor growth, without ad-

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