By excluding the new components from the purine nucleotides the ratio of purine to pyrimidine nucleotides is 0.92. Two of the unknown components are very likely to be derivatives of guanine due to the similarity of their spectral ratios with those of guanylic acid. If this is the case, the ratios of purine to pyrimidine will be close to unity.

SUMMARY

The method of CRESTFIELD, SMITH AND ALLEN[3] for the isolation of the ribonucleic acids from yeast has been modified and applied to the isolation of the ribonucleic acids of pancreas. In order to assess the possibilities of enzymic degradation and fractionation, the nucleotide composition of the isolated ribonucleic acids has been compared with that found for the ribonucleic acids prior to isolation from pancreatic tissue and found to be identical. The ratios of purine to pyrimidine are unity which are similar to those for undegraded ribonucleic acids from other sources.

The fifth nucleotide which has been reported by DAVIS AND ALLEN[4] to be present in the fractions of the ribonucleic acids from yeast has been found to be present in the ribonucleic acids isolated from the pancreas. In addition certain unknown nucleotide components which occur with the guanylic acid fraction in paper chromatography are reported.

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THE EFFECT OF DEUTERIUM OXIDE ON SURVIVAL OF MICE WITH ASCITES TUMOR*

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The improved availability of mass-produced deuterium at reasonable prices ($ 28 per pound for D_2O) has made it of interest to renew the study of metabolic effects of deuterium in plants and animals. The older literature on this subject has been ably

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reviewed by CHANCE AND ALLEN[1] and THORN[2] who include several reports on the effects of deuterium on a variety of tumors. REA AND YUSTER[3] inoculated rats with a sarcoma, and after the tumor was established, injected 0.11% D_2O in and around the tumor every other day for ten treatments. They reported no inhibition of tumor growth. WOGLOM AND WEBER[4] brought the body water of mice to 0.3% and then implanted sarcoma 180 or carcinoma 63 while continuing D_2O treatment. They also reported no effect on the tumor.

These results are not surprising in view of other reports which have indicated that greater than 5% D_2O body-water concentration is needed to produce any gross metabolic changes in animals. BARBOUR AND ALLEN[5] report a significant inhibition of carcinoma and lymphosarcoma growth in mice maintained on 40% D_2O drinking water. This produced a body-water deuterium oxide concentration of about 20%. More recently, WEINBERGER AND PORTER[6] and HOLM-HANSEN, MOSES AND YARBERRY[7] have demonstrated an inhibition of algal reproduction at deuterium water concentrations over about 30%.

In this report we wish to describe the effect of D_2O on the survival of mice with Ehrlich's ascites tumor. At the time of our first report on this work[8], preliminary results on a similar study were presented by FINKEL[9]. More recently, an article by KATZ *et al.*[10] has presented these data in a more detailed form.

EXPERIMENTAL

The body-water concentration of D_2O in young adult male and female C_{57} strain mice was brought up to 20–30% in two days as follows: The mice were injected intraperitoneally daily with 1.5 ml of isotonic 99 + % D_2O water. At the same time different groups were given 25, 30 or 40% D_2O in the drinking water, and food, *ad lib.* Controls were similarly injected and treated, but with H_2O instead of D_2O. On the third day the D_2O-treated mice and controls were each inoculated with 0.1 ml of a tumor suspension, containing about $1 \cdot 10^6$ Ehrlich's mouse ascites tumor cells*. Inoculum from the same sample was used for each group and its controls. The D_2O-treated mice were continued on their 25%, 30% or 40% drinking water. Survival time after tumor inoculation was determined. Each experiment was repeated.

All water D_2O is expressed as volume percent, which is essentially the same as atom percent.

RESULTS

Preliminary experiments on deuterium toxicity in mice had shown that drinking water of 50% D_2O was surely fatal, killing the mice in a few days. However, we were able to maintain mice on 40% D_2O for several months without any deaths. Therefore, 40% D_2O was the highest concentration of drinking water used in our experiments.

In all of our experiments the tumor cells multiplied, swelling the abdomens of the deuterated as well as the normal mice. We found no evidence of actual tumor regression. The survival time curves for the mice treated with 25%, 30% and 40% D_2O drinking water are given in Figs. 1–3. Each group of animals had their own controls, as there is some variation in the lethal characteristics of any given sample of the tumor inoculum. As can be seen from Figs. 1 and 2, the mice given 25% and 30% D_2O drinking water had an appreciably longer survival time than their respective controls. In addition, the deuterated mice continued to be bright and lively in spite of the tumor for a longer period than the controls.

* This tumor has been maintained in C_{57} mice in this laboratory for more than one year.

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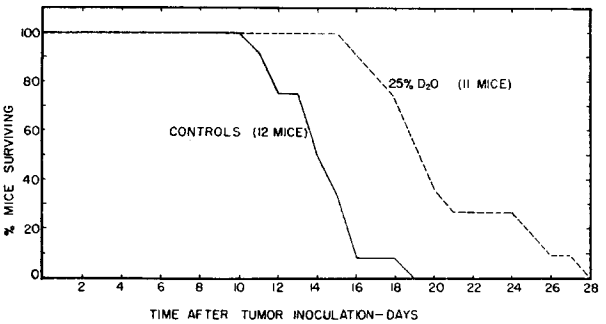

Fig. 1. Influence of 25 % D_2O drinking water on the survival of mice after ascites tumor inoculation The mean survival time was increased 6.3 ± 1.4* days.

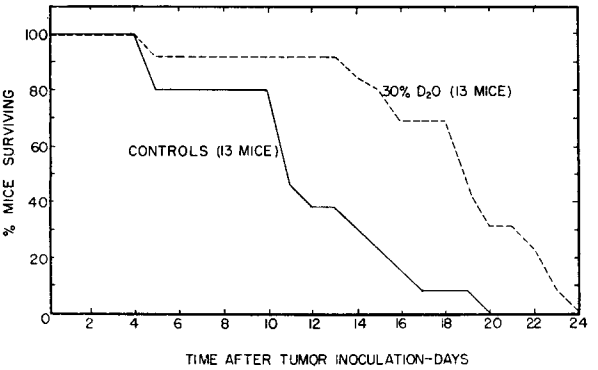

Fig. 2. Influence of 30 % D_2O drinking water on the survival of mice after ascites tumor inoculation. The mean survival time was increased 6.6 ± 1.9* days.

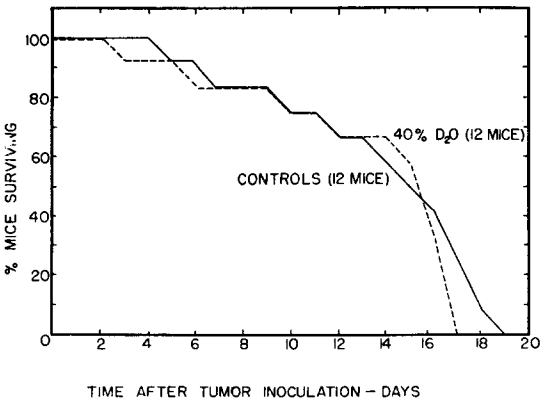

Fig. 3. Influence of 40 % D_2O drinking water on the survival of mice after ascites tumor inoculation. The mean survival time changed from 14.0 days for the controls to 13.5 days for the deuterated mice.

* Standard error for the difference of the mean.

The 40% D_2O drinking water had no inhibitory effect on the ascites tumor. It would appear that it might even potentiate the lethal effect of the tumor. This substantiates the observation of BARBOUR AND ALLEN[5] that although 40% D_2O in the drinking water inhibited the growth of mouse carcinoma and lymphosarcoma, the survival time of the animals was shortened.

DISCUSSION

The data of HOLM-HANSEN, MOSES AND YARBERRY[7] on the division of algae cells in D_2O indicates that moderate deuterium concentrations can inhibit cell division. They found that in unadapted algae, 50% D_2O in effect stopped cell division although the cells were still alive and, in fact, grew in size. It is possible that this same inhibition of cell division by deuterium occurs in higher biological systems, but the toxicity of the deuterium to these systems is such that it is difficult to raise the deuterium oxide levels high enough to make such inhibition truly effective.

Our experiments indicate that 25% and 30% D_2O drinking water provide a moderate inhibition of the tumor growth and increase animal survival. The 40% D_2O is already at a rather toxic level and 50% D_2O cannot be used for this type of experiment. The data of KATZ[10] and FINKEL[9] help confirm our inference that increased survival time of the mice maintained on 25% and 30% D_2O drinking water is due to a decreased rate of cell division.

SUMMARY

The effect of deuterium oxide (D_2O) on the survival of mice inoculated with Ehrlich's mouse ascites tumor has been studied. Mice maintained on 25% and 30% D_2O drinking water showed an improved survival time of about 6 days, whereas 40% D_2O drinking water had no effect on survival time. The effect is interpreted in terms of inhibition of tumor cell division and systemic toxicity.

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