reports of the studies referred to here will be published elsewhere.

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HÆMATOLOGY

Decreased Erythrocyte Survival in Alloxan Diabetic Rat

Although numerous metabolic activities have been investigated in the alloxan diabetic rat, the red cell survival has not been reported. Derangement in the metabolism of the human erythrocyte in diabetes mellitus was shown recently by Long and Carson[1]. The present communication reports a reduction in the red cell life-span in the alloxan diabetic rat.

Albino rats were rendered diabetic by the intravenous injection of 40 mg alloxan/kg body-weight. The diabetic animals (blood sugar-levels more than 300 mg per cent) were tagged with 10 μc chromium-51 three weeks after alloxanization in order to minimize the possibility of a direct effect of alloxan on the erythrocytes. The time in days between tagging and the disappearance of the radio-activity from the blood is taken as the maximal survival time. The details of the procedure have been published elsewhere[2].

Table 1. Maximal Survival Time of Erythrocytes of Normal and Alloxan Diabetic Rats*

	Normal		Alloxan diabetic	
	Body-weight (g)	Max. survival (days)	Body-weight (g)	Max. survival (days)
Mean (± *S.D.*)	205 (± 18)	68 (± 3) $P < 0.01$	146 (± 18)	56 (± 1)

* Nine rats in each group.

Table 1 shows that while normal rats had an average maximal survival time of 68 (±3) days, the alloxan diabetic rats had an average value of 56 (± 1) days. These results indicate clearly that alloxan diabetes reduces significantly the survival of red cells in the rat. Although three weeks were allowed between alloxanization and tagging, one cannot exclude the possibility that the observed effect might be, at least in part, due to the direct action of alloxan on the erythrocytes. However, of 11 diabetic rats, 2 recovered spontaneously after tagging, and their erythrocytes were found to have maximal survival times of 60 and 68 days, values which approach those of the normal animals. This tends to provide evidence against the direct effect of alloxan on the red cells. Moreover, György and Rose[3] showed that although alloxan hæmolyses red cells from vitamin E-deficient rats, it had no such effect on those from normal animals.

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PATHOLOGY

Effect of a New Anticancer Agent, 1,4-Dimethyl-1,4-Diphenyl-2-Tetrazene, on a Transplantable Mammary Adenocarcinoma (72*j*) and Spontaneous Mouse Breast Tumours

1,4-Dimethyl-1,4-diphenyl-2-tetrazene[1] (MPT) inhibits the growth of transplanted 72*j* mammary adenocarcinoma carried in C_3H mice. Its activity was found during the screening[2,3] of compounds structurally related to the antineoplastic agent 3,3-dimethyl-1-phenyltriazene[4]. The corresponding 1,4-diethyl[5] and 1,4-di(*p*-nitrophenyl) analogues of MPT were also found active against this tumour. Extensive laboratory evaluation of MPT and synthesis of additional compounds are in progress and will be reported in detail[6,7]. The following biological findings were considered to be of immediate interest.

MPT given subcutaneously or intraperitoneally over a wide range of doses (that is, 2–50 mg/kg/day) prolonged the median survival-time of mice bearing the 72*j* mammary adenocarcinoma to about 60 days, from an average of 30 days in control animals. (Treatment was started 17 days following transplantation. Experimental design in both the transplanted and spontaneous tumour test systems was that introduced by Goldin[8].) In contrast, THIO-TEPA, a known clinically useful anticancer agent, was active over a much narrower range of doses (that is, 0·8–2 mg/kg/day), and had an estimated maximal median survival-time of 50 days. MPT fed in the diet resulted in prolongation of the median survival-time to about 100 days (500, 1,000 or 2,000 mg/kg/day). This median survival-time is the longest observed in these laboratories with any anticancer agent given to the 72*j* mammary adenocarcinoma bearing mouse.

MPT was also interesting because of its apparent ability to prolong significantly the median survival-time of spontaneous tumour-bearing C_3H mice. MPT given subcutaneously (6 or 20 mg/kg/day) to C_3H mice bearing spontaneous mammary tumours increased the maximum median survival-time from 35 days in control mice (starting from the time the mice were placed on test) to 68 days. The compound showed effects over a wide range of doses: that is, 2–150 mg/kg/day. MPT was less effective when given intraperitoneally. By the oral route the median survival-time was prolonged to 70–80 days (500, 1,000 or 2,000 mg/kg/day) versus 37 days for control animals (see Table 1 for results of diet administration).

Table 1. Survival Data of *C3H* Mice Bearing Spontaneous Mammary Tumours

Compound	Estimated daily dose (mg/kg)	No. of mice/ group	No. of exp.	Mean median survival (days)
MPT (in diet)	2,000	5	5	77*
	1,000	5	5	78*
	500	5	5	73*
THIO-TEPA (in drinking water)†	6·7	5	2	42
	4·5	5	2	37
	3·0	5	2	39
	2·0	5	2	43
	1·3	5	2	46
	0·9	5	2	34
Controls (no treatment)	—	5	7	37

* Significant prolongation of median survival $P = 0.01$.
† Solutions were made up fresh daily.

In contrast, THIO-TEPA (by any route of administration) had no effect on the median survival-time of spontaneous tumour-bearing mice.

An earlier report indicated that marked bone marrow destruction was found concomitant with antitumour activity in the laboratory evaluation of alkylating agents and many antifolic compounds[9]. In similar experiments MPT caused no depression of the marrow concomitant with tumour inhibition; moreover, this compound was not identified as an alkylating agent when tested chemically by the Friedman and Boger method[10]. MPT was completely ineffective against the $6C_3HED$ lymphosarcoma