RADIOPROTECTIVE ACTION OF IPRONIAZID

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INTRODUCTION

This experiment was a special laboratory project designed to explore the capacity of a monoamine oxidase inhibitor as a radioprotective agent. In previous work (1) serotonin has shown promise in diminishing the injurious effects of radiation. It is well established that a monoamine oxidase inhibitor will increase body serotonin (2 & 3). Iproniazid is one of the more effective monoamine oxidase inhibitors. Thus we had reason to anticipate that it would exhibit a protective capacity comparable to that of serotonin.

EXPERIMENTAL METHOD

The experimental animals were adult male white mice which weighed approximately 35 grams each. The diet was Purina Laboratory Chow allowing water *ad lib*. We used 18 mice, housed at room temperature. Five mice were injected intraperitoneally with 75mg./kg. of serotonin (about ¼ of the intraperitoneal LD_{50}), five mice with 75mg./kg. of iproniazid (about 1/10 of the IP LD_{50}), and five mice with 150mg./kg. of iproniazid (about 2/10 of the IP LD_{50}). The remaining three served as untreated controls.

The mice were injected from 12:15 to 1:35 p.m. and radiated between 8:00 and 8:40 p.m. the same day. The purpose of the time interval was to allow the drugs to reach a maximal level of monoamine oxidase inhibition before irradiation. Green and Erickson (3) found with one oral dose of 100mg./kg. of iproniazid, inhibition of monoamine oxidase was maximal within 3 hours and after 16 hours slowly returned toward the normal level over a period of 11 days.

During irradiation eight and ten mice were placed in each of two clear plastic containers measuring about 20cm. x 20cm. x 4cm. and provided with holes for breathing.

The mice were exposed to 800r. of whole-body x-ray at 200KV., 15ma. with a half value layer of 1.8mm. of copper. The exposure was over a 10 minute interval at 80r./minute.

RESULTS

We used survival time as a measure of protection with these results:

TABLE I

Group	Mortality Ratio by Days												
	1	2	3	4	5	6	7	8	9	10	11	12	13
Control	0/3	0/3	1/3	1/3	1/3	1/3	2/3	0/3					
75mg./kg. Serotonin	0/5	0/5	0/5	0/5	2/5	2/5	2/5	2/5	3/5	3/5	3/5	4/5	5/5
75mg./kg. Iproniazid	0/5	0/5	0/5	0/5	0/5	0/5	1/5	2/5	2/5	2/5	2/5	3/5	5/5
150mg./kg. Iproniazid	0/5	0/5	0/5	0/5	0/5	0/5	0/5	3/5	3/5	4/5	4/5	5/5	

The (ST_A) average survival time (number of days/number of mice in group) and the level of statistical significance is shown for each group in Table II.

TABLE II

Group	ST_A in Days	ST_A Difference from Control
Control	6.3	
75mg./kg. Serotonin	8.8	2.5*
75mg./kg. Iproniazid	10.6	4.3**
150mg./kg. Iproniazid	9.2	2.9***
Iproniazid (groups combined)	9.9	3.6****

*Significant at the 0.20 level.
**Significant at the 0.05 level.
***Significant at the 0.15 level.
****Significant at the 0.10 level.

The Air Force report (1) showed serotonin to be effective in a radioprotective capacity. Our study has demonstrated that iproniazid is at least equal to serotonin as a radioprotective agent. Due to the small number and the age of the mice used our results are not definitive, but are suggestive of an avenue for further study.

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