Effect of Cholinesterase Inhibitor Malathion on Whole Body Irradiated Rats

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INTRODUCTION

It is well known that acute doses of malathion induce hyperglycaemia and increase plasma sodium and glycogen content of various tissues (KLOTZSCHE, 1955, GUPTA and PAUL 1972 and GUPTA, 1974). Recently we have observed that small doses of malathion do have significant effect on phosphatases and succinic dehydrogenase of irradiated rats, even though no effect was observed in normal rats (GUPTA et al. 1975 and GUPTA and KAPOOR, in press). As an extension of these observations the effect of malathion and radiation separately and jointly has been studied on blood glucose, plasma electrolytes and glycogen content of various tissues in 12 hr-fasted female albino rats.

MATERIALS AND METHODS

One hundred and twenty female Albino rats ranging between 150-200g were used in this study. Rats were maintained on commercial diet ad libitum except that before sacrifice they were fasted for 12 hrs so that the same 12 hrs-fasting period was used for all the animals. The animals were divided at random into four equal groups.

First group served as control and received propylene glycol, the second group received a dose of 50 mg/kg malathion in propylene glycol intraperitoneally. The rats in the 3rd group served as irradiation controls while the rats in the 4th group received 50 mg/kg malathion half an hour after irradiation. For irradiation animals were exposed at the abdominal region to a single dose of gamma rays emitted from Co^{60} source at the rate of 37.1 R/min

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for 24.30 min; total dose being 900 Rads. Six animals from each group were sacrificed and blood and tissue samples were collected at predetermined time intervals (see results).

Blood glucose was measured as described by HAWK et al. (1954) and expressed in mg/100 ml. The procedures for measuring plasma sodium and potassium were the same as described previously (GUPTA and PAUL, 1972). Glycogen content of various tissues was estimated by the method of FONG et al. (1953).

RESULTS

TABLE 1 summarises the results of blood glucose, plasma sodium and potassium estimation of rats exposed to various treatments. The results are expressed as the average (±SE) of 4 to 6 rats in each group. Malathion alone at the dose levels, used in this study (50 mg/kg) had no effect on any of the three parameters. Radiation caused a significant increase in blood glucose for a period of 12 to 24 hrs after exposure. Thereafter, the values returned to control levels. A fall in plasma sodium and a rise in plasma potassium levels was also apparent between 12 to 24 and 12 to 48 hrs after irradiation respectively.

In pre-irradiated rats given malathion, increase in blood glucose was observed as early as 2 hrs and the values persisted up to 12 hrs after treatment. Similarly malathion mitigated or reduced the duration of effect of irradiation on plasma electrolytes. Thus in pre-irradiated rats given malathion, no significant change in potassium levels was observed while the decrease in sodium level was only of a minor degree and for a shorter period.

Mean values of glycogen content of various tissues including SE of the observations are shown in TABLE 2. Here again at the dose level of 50 mg/kg malathion produced no noticeable changes in glycogen content of any of the tissues. Radiation on the other hand caused an increase in glycogen content of liver, spleen and brain between 12-48 hours, but there was no change in any of the other organs.

Administration of malathion to pre-irradiated rats further added to the effects of radiation. The increase in glycogen content was earlier and more marked in liver, spleen and brain of irradiated animals given malathion as compared to irradiated controls.

TABLE I

Blood Glucose (mg/100 ml) and Plasma Sodium & Potassium (m.eg/liter) of 12 Hr-Fasted Rats.

Hr		Control	Malathion (50 mg/kg,ip)	Radiation (900R)	Radiation (900R) + Malathion (50 mg/kg,ip)
2	glucose	81.4±6.2	85.1±5.8	80.6±2.1	139.0±1.9*
	Na	134.4±3.2	132.4±0.6	136.4±2.2	142.0±2.2*
	K	7.6±0.3	7.7±0.5	7.1±1.0	6.9±0.8
6	glucose	75.6±4.2	79.2±7.2	82.4±6.0	146.0±6.2*
	Na	130.0±2.7	136.2±1.4	131.7±4.0	138.2±4.2
	K	7.0±0.6	6.9±1.4	6.8±0.9	8.1±1.4
12	glucose	80.6±3.1	82.5±3.9	139.1±6.3*	142.0±4.0*
	Na	134.0±2.5	131.4±3.0	122.1±2.3*	128.7±2.9
	K	8.2±1.4	7.4±0.1	10.4±0.2	7.1±0.4
24	glucose	78.4±2.8	80.4±4.8	142.6±3.1*	86.5±4.2
	Na	132.0±0.3	134.2±0.9	118.4±1.8*	124.4±2.2*
	K	6.8±1.0	7.6±0.2	9.2±0.2*	8.2±0.6
48	glucose	83.3±2.5	91.2±5.1	88.4±7.1	78.4±4.9
	Na	134.4±1.8	130.9±2.3	136.5±5.6	136.2±1.8
	K	7.5±0.6	7.9±0.9	8.7±0.1	7.3±0.6

± SE for 4 to 6 animals at each time interval.
*=P≤0.05 = Significant difference from control values.

TABLE 2

Glycogen Content (mg/100 gm) in 12 Hr-Fasted Rats

Hr	Tissue	Control	Malathion (50 mg/kg ip)	Radiation (900R)	Radiation (900R) + Malathion (50 mg/kg ip)
2	Liver	74.0±9.1	81.0±4.0	75.4±6.1	76.1±4.5
	Spleen	12.1±1.6	10.4±1.9	11.6±2.0	9.8±2.3
	Brain	3.8±0.4	4.1±0.0	3.4±0.8	3.5±0.2
6	Liver	79.5±6.4	82.0±8.2	73.6±1.9	83.5±4.6
	Spleen	11.4±1.6	14.3±2.7	10.6±0.7	12.2±3.4
	Brain	2.9±1.1	3.5±0.3	3.8±1.0	8.4±1.4
12	Liver	82.4±3.6	85.2±0.0	80.6±6.1	182.6±23.5*
	Spleen	12.8±2.1	11.6±1.8	13.2±2.4	19.6±3.4 *
	Brain	4.1±0.5	4.5±0.9	7.2±0.4	12.3±2.0 *
24	Liver	73.9±3.4	72.0±8.6	116.4±7.1*	375.2±36.4*
	Spleen	10.8±0.8	11.2±0.6	18.0±2.6*	17.4±3.6 *
	Brain	4.3±0.2	3.7±0.5	13.2±2.4	15.9±4.1 *
48	Liver	78.9±7.6	69.0±11.0	125.6±13.9*	193.6±25.6*
	Spleen	11.3±0.7	12.1±0.4	15.4±2.6	13.0±1.8
	Brain	4.1±0.4	3.2±0.7	14.1±1.6 *	12.5±2.3 *

± SE for 4 to 6 animals at each time interval.
*=P≤0.05 + Significant difference from control values.

DISCUSSION

At a dose level of 50 mg/kg as used in the present study malathion caused no significant change in blood glucose, plasma electrolytes and glycogen content of various tissues of rat, even though higher doses of malathion are known to cause hyperglycaemia and an increase in liver glycogen as well as an increase in plasma sodium (GUPTA, 1974).

Radiation alone caused hyperglycaemia and slight increase in liver glycogen. When a small dose of malathion was given to irradiated rats the general effect of the combined treatment was in the same direction. In fact, the effect appeared to be enhanced in time to a degree. Thus with radiation alone the blood glucose level reached maximum between 12-24 hrs; with combined treatment the maximum, which was slightly higher, was reached in six hrs. Hyperglycaemia following radiation has been reported to be due to gluconeogenesis related to 11-OXY steroids (ORD and STOCKEN, 1961). Malathion appears to add to and enhance that effect. Glycogen deposition in liver and other organs seems to follow a spell of hyperglycaemia with either treatments.

The effects on plasma electrolytes by radiation; decrease in Na and increase in K, appears to be due to an interference with the active mechanism at the cell membrane level (OKADA, 1970). Inhibition of such a mechanism will allow the effects of physical factors, osmosis, permeability, etc. to prevail. Malathion in large doses, however, caused increase in plasma Na without much effect on K. This has been speculated by GUPTA (1974) as a non-specific stress leading to release of corticosteroids and consequent Na retention and K loss. Therefore, malathion given to irradiated rats appears to neutralize the effect of radiation on the cell membranes. Thus in animals with combined treatment there is lesser fall of Na and lesser rise in K levels of plasma.

One could therefore speculate that simple non-specific stress caused by malathion adds to the similar effect of radiation enhancing the hyperglycaemia and glycogen deposition that follows. On the other hand the same action of malathion appears to alleviate the effect of radiation directly on the Na K pump mechanism at the cell membranes.

KLOTZSCHE, V. C. Arzneim. Forsch. 5 (1955) 436.

GUPTA, P. K. and Paul, B. S. Poultry Sci. 51, (1972) 1574.

GUPTA, P. K. Acta, Pharmacol. et Toxicol. 35, (1974) 191.

GUPTA, P. K., DHAR, U. and BAWA, S. R. Environ. Physiol. Biochem. 5, (1975) 59.

GUPTA, P. K. and KAPOOR, V. Environ. Physiol. Biochem. (In Press)

HAWK, P. B., OSER, B. L., and SUMMERSON, W. H. Practical Physiological Chemistry, McGraw-Hill Book Company, Inc., New York, Toronto London, 13 ed; (1954).

FONG, J., SCHAFFER, F. L. and KIRK, P. A., Arch. Biochem. & Biophys. 45, (1953) 319.

ORD, M. G. and STOCKEN, L. A. The biochemical lesion *in vivo* and *in vitro*. In: Mechanism in Radiobiology Vol 1, p. 259 (Eds. M. Errera and A. Foressberg) Academic Press, New York (1961).

OKADA, S. Radiation biochemistry, Vol. 1, Cells. Academic Press, New York and London (1970).