EFFECT OF MALATHION ON BLOOD GLUCOSE, LIVER GLYCOGEN, PLASMA CORTICOSTERONE AND ELECTROLYTES CONCENTRATIONS AND EOSINOPHIL COUNT IN ADRENAL DEMEDULLATED RATS

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ABSTRACT

Malathion produced hyperglycaemic and hyperhepatic glycogenic effects in Sham operated animals whereas it produced only non-significant rise in adrenal demedullated rats indicating the involvement of adrenal medulla in mediating these effects partially. Malathion produced a significant rise in the level of plasma corticosterone in Sham operated as well as adrenal demedullated rats. Malathion at this dose (170 mg/kg i. p) caused significant eosinopaenia in both Sham operated and adrenal demedullated rats which might be due to the non-participation of adrenal medulla in causing this effect. Malathion did not produce any change in the levels of plasma sodium and potassium in either Sham operated or adrenal demedullated rats which showed that there was neither any effect of malathion on these electrolytes nor involvement of adrenal medulla.

INTRODUCTION

MALATHION brings about hyperglycaemia and increased liver glycogen deposition[1, 2]. Earlier studies on rats with malathion have shown that it acts as a stressor[1, 3] by producing hyper adrenal activity along with eosinopaenic response and further, it is also shown that there is involvement of adrenal glands in causing hyperglycaemic and hyper hepatic glycogenic effects as these effects are seen in intact animals but not in adrenalectomised rats[4]. Similarly another insecticide guthion and herbicides like paraquat and diquat have failed to elicit this response in adrenalectomised animals but not in intact animals[5, 6]. In continuation of the above research project, the present study was undertaken in adrenal demedullated rats to find out the participation of adrenal medulla in mediating these effects.

MATERIALS AND METHODS

The experiment was conducted on Wister strain of male Albino rats weighing from 120 to 150 g. The animals were procured from the animal house of this institute and were maintained on standard feeding schedule and management conditions. The feed and water were provided *ad lib.*

Malathion [0,0-Dimethyl S(1,2-dicarbo-ethoxy ethyl) phosphorodithioate] of technical grade (97.2%) after dissolving in arachis oil was administered intraperitoneally. The animals were divided into four different groups namely 1. Sham operated control, 2. Sham operated with administered malathion. 3. Adrenal demedullated control and 4. Adrenal demedullated administered malathion. Each group consisted of six animals. The rats were demedullated bilaterally according to the method outlined by Zarrow *et al*[7] and after demedullation the animals were maintained for 30 days for complete regeneration of adrenal cortices. In the case of Sham operated animals the entire operation of adrenal demedullation was performed except the removal of adrenal medulla. During the first weak following operation, the animals were provided with a drinking solution containing one per cent sodium chloride and five per cent glucose in the case of adrenal demedullated rats and only glucose solution in the case of Sham operated rats. Later they were kept on normal feed and water. After one month these animals were used for experimentation. Malathion was administered at a dose of 170 mg/kg which is approximately 1/7th of LD-50 (1150 mg/kg). Controls received an equivalent volume of arachis oil without malathion. All the animals were sacrificed after two hours of malathion administration. This interval was selected because in previous studies with malathion at 170 mg/kg, the peak effect was observed at two hours after its administration[1]. The rats were anaesthetised with pentobarbitone at 50 mg/kg given

intraperitoneally before sacrifice. The chest was opened and the blood was collected directly from the heart in heparinised test tubes. A part of it was used for the estimation of blood glucose[8] and eosinophil counting[9] and the remainder was centrifuged and the plasma obtained was used for the estimation of corticosterone[10], sodium and potassium levels. After opening the peritoneal cavity, the liver was taken out for estimating glycogen[11]. The experimental data were analysed statistically[12] and student's 't' test was applied to determine the significance.

RESULTS AND DISCUSSION

Malathion produced a significant hyperglycaemic effect in Sham operated animals, the level of glucose increased from 69.4 to 125.7 mg per 100 ml of blood, whereas it had only a little insignificant effect in adrenal demedullated rats, the level of glucose rising from 67.2 to 75.1 mg per 100 ml of blood (table 1). Malathion caused a significant rise in liver glycogen in Sham operated rats. In these animals the level of glycogen increased from 27.1 to 54.6 mg/g of liver, whereas it caused an insignificant increase in adrenal demedullated rats, the level of glycogen rising from 26.5 to 32.0 mg/g of liver (table 1). Since malathion produced much smaller effect in adrenal demedullated animals as compared to Sham operated animals, the role of adrenal medullary catecholamines in bringing these effects cannot be ignored. In previous studies with malathion, the involvement of adrenal glands was observed in mediating hyperglycaemic and hyper hepatic glycogenic effects as these effects were seen in Sham operated but not in adrenalectomised rats[4]. Therefore, hyperglycaemic effect and increased glycogen deposition in liver appear to be dependant on the normal functioning of both adrenal medulla and cortex.

Corticosterone can bring about hyperglycaemia by rapid mobilisation of amino acids and fats from cellular stores thus making these available for synthesis of glucose[13] and also increase glycogen deposition in liver by preventing peripheral utilization of glucose probably by acting as anti-insulin factor[13, 14]. This observation has been further confirmed indirectly in our earlier studies[1, 4]. However, the observation in demedullated rats indicating hyperglycaemia and increased liver glycogen deposition in the present study are probably dependant on the adrenal medullary activity also. Medullary catecholamines can bring about faster muscle glycogenolysis leading to more of lactic acid that gets ultimately converted to glycogen in liver[15].

In our previous studies[4] on the effect of malathion in adrenalectomised rats it revealed the total absence of significant response with respect to increase blood

Table 1 *Effects of malathion treatment on blood and liver components*

	Adrenal demedullation	Control	Malathion treated	Per cent control
Blood glucose (mg/100 ml)	–	69.4 ± 3.7	125.7 ± 3.5**	181
	+	67.2 ± 2.0	75.1 ± 5.4	112
Liver glycogen (mg/g)	–	27.1 ± 2.9	54.6 ± 3.9**	201
	+	26.5 ± 2.4	32.0 ± 1.7	121
Plasma corticosterone (μg/100 ml)	–	23.9 ± 2.1	69.1 ± 3.8**	289
	+	19.1 ± 1.6	60.6 ± 4.3**	317
Eosinophil count (Counts/cmm)	–	891 ± 55	125 ± 12**	14
	+	851 ± 27	244 ± 24**	29
Plasma sodium (mEq/L)	–	157.3 ± 1.8	155.3 ± 2.9	99
	+	152.5 ± 1.4	152.8 ± 4.6	100
Plasma potassium (mEq/L)	–	4.7 ± 0.2	5.1 ± 0.4	108
	+	4.7 ± 0.9	5.0 ± 0.3	106

Animals were sacrificed two hours after the administration of malathion.
** $P < 0.01$ as compared to their respective controls in all attributes.

glucose and liver glycogen values in comparison to their control groups. But the present study in adrenal demedullated rats at two hours of malathion administration demonstrated the partial response of hyperglycaemia and increased liver glycogen values in comparison to their respective control groups indicating the participation of medulla. However, it would be interesting to find the degree and duration of such participation in demedullated rats to assess the differential participation of medulla and cortex.

The rats showed symptoms of slight convulsions and other cholinergic stimulation at the dose of malathion used requiring higher uptake of glucose by brain. The animals became normal subsequently after exhibiting the symptoms.

Melathion produced a significant rise in level of plasma-corticosterone in Sham operated as well as adrenal demedullated rats, which is due to the presence of intact cortex in adrenal demedullated rats Malathion at this dose caused a significant eosinopaenic response in both Sham operated and adrenal demedullated groups. Eosinophils reduced from 891 to 125 counts/cmm in Sham operated and from 851 to 244/cmm in adrenal admedullated rats (table 1). This indicates probably the non-participation of adrenal-medulla in bringing this effect. No significant change in the levels of plasma sodium and potassium were observed when malathion was administered either to Sham operated or adrenal demedullated rats. This showed that there was neither any effect of malathion on electrolytes nor involvement of adrenal medulla.

Murphy and Porter[5] found that the hyperglycaemic and hyperhepatic glycogenic actions of guthion another insecticide were not seen in either adrenalectomised or adrenal demedullated rats which showed that both adrenal cortex and medulla are important in mediating these effects. Toshio *et al*[16] observed the elevation of blood glucose in intact rats after administration of 3-phenyl = 5-(2-peridinioethyl) isoxazole citrate but not in adrenal demedullated or adrenalectomised rats and the authors drew a similar conclusion as above.

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