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Effect of 2-piperazino-4(3H)-quinazolinone monoacetate on some aspects of carbohydrate metabolism of albino rats*

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IT HAS been demonstrated that 2-piperazino-4(3H)-quinazolinone monoacetate (Compound I) is a potent, new hypoglycaemic agent.[1] The action of this compound on some parameters of carbohydrate metabolism in albino rats is reported in this paper.

Fifty-two adult male albino rats from this Institute's colony were used. Animals weighing 110–160 g were maintained on a standard animal house pellet diet. The rats were fasted for 18 hr prior to the experiment. Eight rats were stunned by a blow on the head and decapitated. Liver and skeletal muscle (gastrocnemius) were quickly excised, placed in a mixture of ice and sodium chloride at −2° and weighed. Glycogen was estimated by the method of Good *et al.*[2] Twenty rats were intubated with a solution of Compound I (100 mg/kg body weight). They had access to water *ad lib.* Liver and muscle were excised from four rats at 2·5, 4, 8, 16 and 24 hr after administration of Compound I for glycogen estimation.

Blood was collected from 12 albino rats by cardiac puncture and estimations of lactic acid, pyruvic acid and Pi (inorganic phosphate) were carried out by the methods of Barker and Summerson,[3] Friedman and Haugen,[4] and Taussky and Shorr.[5] respectively. Compound I was administered at 100 mg/kg to 12 rats by intubation. After 2 hr, blood was again collected from the rats for the estimations as above. Each compound was estimated in duplicate.

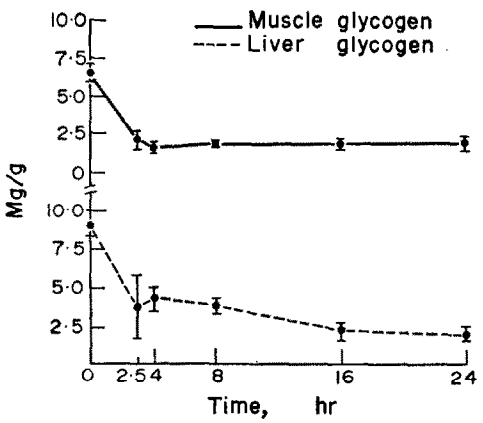

FIG. 1.

The decrease of glycogen in skeletal muscle and liver can be seen in Fig. 1, from the time of feeding (Compound I) until 24 hr later. However, a very rapid decrease in the muscle glycogen level at 2·5 hr, from 6·78 ± 0·61 to 2·14 ± 0·64 mg/g wet wt of muscle (i.e. almost one-third of its initial value) was observed. A marked decrease in the liver glycogen could also be observed, the initial level falling from 8·19 ± 0·12 to 3·66 ± 1·93 mg/g wet wt of liver (i.e. less than one-half of its initial value).

After administration of Compound I, significant changes in the blood lactic acid and inorganic phosphate were observed. The level of pyruvic acid remained unchanged. The lactic acid level rose from 17·35 ± 2·32 to 49·00 ± 8·79 mg/100 ml of blood (i.e. 2·5 times its initial value) and inorganic phosphate rose from 4·39 ± 0·3 to 6·06 ± 0·26 mg/100 ml blood after 2 hr (Table 1).

Liver and muscle glycogen depletion, and increase in inorganic phosphate associated with rise in blood lactic acid level was found in animals made hypoglycemic by administration of guanidine and its derivatives.[6] Therefore it can be concluded that the action of Compound I on the blood level of Pi,

* Title of this paper was read in the 7th International Congress of Diabetes Federation at Buenos Aires (1970).

TABLE 1. CHANGES IN LACTIC AND PYRUVIC ACIDS AND IN INORGANIC PHOSPHATE OF BLOOD AFTER ADMINISTRATION OF COMPOUND I (100 mg/kg)

	0 (hr)	2 (hr)	*T* between means
Lactic acid	17·35 ± 2·32 (12)	49·00 ± 8·79 (12)	3·4*
Pyruvic acid	2·19 ± 0·1 (9)	2·96 ± 0·26 (9)	2·7
Pi	4·39 ± 0·3 (9)	6·06 ± 0·26 (8)	4·2*

Figures in parentheses indicate number of observations.
* Significant at 5 per cent level.
Values expressed in milligram per cent indicate mean ± S.E. of the mean.

lactic acid and liver and muscle glycogen compares directly with that of guanidine derivatives. Therefore, Compound I may act in a similar manner to guanidine derivatives as speculated by Hollunger.[7]

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Effect of intracellular accumulation of inert carbon particles on the cytochromes P-450 and b_5 levels of rat liver microsomes

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HISTOLOGICAL and ultrastructural studies have shown that carbon particles injected into the blood stream are quickly resorbed by the reticuloendothelial cells, particularly by the Kuppfer cells of the liver.[1–4] Biochemical effects of this intracellular accumulation of carbon in the whole liver are not well known. In this communication we report the results of a systematic study, showing a decrease in the microsomal cytochrome levels.