From the above results, it was found that the enzymatic demethylation of lysergic acid derivatives at position 6 to form nor-derivatives was independent of their physiological actions, and that a side chain at position 8 of normal lysergic acid derivatives was enzymatically attacked to form monoalkylamides or hydroxyalkyl amides. However, an exception occurs when the compound possesses a methyl group at position 1 for then demethylation occurs at position 1 instead of 6.

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Effect of 2-piperazino-4(3H)-quinazolinone monoacetate on the tissue respiration, glucose uptake and lactic acid production by rat hemidiaphragm*

(*Received* 10 *December* 1973; *accepted* 19 *March* 1974)

2-PIPERAZINO-4(3H)-quinazolinone monoacetate (I), is a hypoglycemic agent in some species of normal animals.[1] Also it can effectively lower blood sugar in different species of diabetic animals.[2] When administered by gastric intubation, it causes a remarkable increase in lactic acid and a lowering of liver and muscle glycogen in albino rats.[3] Its effect *in vitro* on the glucose uptake, lactic acid formation and tissue respiration of rat hemidiaphragm suspended in phosphate buffer has been studied and the results are reported.

Albino rats of the Charles Foster strain, body wt 110–160 g, were used. After fasting for 18 hr the rats, with constant access to water, were quickly decapitated and diaphragms were dissected out and collected in phosphate buffer at 4°.[4] Oxygen was bubbled through the buffer for 5 min at room temperature and then for 1 min after the hemidiaphragms had been transferred to Warburg flasks and suspended in 2 ml buffer containing 3 mg glucose/ml, cooled to 4°. (I) was added to give a final concentration of 0, 10^{-3}, 10^{-4}, 10^{-5}, and 10^{-6} M. The flasks were incubated at 37° for 90 min with constant shaking. Manometric readings were taken at 30, 60 and 90 min. Glucose and lactic acid were estimated according to Sunderman *et al.*[5] and Barker and Summerson,[6] respectively, after 90 min incubation. The hemidiaphragms were weighed on a torsion balance after carefully pressing between two filter papers to remove the buffer solution. The weight of hemidiaphragms ranged from 120 to 200 mg.

There was an increase in glucose uptake and lactic acid production by diaphragms in flasks containing 10^{-4} M and 10^{-5} M(I) compared with the untreated control flasks (Table 1). There was no significant change in glucose uptake or lactic acid production in the presence of 10^{-3} M or 10^{-6} M(I).

It is evident from Fig. 1 that 10^{-4} M(I) caused maximum O_2 uptake by hemidiaphragm. On the other hand 10^{-3} M(I) inhibited the tissue respiration and the stimulating effects of (I) gradually waned beyond 10^{-4} M.

* Communication No. 1915 from Central Drug Research Institute, Lucknow, India.

TABLE 1. SHOWING GLUCOSE UPTAKE, LACTIC ACID RELEASE AND OXYGEN CONSUMPTION IN HEMIDIAPHRAGMS INCUBATED WITH 10^{-4} M AT 37° FOR 90 MIN

	Experimental	Control	*t*
Glucose uptake (μg glucose/ml buffer/mg diaph.)	2·920 ± 1·52	0·830 ± 0·26	3·2
Lactic acid (μg lactic acid/ml buffer/mg diaph.)	3·5 ± 0·04	3·2 ± 0·03	6·0
Oxygen uptake (μl O_2 uptake/ mg diaph.)	243 ± 8·71	160 ± 28·8	2·7

Results expressed as mean ± S.E.M. for six determinations.

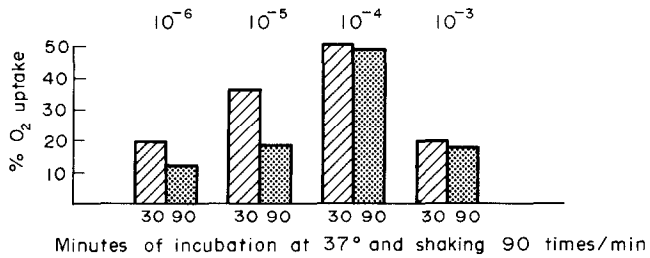

FIG. 1. Percentage oxygen uptake at various molar concentrations of the compound (each value has been compared with its paired control).

An optimal concentration of 10^{-4} M(I) increased the O_2 and glucose uptake, and lactic acid formation by hemidiaphragms *in vitro*. This corroborates previously reported results *in vivo*.[3]

The *in vitro* effect shown by (I) may be due to its direct action on the diaphragm. Such a possibility has been envisaged for the mechanism of action of biguanides.[7]

Acknowledgements—The author's thank Drs. C. M. Gupta, A. P. Bhaduri and N. M. Khanna for supplying (I). Sincere thanks are also due to Messrs. M. A. Hai, H. M. Chakravarti and Rama Nand for their technical assistance.

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