

## Effects of lithium on the activity of pyruvate kinase and other magnesium dependent enzymes

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It has been proposed that the many various pharmacological effects of lithium might be explained by its competition with magnesium and calcium (Birch, 1973). Many enzymes are magnesium dependent and it was decided to determine the effect of lithium on the activity of a number of those which were commercially available. Preliminary experiments were carried out on the following: pyruvate kinase, alkaline phosphatase, hexokinase, glucose-6-phosphate dehydrogenase, 3-phosphoglycerate kinase. Hexokinase was obtained from Sigma Ltd, all others from Boehringer Ltd.

The first three enzymes were inhibited by lithium concentrations of 6 mmol/l (50%), 2 mmol/l (50%) and 14 mmol/l (30%) respectively. The remaining two were not inhibited in the preliminary experiments though their investigation was not exhaustive.

Lithium inhibition of pyruvate kinase has been previously reported (Kachman & Boyer, 1953) though the concentration used (100 mmol/l) was far in excess of the plasma level (0.6-1.4 mmol/l) obtained during treatment of recurrent affective disorder (Hullin, McDonald & Allsopp, 1972). The effects of lithium in the pharmacological dose range was therefore determined by the disappearance of NADH (estimated spectrophotometrically at 340 nm) in 3 ml aliquots of the test system: pyruvate kinase (0.66 mg/l), lactate dehydrogenase (13.32 mg/l), ADP (0.5 mmol/l),  $MgCl_2$  (1.5 mmol/l) and KCl (40 mmol/l). Lactate dehydrogenase was shown to be unaffected by lithium at the concentrations prevailing.

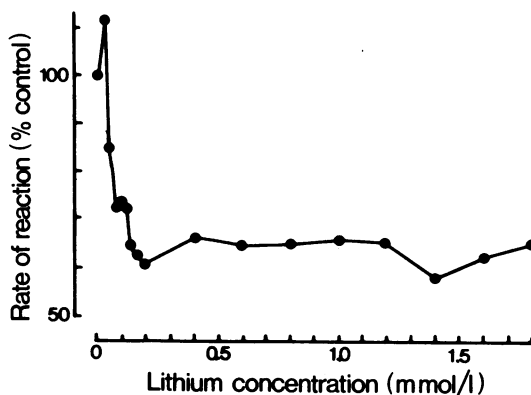


Fig. 1 The effects of various concentrations of lithium on the activity of pyruvate kinase expressed as percentage of control values.

Figure 1 shows the effect of various concentrations of lithium on the activity of pyruvate kinase. A significant inhibition occurs at normal pharmacological concentration of lithium.

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### References

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## The effects of the anticonvulsant ethosuximide on adenosine triphosphatase activities of synaptosomes prepared from rat cerebral cortex

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The results of recent experiments in our laboratory have indicated that the anticonvulsant

ethosuximide inhibits the sodium, potassium-activated, magnesium-dependent adenosine triphosphatase ( $Na,K$ -ATPase) activity of nerve terminals (synaptosomes) prepared from rat cerebral cortex. The results also suggested that the synaptosomes contain a sodium-activated, magnesium-dependent ATPase ( $Na$ -ATPase) in addition to the  $Na,K$ -ATPase usually associated with the sodium pump (Gilbert, Scott & Wyllie, 1974). In contrast to the  $Na,K$ -ATPase, the  $Na$ -ATPase was not inhibited by ethosuximide ( $2.5 \times 10^{-4}$  –