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SHORT COMMUNICATIONS

The effect of chlorpromazine on the aconitase in kidney particle preparations

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IN the course of some other work, the writer tried the effect of chlorpromazine on the metabolism of kidney particles from the guinea pig. The experiments were arranged so that in 30 min the particles almost completely metabolized 10 μmole citrate, added at the start of the experiment. Figure 1, compiled from four experiments, shows that addition of chlorpromazine stopped citrate metabolism; $4{\cdot}7 \times 10^{-4}$M had an effect over 50 per cent, whereas $1{\cdot}88 \times 10^{-4}$M did nothing. Many of the biochemical observations made in this field appear to be rather unspecific, though recent observations on cytochrome oxidase[1] are more definite. One possible explanation of the aconitase results is that the chlorpromazine forms a non-ionized compound with the citrate which then becomes inaccessible to the enzyme. The steepness of the curve would be consistent with this. If this be the explanation, observations upon compounds formed between ATP and chlorpromazine and other substrates may show similar complexing effects. This may well explain the lack of specificity in action upon mitochondrial reactions which has been reported, for instance, by Berger.[2]

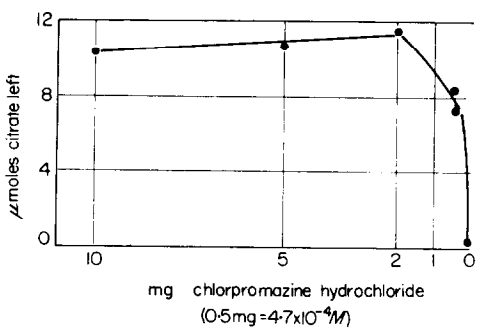

FIG. 1. Relation between concentration of chlorpromazine and the disappearance of added citrate with kidney particles.

Experiment: Kidney particles (guinea pig) were homogenized by our usual methods,[3] centrifuged and made up in 1 % KCl containing 0·1 M phosphate buffer, pH 7·2, so that the particles from one guinea pig made up a volume of 26 ml. Flasks for experiment contained 1·9 ml enzyme suspension Mg^{2+} 0·1 ml (4 μmoles), ATP 0·1 ml (1·2 μmoles) Na citrate 10 μmoles, chlorpromazine hydrochloride (neutralized) and enough 1 % KCl to bring the total volume to 3·0 ml. The reaction was run for 30 min at 37 °C, after which trichloracetic acid was added to 8 per cent. Citrate was determined by TAYLOR'S[4] method. Chlorpromazine hydrochloride was "Largactil".

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