Therapeutic application of these antidotes, either alone or in combination, to rats intoxicated with organophosphates results in a separation of the LD90 (untreated) and the LD10 (treated) values (Table 1). This separation is regarded as a more meaningful criterion of the therapeutic efficiency of these antidotal regimens than is protection against the lethal effects of multiples of the LD50.

Cholinesterase in endplates of rat and chick: relationship of activity to log-dose response curves and the effects of some inhibitors.

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Although the cholinesterases of muscle have been extensively studied using homogenates, few workers have studied the properties of the enzymes *in situ*. This report is concerned with some aspects of the biochemistry and pharmacology of cholinesterase in motor endplates of chicks and rats. Single endplates were dissected, and cholinesterase estimated as described previously (Buckley & Heaton, 1968). Parallel measurements were made using single endplates and homogenates of fifty dissected endplates.

Homogenates of endplates from posterior latissimus dorsi of chick and from rat gastrocnemius showed a typical log dose/response curve with an optimum substrate concentration of 3–7 mM. Single whole endplates of chick muscle did not differ markedly from homogenates, but endplates of rat gastrocnemius showed no substrate inhibition with concentrations of acetylcholine less than 20 mM (Fig. 1).

A comparison of the effects of some inhibitors on endplate cholinesterase and homogenate cholinesterase showed further differences between chick muscle and rat gastrocnemius. Eserine ($2{\cdot}25\times10^{-7}$M) and choline (10·7 mM) produced the same inhibition in homogenates of chick and rat endplates, but the inhibition of single endplates from chick was approximately twice that of the rat endplates. According

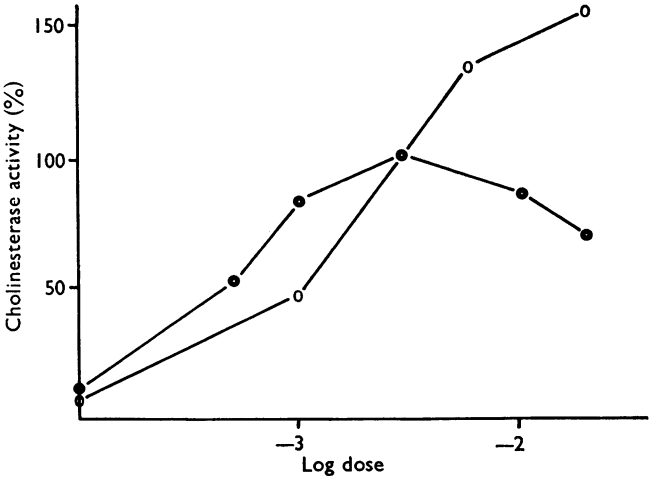

FIG. 1. Cholinesterase log dose/response curves for endplates from rat gastrocnemius (○) and chick posterior latissimus dorsi (●). In each case cholinesterase activity at 3 mM is taken as 100%.

to Webb (1963) the observation in the chick that endplates are inhibited more than homogenates could indicate the presence of a diffusion barrier for substrate. The observation in the rat that inhibition in endplates is less than in homogenates could indicate free diffusion of substrate but slow diffusion of the inhibitors. These two conclusions are not supported by the log dose/response curves of Fig. 1.

The results can be interpreted as evidence that the organization of the endplate in chick posterior latissimus dorsi differs from that of the rat gastrocnemius.

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Electron microscopy and histochemistry of isolated kallikrein granules.

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Differential centrifugation and sucrose density-gradient analyses of homogenates prepared from submaxillary glands of the guinea-pig have established that kallikrein is stored intracellularly in granules (Bhoola & Ogle, 1966; Bhoola, 1968).

In the present experiments, secretory granules separated at 9,500 *g* on a 1·5 ml cushion of 0·8 M sucrose and 1% glycogen were centrifuged at 25,000 *g* on a discontinuous density-gradient extending from 1·3 M to 2·0 M sucrose. The kallikrein-containing granules equilibrating between 1·6 M and 1·85 M sucrose were recovered and recentrifuged at 180,000 *g* on a second gradient ranging from 1·7 M to 2·0 M sucrose. The fractions containing the various subcellular elements were recovered

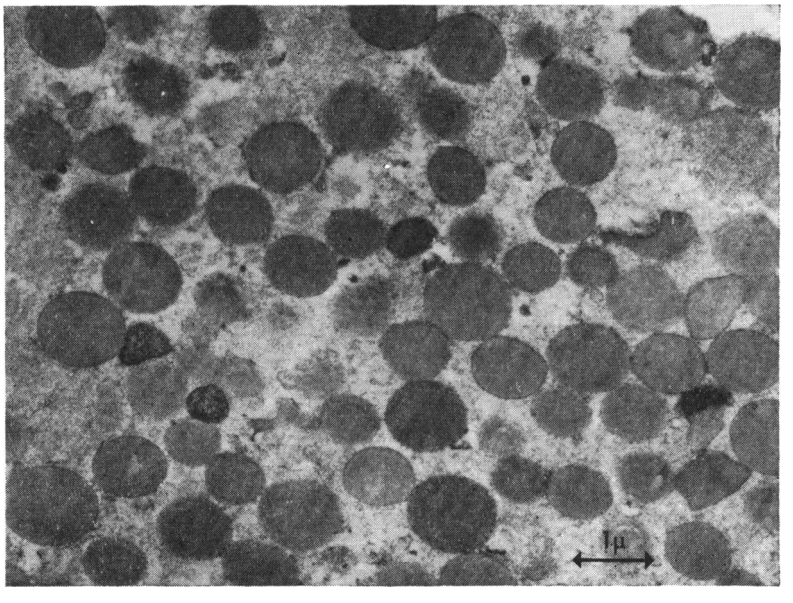

FIG. 1. Electron-micrograph of granules isolated by two sucrose density-gradients from homogenates of guinea-pig submaxillary gland; the granules illustrated in this figure were in equilibrium between 1·8 M and 1·85 M sucrose and contained most of the kallikrein activity.