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COMMUNICATIONS

In communications with more than one author, an asterisk (*) denotes the one who presented the work.

Differential antagonism of the acutely lethal effects of organophosphates in rats.

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The subcutaneous toxicity of some organophosphorus insecticides has been determined in rats and the effect of antidotes (cholinoceptor blocking agents and oximes) on the mortality curves has been examined. Probit analysis of these curves allows the estimation of LD10, LD50 and LD90 values in the absence and the presence of these antidotes. The oximes studied (pyridine-2-aldoxime methiodide (P2S) and obidoxime (Toxogonin, E. Merck, Darmstadt)) are quaternary ammonium compounds, and their reactivating activity against phosphorylated cholinesterase is restricted principally to peripheral sites in the body. The cholinoceptor blocking agents used were methylatropine, which acts mainly peripherally, and atropine sulphate, which exerts its effects both peripherally and centrally.

TABLE 1. *Estimated LD90 (untreated) and LD10 (treated) values for organophosphorus pesticides in female rats in the absence and presence of antidotes (μmol/kg subcutaneously)*

Antidotal regimen		Azodrin†	Bidrin†	Chlorfenvinphos†	Ciodrin†	Dichlorvos†	Mevinphos†
Untreated	LD90	38·1	43·9	69·7	208·9	60·4	6·0
Methylatropine 18·02 mg/kg s.c.	LD10	79·7	73·9	32·3	178·4	51·9	5·0
Atropine sulphate 17·40 mg/kg s.c.	LD10	266·0	208·5	66·4	247·0	123·3	6·4
P2S, 50 mg/kg s.c.	LD10	60·8	77·5	39·4	184·0	182·8	6·0
Obidoxime 90 mg/kg s.c.	LD10	104·2	99·3	67·8	153·8	270·1	8·3
Atropine sulphate 17·40 mg/kg s.c.+ P2S, 50 mg/kg s.c.	LD10	591·0	186·6	122·4	235·1	466·5	8·6
Atropine sulphate 17·40 mg/kg s.c.+ obidoxime, 90 mg/kg s.c.	LD10	488·0	291·0	570·0	207·9	795·8	15·2

† Products of Shell International Chemical Company.

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

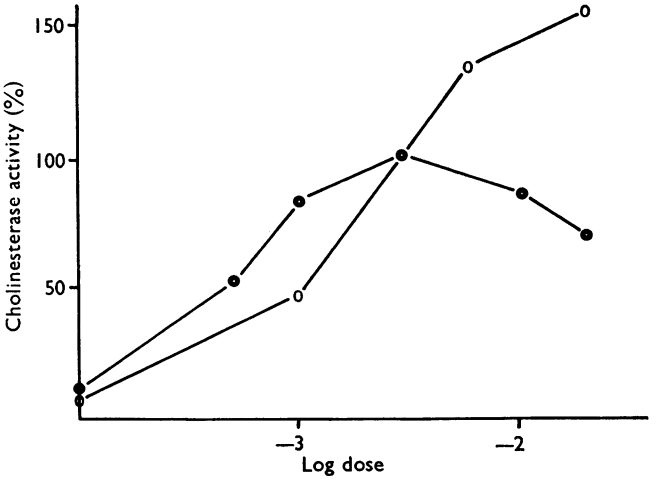

FIG. 1. Cholinesterase log dose/response curves for endplates from rat gastrocnemius (○) and chick posterior latissimus dorsi (●). In each case cholinesterase activity at 3 mM is taken as 100%.