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

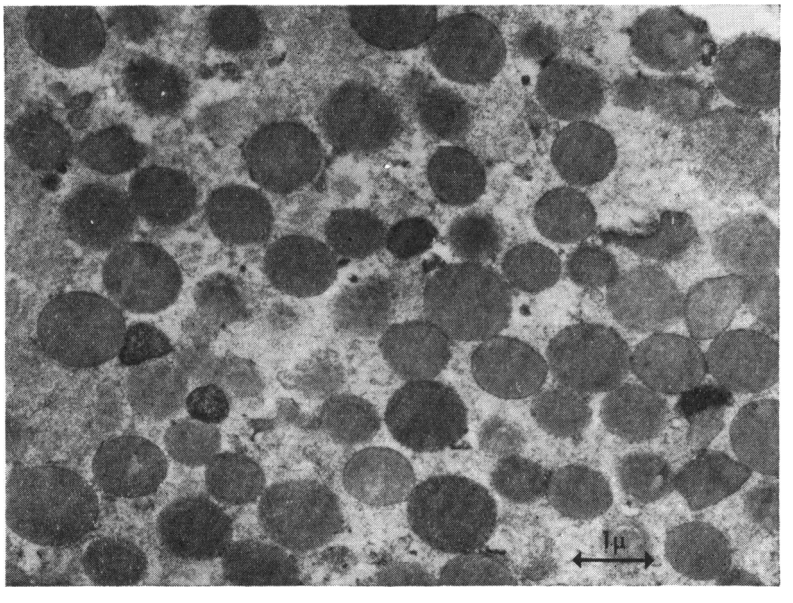

FIG. 1. Electron-micrograph of granules isolated by two sucrose density-gradients from homogenates of guinea-pig submaxillary gland; the granules illustrated in this figure were in equilibrium between 1·8 M and 1·85 M sucrose and contained most of the kallikrein activity.

separately by cutting each centrifuge tube (Beckman, cellulose nitrate) into four sections with a specially designed cutter. Aliquots of all fractions were taken for biochemical estimations. For electron microscopy some of the fractions containing particulate material were recentrifuged to form pellets which were first fixed in a triple aldehyde mixture (2·5% w/v glutaraldehyde—4% paraformaldehyde—2% acrolein) and then fixed in 1% osmium tetroxide. For histochemistry the pellets were fixed only in the aldehydes.

The secretory granules separated between 1·7 M and 1·85 M sucrose on the second density-gradient showed peak kallikrein activity. These organelles were almost completely free of other subcellular particles as determined by electron microscopy and by subcellular enzymes (succinate-neotetrazolium reductase for mitochondria and ß-glucuronidase and acid phosphatase for lysosomes). The isolated secretory granules reacted strongly with toluidine blue and periodic acid-Schiff reagents. The ultrastructure of the granules containing kallikrein resembled the electron-dense secretory (zymogen) granules observed in the intact guinea-pig submaxillary gland (Heap & Bhoola, 1969).

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Oxidative phosphorylation in heart mitochondria isolated from chlorpromazine-treated animals.

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Guinea-pigs, rats and cats were treated orally with either chlorpromazine (10, 15 and 20 mg/kg per day), saline, or placebo tablets for periods of 3 to 7 months. While under treatment the animals appeared healthy: their growth rate was normal and their body temperature remained at normal levels.

At the conclusion of treatment, mitochondria were isolated from ventricular myocardium by an adaptation (Zaimis, Papadaki, Ash, Larbi, Kakari, Matthew & Paradelis, 1969) of the method of Safer & Schwartz (1967). Respiration of the mitochondria was measured at 37°C with an oxygen electrode in the presence (state 3) and absence (state 4) of adenosine diphosphate (ADP) (Chance & Williams, 1956). The ratio of these two oxidation rates (state 3/state 4) gives an index (RCI) of respiratory control. The ADP:oxygen ratio, a measure of the efficiency of adenosine triphosphate (ATP) synthesis, was obtained by measuring the oxygen consumed in the conversion of a given quantity of ADP to ATP.

In each experiment the respiration of the mitochondria was studied (*a*) immediately after their isolation; and (*b*) after they had been stored at 0°C for 4 hr.