which is maximal at C_{10} (mark 24). At the same mark, the upper muscle receives hyoscyamine C_9 with practically no effect.

In my experiments the lowest active dose of hyoscyamine was C_{17}. It can be seen that hyoscyamine in very low concentrations contracts the frog's rectus, whereas concentrations of ten thousand up to one billion times greater fail to do so.

The amplitude of the maximal contraction produced by hyoscyamine increases by 6–10 times after paraoxon and is generally higher than that elicited by acetylcholine in concentration C_6 on untreated muscle. Concentrations of hyoscyamine, one million to one billion times higher than the threshold ones, are ineffective on treated, as well as on untreated, rectus muscles.

The contractions produced by small hyoscyamine concentrations are relaxed by stronger concentrations of this same alkaloid, by D-tubocurarine, in concentration C_6, and by magnesium chloride of concentration C_3.

These results suggest strongly that hyoscyamine acts on the rectus muscle as a contracting drug through a cholinergic mechanism, possibly by setting free an amount of acetylcholine at the level of its action. The closer pharmacological analysis of the site of this effect, details of which will be published elsewhere, demonstrates that these small concentrations of hyoscyamine act at the level of the neuromuscular junction and not on the contractile substance itself.

Methylatropine and scopolamine have no such effects. Other drugs may also act by releasing acetylcholine through a similar mechanism. I demonstrated it for barium chloride in concentrations between C_5 and C_3 and for neostigmine, in concentrations C_6 and C_5.

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Serum Changes in the Rat following Oral Administration of Cadmium

THE comparatively sudden and pronounced drop in hæmoglobin-levels and the resultant anæmia following oral administration of low doses of cadmium to rats has been reported by several workers[1–4]. Starch-gel electrophoresis was performed on the serum proteins of rats similarly dosed, using the apparatus described by Smithies[5], and a modification of the discontinuous buffer system described by Poulik[6], in which low melting point *tris*(hydroxymethyl)-aminomethane (m.p. 125° C.) was used instead of the usual form (m.p. 171° C.).

Sixteen male rats, Chester Beatty strain, aged three weeks and weighing 80–100 gm., were fed on diet 41*B* and allowed unlimited drinking water, containing 50 p.p.m. of cadmium as cadmium chloride. Blood specimens were taken from the tail at fortnightly intervals by rota, and severe anæmia was confirmed after four weeks. Despite continued oral administration of cadmium for a further three months, the degree of anæmia remained constant. Certain modifications of the normal serum protein pattern were observed after a similar time, but again, despite continued dosing, no further change was observed.

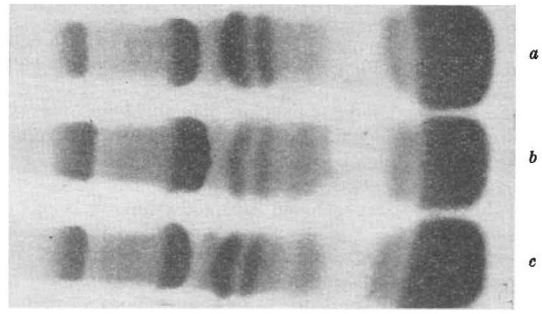

Fig. 1. Starch gel-electrophoresis pattern of the sera of rats given drinking water containing 50 p.p.m. of cadmium as cadmium chloride for four weeks. *a*, Cadmium rat serum; *b*, normal rat serum; *c*, cadmium rat serum. *A*, Unknown; *B* and *C*, transferrin bands

Two abnormalities in the serum protein pattern were seen to occur (Fig. 1). The component at point *A* was considerably diminished in the cadmium-dosed rats, compared with the control rats. The components at points *B* and *C* were noticeably enhanced by comparison with the controls and the possibility that they might be transferrin bands was examined, using the method of Giblett, Hickman and Smithies[7]. 1 μc. of radioactive iron-59 (as ferric chloride) was added to 0·2 ml. of normal rat serum and the specimen was subjected to starch-gel electrophoresis as before. The gel was sliced into two wafers, one slice being stained with a saturated solution of naphthalene black 10*B* 200 in methanol/water/glacial acetic acid (5:5:1) and the other slice, sealed in 'Saran Wrap', was placed in contact with Kodak 'No Screen' X-ray film for 12 hr., followed by development for 3 min. in Kodak *D*8 developer. Comparison of the stained gel and the final X-ray film showed that bands *B* and *C* had bound the radioactive iron exclusively. The result was confirmed by sectioning the starch block into the various bands, digesting the sections in 50 per cent nitric acid containing added carrier iron, and finally assaying the activity using an *M6H* liquid counter.

Benzidene staining of the gel revealed the presence of hæmoglobin in the space between the bands *A* and *B*, and further investigation indicated a 'ghost' band in this area, which was apparently the component which reacted positively to the stain.

Estimations of the copper oxidase-levels of the sera by the method of Ravlin[8] indicated no significant difference between the cadmium-dosed rats and the controls.

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