rat anterior tibialis preparation of the cat tibialis preparation demonstrated that RX 67668 was effective in reversing tubocurarine-induced muscle blockade at doses in the range 0·3–1·0 mg/kg, i.v. At these doses, unlike animals treated with comparable doses of other anticholinesterases, the RX 67668-treated animals exhibited no signs of muscarinic stimulation such as salivation, lachrymation, urination or defaecation.

This apparent lack of muscarinic activity was investigated by studying the effect of RX 67668 on the flow of saliva induced by electrical stimulation of the chorda tympani nerve in the cat. It was found that, although RX 67668 increased the flow of saliva produced in response to electrical stimulation at doses greater than 0·3 mg/kg, i.v., the drug did not induce a spontaneous flow of saliva at doses up to 20 mg/kg, i.v. In contrast neostigmine produced a spontaneous flow of saliva at doses greater than 0·03 mg/kg, i.v.

REFERENCES

BURGEN, A. S. V. (1949). Assay of anticholinesterases by the chromodacryorrhoea response in rats. *Br. J. Pharmacol.*, **4**, 185–189.

MICHEL, H. O. (1949). An electrometric method for the determination of red blood cell and plasma cholinesterase activity. *J. Lab. Clin. Med.*, **34**, 1564–1568.

SCHNEIDER, R. (1970). A test for the assessment of the duration of the action of neostigmine and of the relative potencies of various anticholinesterases using the pupil of the mouse. *J. Pharm. Pharmac.*, **22**, 298–301.

Differential effects of drugs on the acetylcholine output from the myenteric plexus and the responses of the longitudinal muscle of the guinea-pig ileum

H. W. KOSTERLITZ and ANGELA A. WATERFIELD*

Department of Pharmacology, University of Aberdeen

In the myenteric plexus-longitudinal muscle preparation of the guinea-pig ileum, morphine (1–2·5 μM), noradrenaline (3 μM) and adrenaline (0·3–0·6 μM) inhibit the contractile responses to electrical field stimulation at low frequencies (0·017–1 Hz) and reduce the output of acetylcholine (ACh) obtained in the presence of eserine (7·7 μM) by 65–85%, whereas the responses and output obtained at 10 Hz are unaffected (Cowie, Kosterlitz & Lydon, 1968; Paton & Zar, 1968; Paton & Vizi, 1969; Kosterlitz, Lydon & Watt, 1970).

Similar depressions of ACh output were obtained with hexamethonium (140 μM) (Greenberg, Kosterlitz & Waterfield, 1970) and $MnCl_2$ (125 μM) but, in contrast to the findings with morphine and the catecholamines, the contractile responses were not inhibited. When the release of ACh was depressed by about 80% by hexamethonium, addition of morphine reduced the ACh output by a further 10%; the contractile response obtained in the absence of eserine was not reduced by hexamethonium but was depressed by hexamethonium plus morphine. Similar results were obtained with $MnCl_2$ (125 μM) and morphine (1 μM).

It is possible that the ACh output observed in the presence of eserine is not identical with the output responsible for the contraction of the longitudinal muscle and that hexamethonium and Mn-ions depress only the output in the presence of eserine. Another possibility is a release of ACh from two different pools of ACh; both pools would be sensitive to the depressant actions of morphine and adrenaline

and noradrenaline but only one of them would be sensitive to Mn-ions and hexamethonium.

Supported in part by a grant from the Committee on Problems of Drug Dependence of the U.S. National Academy of Science—National Research Council.

REFERENCES

COWIE, A. L., KOSTERLITZ, H. W. & WATT, A. J. (1968). Mode of action of morphine-like drugs on autonomic neuro-effectors. *Nature, Lond.*, **220**, 1040–1042.

GREENBERG, R., KOSTERLITZ, H. W. & WATERFIELD, A. A. (1970). The effects of hexamethonium, morphine and adrenaline on the output of acetylcholine from the myenteric plexus-longitudinal muscle preparation of the ileum. *Br. J. Pharmac.*, **40**, 553*P*.

KOSTERLITZ, H. W., LYDON, R. J. & WATT, A. J. (1970). The effects of adrenaline, noradrenaline and isoprenaline on inhibitory α- and β-adrenoceptors in the longitudinal muscle of the guinea-pig ileum. *Br. J. Pharmac.*, **39**, 398–413.

PATON, W. D. M. & VIZI, E. S. (1969). The inhibitory action of noradrenaline and adrenaline on acetylcholine output by guinea-pig ileum longitudinal muscle strip. *Br. J. Pharmac.*, **35**, 10–28.

PATON, W. D. M. & ZAR, M. A. (1968). The origin of acetylcholine released from guinea-pig intestine and longitudinal muscle strip. *J. Physiol., Lond.*, **194**, 13–33.