REFERENCES

ARBAB, A. G. & TURNER, P. (1971a). The fluorimetric determination of thymoxamine in plasma. *J. Pharm. Pharmac.*, **23**, 719–721.

ARBAB, A. G. & TURNER, P. (1971b). Influence of pH on absorption of thymoxamine through buccal mucosa in man. *Br. J. Pharmac.* **43**, 479*P*–480*P*.

COUPAR, I. M. & TURNER, P. (1970). Relative affinities of some α-adrenoceptor blocking drugs in isolated human smooth muscle. *Br. J. Pharmac.*, **40**, 155*P*–157*P*.

SCHILD, H. O. (1957). Drug antagonism and pA_x. *Pharmac. Rev.*, **9**, 242–246.

Comparison of the potencies of edrophonium, neostigmine and eserine with a new anticholinesterase drug RX 67668 on human tissues

P. TURNER and DINAZ M. VARIAVA

Department of Clinical Pharmacology, St. Bartholomew's Hospital, London EC1

RX 67668 (cis-2-phenyl-1-(N-pyrrolidinyl) cyclohexane hydrochloride) is a novel anticholinesterase compound which appeared in animal studies (Doxey, Metcalf, Smith & Whittle, 1972) to have greater affinity for nicotinic receptors at the neuromuscular junction than for muscarinic receptors, although human studies have not confirmed this (Gillett, Hedges, Metcalf, Richens & Royds, 1972). Anticholinesterase activities of established compounds have been compared with that of RX 67668 on isolated human tissues and blood. pP_2 determinations (Edge, 1967) were performed on strips of human smooth muscle from surgical specimens of stomach, ileum and colon, and biochemical estimations of anticholinesterase activity on human blood using a modification (Glegg & Turner, 1971) of the method of Fleisher & Pope (1954).

The mean pP_2 of RX 67668 was 6·82 which compared closely with edrophonium, 6·76. Neostigmine, 7·35, was ten times more potent than RX 67668. In Table 1 the

TABLE 1. *Mean ID50 values for anticholinesterase activity of RX 67668, neostigmine, edrophonium and eserine estimated biochemically on human blood and mean pP_2 values reduced to their molar equivalents measured on isolated human smooth muscle*

Drug	Mean ID50	Mean pP_2 (moles)
RX 67668	$2{\cdot}65 \times 10^{-7}$	$1{\cdot}54 \times 10^{-7}$
Neostigmine	$5{\cdot}81 \times 10^{-8}$	$4{\cdot}57 \times 10^{-8}$
Edrophonium	$5{\cdot}32 \times 10^{-5}$	$1{\cdot}76 \times 10^{-7}$
Eserine	$2{\cdot}50 \times 10^{-10}$	$8{\cdot}0 \times 10^{-11}$

mean anticholinesterase ID50 for the compounds using the biochemical method are compared with their pP_2 values reduced to their molar equivalent in moles, obtained from the isolated tissue studies. Although the ID50 and pP_2 values are comparable for RX 67668, neostigmine and eserine, the values for edrophonium did not correlate so closely. This might be due to variation in stability of the complex formed between edrophonium and the anionic site of the cholinesterase enzyme.

RX 67668 was supplied by Reckitt and Colman Ltd. We thank the Peel Medical Research Trust, the Chest and Heart Association, and the Board of Governors of St. Bartholomew's Hospital for financial support.

REFERENCES

DOXEY, J. C., METCALF, G., SMITH, M. H. & WHITTLE, B. A. (1972). Some pharmacological properties of RX 67668—a new anticholinesterase. *Proc. Br. Pharmac. Soc., Sept.*

EDGE, N. D. (1967). pPy a measure of potentiating activity. *Nature (Lond.)*, **216**, 1014–1015.

FLEISHER, J. H. & POPE, E. J. (1954). Colorimetric method for the determination of red blood cell cholinesterase activity of whole blood. *A.M.A. Arch. Indust. Hyg.* **9**, 323–334.

GILLETT, G. B., HEDGES, A., METCALF, G., RICHENS, A. & ROYDS, R. B. (1972). Reversal of competitive neuromuscular blockade by RX 67668 in normal volunteers. *Proc. Br. Pharmac. Soc., Sept.* 1972.

GLEGG, A. M. & TURNER, P. (1971). Cholinergic interactions of methysergide and cinanserin on isolated human smooth muscle. *Arch. int. Pharmacodyn.*, **191**, 301–309.