a square wave stimulus of 1 ms duration applied through silver button skin electrodes. The twitches were recorded isometrically with a strain gauge and displayed on moving paper. When a steady baseline had been achieved D-tubocurarine was slowly injected over 5–15 min until the twitch amplitude had been reduced to approximately 50% of the control level. The total dose varied between 6 and 13 mg, but this was never sufficient to impair breathing. Three minutes later neostigmine (2·5 mg, preceded by 1·2 mg of atropine), RX 67668 (0·4 or 0·6 mg/kg) or an equivalent volume of saline was injected and the rate of recovery followed. Each subject received the three treatments on separate occasions, and was unaware of which treatment he had received.

Full recovery from the curare block was achieved in an average of 16 min after the injection of neostigmine. At the same point in time following the saline and RX 67668 (0·4 mg/kg) injections the recoveries were to 72% and 84% of the control values respectively (mean values of 2 subjects). The higher dose of RX 67668 produced no greater reversal than the low dose (85%, mean of 2 subjects).

Few adverse effects were seen with the low dose, but 0·6 mg/kg of RX 67668 produced nausea and distortions of body image. In a concomitant study, doses of up to 1 mg/kg were given to 5 healthy volunteers. These doses caused more severe adverse effects, including vomiting, dizziness and profuse sweating, in addition to the above effects. Muscarinic effects began to appear at doses above 0·6 mg/kg, but were slight.

It is concluded that RX 67668 produces marked central adverse effects in doses which have a weaker anticholinesterase effect than neostigmine at the human neuromuscular junction. It would therefore be unsuitable for clinical use.

REFERENCE

DOXEY, J. C., METCALF, G., SMITH, M. H. & WHITTLE, B. A. (1972). Some pharmacological properties of RX 67668—a new anticholinesterase. Proceedings of the British Pharmacological Society, September 1972.

Simplified extraction, chromatography and bioassay of prostaglandins in biological extracts (T)

A. L. WILLIS

Department of Physiology, Stanford University, California, U.S.A.

Automatic programme control for Skinner box experiments (T)

J. E. OLLEY and M. E. WEIR

School of Studies in Pharmacology, University of Bradford

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H. B. MILNE and C. R. WHYTE

Drug Dependency Unit, Lynfield Mount Hospital, Bradford

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P. A. LINLEY and JUDITH SENIOR

Postgraduate Schools of Studies in Pharmacy and Pharmacology, University of Bradford.