On the specificity of the reversal of reserpine hypothermia for the evaluation of antidepressant effect

SIR,—The test to establish potential antidepressant activity based on the calorigenic effect in reserpinized animals has recently been considered unreliable (Whittle, 1967). Evidence was presented that compounds commonly considered not to have an antidepressant effect, such as chlorpromazine, aspirin and morphine were able to increase body temperature in mice previously made hypothermic by a large dose of reserpine.

Since experiments from this laboratory on interactions between tricyclic antidepressant agents and reserpine (Garattini & Jori, 1966; Bonaccorsi & Garrattini, 1966; Manara & Garattini, 1967) have always been made in rats we have repeated Whittle's experiments in this species.

Sprague-Dawley female rats weighing 150 ± 10 g were treated with reserpine (5 mg/kg i.v.) and 16 hr later were given drugs or solvent orally. Body temperature was measured before treatments and at regular intervals as much as 6 hr later by means of a thermistor. The experiment was at a room temperature of 20° with 56% relative humidity.

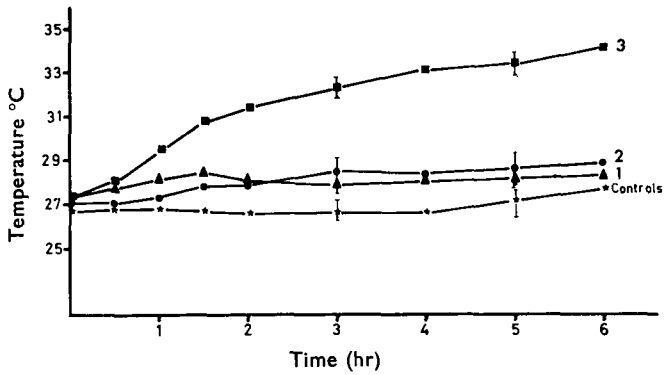

Fig. 1. Changes of body temperature induced by, (1) aspirin (300 mg/kg oral) (2) chlorpromazine (10 mg/kg oral) or (3) desipramine (3 mg/kg oral) in rats receiving reserpine (5 mg/kg i.v.) 16 hrs before the experiment. Vertical bars represent the standard error.

Fig. 1 shows that desipramine but not chlorpromazine or aspirin, induces a significant increase of body temperature in resperpinized rats. Our results with rats differ from those obtained by Whittle (1967) and by Morpurgo & Theobald (1965) (who tested chlorpromazine only) both using mice.

This discrepancy underlines the importance of species difference in comparing experiments and in extrapolating conclusions.

From the data available for rats it thus can be seen that the reversal of the reserpine-induced hypothermia allows a differentiation between tricyclic antidepressant agents and other classes of drugs to be made.

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N-(3-Benzylthio-2,6-dichlorophenyl)anthramyl acid (ASD 30): a non-competitive antagonist of bradykinin

SIR,—In 1966 methixene was reported to be a non-competitive antagonist of bradykinin (van Riezen, 1966). Recently Drs M. Taeschler and A. Fanchamps informed us that ASD 30 was a selective bradykinin antagonist. We have now examined the mechanism of action of this compound by the method used for methixene.

Guinea-pig ileum was bathed in a 10 ml bath with a Tyrode solution saturated with a mixture of oxygen 95% and carbon dioxide 5% at 37°. Two cumulative

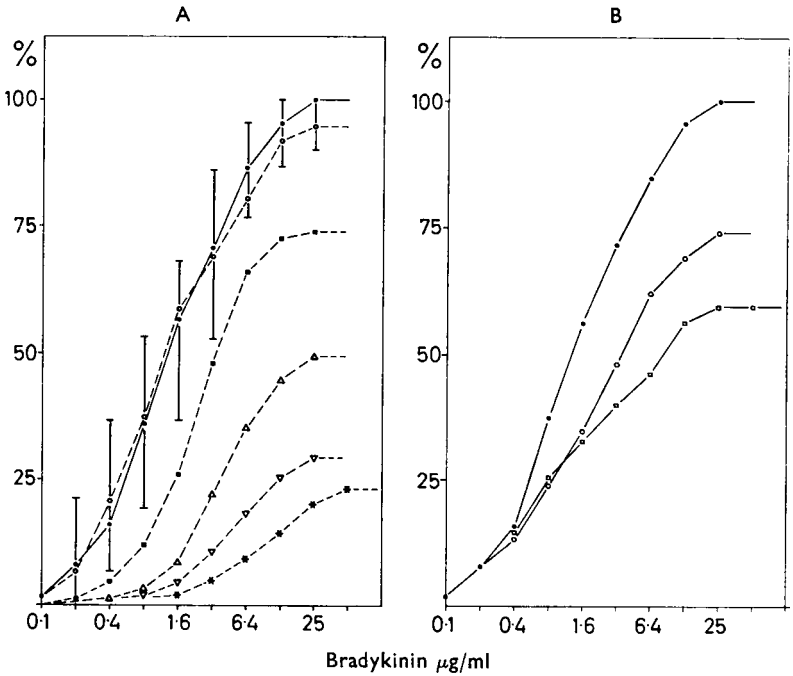

FIG. 1A. Cumulative dose response curves of guinea-pig ileum in Tyrode solution saturated with oxygen 95% and carbon dioxide 5% at 37° to bradykinin. With ASD 30 (mole/ml): ○- - - - -○ 1.10^{-6} (4); □- - - - -□ 3.10^{-6} (6); △- - - - -△ 1.10^{-5} (6); ▽- - - - -▽ 2.10^{-5} (2); *- - - - -* 5.10^{-5} (2). ●——● Control (20) 95% confidence limits. In parentheses: number of individual curves from which the curve is calculated.

B. In this experiment, the period of 30 min washing was followed by a second because the bradykinin curve was still below its control value. After this second wash the 1 hr curve ○——○ (2.10^{-5}mole/ml) was made. Then the preparation was again incubated with ASD 30 (2.10^{-5}mole/ml) for 20 min and the procedure repeated: curve □——□.