Table 1 Dose ratios (D.R.) produced by bicuculline (BIC), picrotoxin (PTX), iso-propyl bicyclo phosphate (IPTBO) and mixtures of pairs of these compounds

	Mean D.R.	*Mean D.R. with*	
	Alone	*BIC*	*PTX*
BIC	3.5 (3)	—	10 (1)
PTX	2.5 (3)	10 (1)	—
IPTBO	6.9 (3)	32 (2)	5.0 (3)

Number of experiments shown in brackets.

by PTX (10 μM), BIC (50 μM), IPTBO (100 μM), and mixtures of pairs of these compounds, was expressed as a dose ratio (DR) of shift of the dose response curve to GABA. These values are shown in Table 1.

If two antgonists act competitively at the same site, the DR for a mixture of the two would be expected to be $DR_1 + DR_2 - 1$, but if one of the antagonists were non-competitive it would then be $DR_1 \times DR_2$ (Abramson, Barlow, Mustafa & Stephenson, 1969). From Table 1, IPTBO + PTX gave the former relationship while IPTBO + BIC and PTX + BIC gave the latter, suggesting that PTX and IPTBO share a common mode of action while BIC exerts its antagonism by a different mechanism. This may reflect a difference between competitive and non-competitive antagonism or in this preparation antagonists may be acting at two distinct sites in the sequence of events triggered by GABA.

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The effect of (±)-6-fluorotryptophan on sleep and brain monoamine levels in the rat

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(±)-6-Fluorotryptophan (6-FT) has been reported to be a short-acting, competitive inhibitor of brain tryptophan hydroxylase, with a specificity of action superior to that of the widely-used inhibitor, p-chlorophenylalanine (pCPA) (McGeer, Peters & McGeer, 1968; Peters, 1971). 5-hydroxytryptamine (5-HT) is generally accepted to play an important role in the control of sleep mechanisms (Jouvet, 1972). However, in depletion experiments in the rat using pCPA (Rechtschaffen, Lovell, Freedman, Whitehead & Aldrich, 1973) or 5,7-dihydroxytryptamine (Ross, Trulson & Jacobs, 1976), results have been obtained which are not consistent with this hypothesis. This report describes the effects on sleep of an alternative inhibitor to pCPA.

Male Sprague-Dawley rats (200–250 g) under pentobarbitone sodium anaesthesia (60 mg/kg intraperitoneally) were prepared for EEG recording by implanting electrodes onto the cortical surface (Timo-Iaria, Negrão, Schmidek, Hoshino, de Menezes & da Rocha, 1970). Following surgery, all rats were housed individually for at least one week; food and water *ad libitum*, lights on 0800–2000 h, ambient temperature 20 ± 2°C. In each experiment, recordings were made on 3 consecutive days (pre-drug, drug and post-drug days) from either 1200 to 1600 h ($n=4$) or

1200–2000 h ($n=4$). 6-FT (120 mg/kg, i.p.) or vehicle was administered at the start of a recording period. The EEG was scored visually in 20 s epochs for awake (W), slow-wave sleep (S) and paradoxical sleep (PS).

Data from pre- and post-drug days were averaged and compared with drug day data using the Wilcoxon signed-ranks test. Rats used for biochemical determinations were housed for at least one week under identical conditions to the sleep-recorded rats. After decapitation, brains were dissected, using a modification of the procedure of Glowinski & Iversen (1966), into 4 regions; medulla oblongata, hypothalamus, midbrain and 'cortex' (cerebral cortex, corpus striatum and hippocampus). Brain tissue was immediately frozen on a stainless steel plate cooled by solid CO_2, stored at −20°C, and assayed for 5-HT (Curzon & Green, 1970) and noradrenaline (Miller, Cox, Snodgrass & Maickel, 1970). Determinations were made on groups of 15 rats at various times after drug administration.

Over the first 4 h period 6-FT significantly decreased S ($P<0.02$) and PS ($P=0.0078$); W being significantly increased ($P=0.0078$). These effects were apparent only during the second and third hour of recording. 6-FT also significantly reduced sleep latency ($P=0.05$) and increased the number of awakenings ($P<0.02$). No changes in any sleep parameter were apparent during the 1600–2000 period of recording. Brain 5-HT was maximally depleted 3 h after drug injection. The greatest depletion was obtained in the medulla (35% of control) and least in the hypothalamus (58% of control). However, noradrenaline levels were also significantly lowered in all brain regions at this time.

The sleep changes produced by 6-FT appeared to follow a similar time-course to the depletion of brain monoamines. However, the biochemical effects of 6-FT were non-specific. This is surprising in view of a previous report indicating a high degree of specificity (Peters, 1971). The fact that our rats were isolated and of a different strain may account for this discrepancy.

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Interactions between intravenous anaesthetic agents and suxamethonium in mice

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In man, the duration of apnoea and respiratory depression produced by suxamethonium is increased when this drug is administered following induction of anaesthesia with propanidid. No similar potentiation is found with methohexitone or thiopentone (Clarke, Dundee & Daw, 1964).

Interactions between currently used agents have been investigated in mice, to establish the validity of a model for the prediction of similar interactions between suxamethonium and potential new anaesthetic agents.

Two groups of 10 male Alderley Park mice (18–20 g) were used for each combination investi-