determined by the chelate formation with pentacyanoaquaferroate (6). *p*-Aminobenzoic acid (ABA) was determined by the method of Fouts and Brodie (1).

Table 1 shows that NADPH-linked reduction of *p*-nitrobenzoic acid to *p*-hydroxyaminobenzoic acid is mainly localized in microsomes, whereas NADH-linked nitroreduction is localized in supernatant. The activity of NADPH- and NADH-linked nitroreduction is almost same in supernatant. Moreover, the reduction of *p*-hydroxyaminobenzoic acid is done in both microsomes and supernatant, but the activity is higher in microsomes than that in supernatant.

The NADPH-linked activity is about 50% higher than the NADH-linked activity in microsomes. Thus, the NADH-linked reduction of *p*-nitrobenzoic acid to *p*-aminobenzoic acid is negligible in microsomes, but the NADH-linked reduction in microsomes+supernatant is about 30% of the NADPH-linked activity in accord with results of Fouts and Brodie (1). These results suggested that the first step of the NADH-linked reduction of *p*-nitrobenzoic acid to *p*-aminobenzoic acid is mainly done by supernatant and the second step is mainly mediated by microsomes. The NADPH-linked reduction of *p*-nitrobenzoic acid to *p*-hydroxyaminobenzoic acid is the important step for all over nitroreduction and this step is likely the rate limiting step.

In further experiments it was shown that the NADPH-linked reduction of *p*-nitrobenzoic acid to *p*-hydroxyaminobenzoic acid was inhibited by oxygen and stimulated by FMN or FAD and the microsomal activity was stimulated by phenobarbital. The NADPH-linked nitroreductase of microsomal fraction likely differed from that of supernatant, because the former was stimulated by phenobarbital and inhibited by oxygen, whereas the later was not stimulated by phenobarbital and only partially inhibited by oxygen. The detailed results will be published elsewhere (7).

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ANTITREMOR ACTION OF A NEW *BETA* RECEPTOR BLOCKING AGENT (I.C.I. 50, 172)

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In a previous communication (1) it was reported that propranolol (Inderal) a *beta* receptor blocking agent abolishes tremor induced by tremorine. A number of structurally similar adrenergic *beta* receptor blocking agents have been synthesized recently and their actions are almost similar qualitatively in that they all block *beta* receptor but they differ quantitatively. A new *beta* receptor blocking agent (I.C.I.50, 172), which does not block all the receptors (2) have been studied in rats to find out the action if tremorine (1,4-dipyrdino-2-butyne) induced tremor and its cholinergic effects are blocked by this new *beta* receptor blocking agent I.C.I. 50, 172.

Methods: Experiments were carried out in albino rats (C.D.R.I., Strain) of both sexes weighing between

TABLE 1. Effect of I.C.I. 50, 172 in tremorine induced tremor in albino rats.

Groups	Dose mg/kg	No. of animals pretreated No. of animals protected	% protection	Occurrence of diarrhoea and salivation	Abnormal behaviour
1	0.5	10/0	0%	profuse	Nil
2	1.0	10/2	20%	moderate	Nil
3	2.0	10/3	30%	slight	Nil
4	4.0	10/6	60%	absent	Nil
5	6.0	10/8	80%	absent	Nil
6	8.0	10/9	90%	absent	Nil

TABLE 2. Comparison of antitremorine potency of atropine and the new compound I.C.I. 50, 172.

Drugs	ED ₅₀ mg/kg with S.E.	Potency ratio
Atropine sulphate	1.30 ± 0.291	1
I.C.I. 50, 172	3.05 ± 0.554	0.426

100–150 g at room temperature (average of 36°C). The concentration of the compound was such that the required dose could be given in volume of 0.5 ml/100 g of body weight. Groups of ten animals were pretreated subcutaneously with the test drug prior to the test. Fifteen mg/kg of tremorine was given intraperitoneally 20 minutes before the test. The antitremor effect was measured by Rota-Rod test (3). The median effective dose (ED₅₀) was calculated by the method of Miller and Tainter (4). The incidence of diarrhoea and salivary secretion was noted.

Results: Six groups of animals were pretreated with various doses e.g. 0.5, 1.0, 2.0, 4.0, 6.0 and 8.0 mg/kg. Twenty% protection was obtained with 1.0 mg/kg, whereas with 8 mg/kg 90% protection was seen. The results are summarized in Table 1.

The results from Table 1 indicate that the effect of I.C.I. 50, 172 on tremorine induced tremor is dose-dependent. The incidence of salivary secretion and diarrhoea (cholinergic effects) was present up to dose of 2 mg/kg. With the increase of dose up to 4 mg/kg the diarrhoea and salivation was absent. The animals did not show any abnormal behaviour or toxic effects at the above dose level. The ED₅₀ was calculated according to the method of Miller and Tainter (4). The calculated ED₅₀ was 3.05 ± 0.554 mg/kg. The potency of I.C.I. 50, 172 was compared with atropine and is shown in Table 2.

Discussion and conclusion: The present study revealed that the new *beta* adrenergic blocking agent (I.C.I. 50, 172) not only blocked the tremorine induced tremor but also the incidence of salivation and diarrhoea, while Inderal (propranolol) gave 90% protection at a dose level of 4 mg/kg but the salivation and diarrhoea was not abolished. The effect of Inderal and the I.C.I. 50, 172 on the abolition of tremorine induced tremor perhaps gives further evidence to the theory that catecholamines have some role in the causation of both tremorine induced tremor and Parkinson's disease. Further work is necessary to elucidate the mechanism of blockage of salivation and diarrhoea by this new compound I.C.I. 50, 172.

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