Chlorpromazine and other phenothiazines are known to antagonize the emetic action of apomorphine and morphine. As such it was considered likely that the bradycardiac effect of morphine could be antagonized by the phenothiazines. However, we observed that chlorpromazine (5-10 mg/kg) and perphenazine (0.5 mg/kg) did not antagonize morphine induced bradycardia in rabbits.

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REFERENCES


ANTI-TREMOR ACTION OF PROPRANOLOL (INDERAL)

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Herring (1) reported that pronethalol reduces the tremor in Parkinson's disease. Marsden and Owen (2, 3) demonstrated that pronethalol and the newer beta blocking agent-propranolol both abolished the increase in tremor of patients with Parkinson's disease during infusions of epinephrine. The present study was undertaken to explore the possibility of propranolol (Inderal) as a blocking agent in tremorine (1,4-dipyrrolidino-2-butyne) induced tremor in albino rats.

Methods: Experiments have been carried out in albino rats (Central Drug Research Institute, Lucknow, Strain) of both sexes weighing between 100-150 g at room temperature (average of 30°C). The concentration of drug was such that required dose could be given in volume of 0.5 ml/100 g of body weight. Groups of ten animals were pretreated subcutaneously with test drug 30 minutes prior to Rota rod test (4). Fifteen mg/kg of tremorine was given intraperitoneally 20 minutes prior to the test. Anti-tremor effect of compound was measured by determining of the ability to restore the capacity of tremorine injected rats to remain on slowly rotating rod (5 rotations per minute) during one minute period. The median effective dose (ED50) was calculated by the method of Miller and Tainter (5). The incidence of salivary secretion and diarrhoea was also noted.

Results: Atropine sulphate is a powerful antagonist against tremorine and hence was chosen as standard drug (6). Various doses ranging from 2 to 8 mg/kg body weight were given to eight groups of rats. The ED50 obtained from such experiments was 1.30±0.291 mg/kg. The drug completely antagonized tremor, salivation and diarrhoea. The ED50 dose was taken as unity and the potency ratio of the compound has been calculated in respect of atropine.
TABLE 1. Comparison of anti-tremorine potency of propranolol with atropine.

<table>
<thead>
<tr>
<th>No.</th>
<th>Drugs</th>
<th>ED50 in mg/kg with S.E.</th>
<th>Potency ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Atropine sulphate</td>
<td>1.30±0.291</td>
<td>1.0</td>
</tr>
<tr>
<td>2</td>
<td>Propranolol (Inderal)</td>
<td>1.95±0.221</td>
<td>0.666</td>
</tr>
</tbody>
</table>

The data obtained in these experiments demonstrate that propranolol possesses anti-tremor activity. Eight groups of animals were pretreated with various doses e.g. 0.5, 1.0, 1.5, 2.0, 2.5, 3.0, 3.5 and 4.0 mg/kg. With 1 mg/kg dose only 10% protection was observed whereas 90% protection was obtained with 4 mg/kg showing that the anti-tremor activity of propranolol seems to be dose dependant. In did not have any effect on diarrhea and salivation even at 4 mg/kg. The calculated ED50 found for the drug was 1.95±0.221 mg/kg body weight. The potency ratio for the compound is 0.666 in respect to atropine (Table 1). No abnormal behaviour was noticed at doses used in our experiments.

Discussion and conclusion: The present study indicates that propranolol abolished the tremor induced by tremorine although cholinergic effects are not blocked. The LD50 of the compound was 30-40 mg/kg body weight when given intravenously (7) whereas the ED50 found in 1.95±0.221 mg/kg given subcutaneously showing that ED50 is well behind the LD50. Everett et al. (8) suggested that the probable site of production of tremorine tremor is at subcortical level. Evidences so far available show that there is disturbed metabolism of catecholamines in the brain of patients with Parkinson's disease (9) and in rats brain after administration of tremorigenic dose of tremorine (10). The abolition of tremor by propranolol seems to support that catecholamines has some role in the causation of tremorigenic tremor and that of Parkinson's disease. Further work is in progress which may elucidate the mechanism of action of propranolol.

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