

—SHORT COMMUNICATIONS

EFFECT OF LYSERGIC ACID DIETHYLAMIDE (LSD-25) ON
MORPHINE INDUCED BRADYCARDIA

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Several antagonistic interactions between morphine and LSD-25 (lysergic acid diethylamide) have been demonstrated. LSD-25 antagonizes morphine induced analgesia in rats (1) and emesis in dogs (2). It also blocks the miotic action of morphine (3). On the other hand morphine blocks LSD-25 induced pyrexia in rabbits (4) and the central hypotensive effect of LSD-25 in dogs (5). Morphine produces marked bradycardia in rabbits (6) and the present study was undertaken to see if LSD-25 antagonizes this effect of morphine as well.

Twenty-four conscious albino rabbits of either sex weighing from 1.2 to 1.5 kg were used in this investigation. At the time of the experiment the animal was placed on a table. The electrocardiographic tracings (Lead II) were obtained with Cardiopan (Phillips) at intervals of five minutes. When the heart rate was stabilized the test drug was administered intraperitoneally and its effect on heart rate was observed for one hour. The drugs employed in this study were morphine hydrochloride, lysergic acid diethylamide, chlorpromazine hydrochloride and perphenazine hydrochloride. Solutions of the drugs were freshly prepared in distilled water at the time of administration.

TABLE I. Effect of morphine and LSD-25 on heart rate of conscious rabbits.

Drug	No. of animals	Mean control heart rate $\pm$ S.E.	Mean change in heart rate 30 min after the drug $\pm$ S.E.
Morphine (12.5 mg/kg)	12	226 $\pm$ 42.8	-54 $\pm$ 11.5
LSD-25 (150 μ g/kg)	9	220 $\pm$ 25.3	+12 $\pm$ 4.9
Morphine (12.5 mg/kg) 30 min after LSD-25 (150 μ g/kg)	9	232 $\pm$ 29.3	-40 $\pm$ 11.1

The results obtained in this study have been summarized in Table I. It was observed that morphine produced bradycardia in rabbits and the peak effect was attained after 30 minutes. The effect persisted for more than one hour. LSD-25 on the other hand produced a little tachycardia. In animals treated with LSD-25, subsequent administration of morphine produced bradycardia which was slightly less as compared to the group receiving morphine alone. However, this difference was statistically not significant ($P=0.05$). This shows that LSD-25 does not antagonize morphine induced bradycardia. Slight decrease in morphine induced bradycardia after LSD-25 could be attributed to the opposite effects of the two drugs on the heart rate. LSD-25 has also been found not to antagonize other actions of morphine like Straub tail reaction in mice (1) and mania in cats (7).

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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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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.