A screening method for antiarrhythmic agents in the rat

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A method using rats for determining the potential of new compounds as antiarrhythmic agents has been developed. It is based on the antagonism displayed by antiarrhythmic drugs to the ventricular fibrillation that occurs after respiratory arrest induced by chloroform. Similar effects have been observed in mice (Lawson, 1968).

The compounds to be tested are given by intraperitoneal injection to groups of ten rats of either sex and weighing 90 to 100 g. Each group receives a different dose level and the controls receive the vehicle. One hour later each rat is placed in the anaesthetic chamber and anaesthetized with chloroform. Immediately after respiratory arrest electrodes are attached to the animal and the electrocardiogram (Standard lead II) is monitored. If fibrillation occurs during the monitoring period then the time of onset after respiratory arrest is noted. If no fibrillation occurs then the animal is regarded as being protected.

No ventricular fibrillation was observed in animals killed by ether inhalation or cervical dislocation. Therefore the cardiac arrhythmias are probably due to the effects of chloroform on the heart. The three antiarrhythmic agents quinidine, lignocaine and procainamide displayed a clear antagonistic activity to the chloroform induced arrhythmias, their ED50s being respectively 11·5, 17·4 and 20·9 mg/kg.

The effects of drugs that interfere with sympathetic nerve function were also investigated as sympathetic hyperactivity has been implicated in the production of cardiac arrhythmias during chloroform anaesthesia. The adrenergic neurone blocking agents bretylium and guanethidine (1 to 5 mg/kg) were more active in the test than quinidine, and the response to bretylium (5 mg/kg) was antagonized by the concomitant administration of dexamphetamine (3 mg/kg). Inconsistent results were obtained with the ganglion blocking agents hexamethonium and pentacynium. Doses lower than 5 mg/kg exhibited a variable protective action and higher doses did not protect more than 60% of the animals in each group.

REFERENCE

LAWSON, J. W. (1968). Antiarrhythmic activity of some isoquinoline derivatives determined by a rapid screening procedure in the mouse. *J. Pharmac. exp. Ther.*, **160**, 22–31.

The effect of cyproheptadine on food consumption in the fasted rat

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Cyproheptadine is reported to stimulate appetite and to increase body weight in man (Bergen, 1964; Gionta, 1969; Noble, 1969) and in cats (Chakrabarty, Pillai, Anand & Singh, 1967), but not in mature dogs nor mature or weanling rats or guinea-pigs (Bergen, 1964). However, we find increased food consumption in fasted rats.

The rats were pre-trained to an overnight fasting schedule and kept on wire grid floors. Food was removed daily at 16.30 and was replaced the following morning for a 6 h period, 30 min after administering cyproheptadine hydrochloride sub-