monostable to a printing counter. The printer is controlled by a variable timer allowing the printing of numbers of arrhythmias in any desired time interval of between 6 s and 100 minutes.

With the Harris (1950) two-stage coronary artery ligation model of ventricular arrhythmias in the dog, we normally use ECG lead II or CR and allow the counter to be triggered in the negative mode. If, for any reason, the ECG is itself negative, then a switch permits the user to choose positive triggering of the counter. On occasions, the baseline of the ECG may wander because of respiratory or other skeletal muscle movements by the animal and to prevent negative excursions of the baseline giving rise to artefactual counts a d.c. level clamp may be included prior to the amplifier.

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Substituted benzamides as dopamine antagonists

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A number of substituted benzamides have recently been developed for their anti-emetic and anti-psychotic properties. Previous studies with one such compound, metoclopramide (*N*-[diethylaminoethyl]-2-methoxy-4-amino-5-chlorobenzamide) have indicated that it has biochemical and behavioural properties associated with the blockade of cerebral dopamine receptors (Dolphin, Jenner, Marsden, Pycock & Tarsy, 1975; Peringer, Jenner & Marsden, 1975; Donaldson, Jenner, Marsden, Peringer & Miller, 1976). These studies have now been extended to include sulpiride (*N*-[1'ethyl-2'-pyrrolidinyl methyl]-2-methoxy-sulphamoyl benzamide), tigan (*N*-[(2'dimethylaminoethoxy) benzyl]-3,4,5-trimethoxyl benzamide) and clebopride (*N*-[*N'*-benzylpiperidin-4'-yl]-4-amino-5-chloro-2-methoxy-benzamide) and its debenzylated metabolite.

All of these compounds were found to: inhibit the apomorphine (2 mg/kg i.p.) reversal of reserpine (10 mg/kg i.p. 18 h before apomorphine) induced akinesia in mice, inhibit the apomorphine (0.5 mg/kg s.c.) induced circling in mice with unilateral 6-hydroxydopamine induced striatal lesions, induce some degree of catalepsy, induce ipsilateral circling in apomorphine (0.5 mg/kg s.c.) treated rats following their administration via intrastriatal cannulae (25 or 100 μg in 3 μl 0.9% saline).

Thus these compounds all exhibit behavioural properties thought to be associated with blockade of central dopamine receptors. Biochemical studies have shown that these compounds induce a rise in the brain concentration of the dopamine metabolite homovanillic acid and, to a lesser extent, the intraneuronal metabolite dihydroxyphenyl acetic acid. These findings are also consistent with a central blocking action of the compounds on dopamine receptors (Donaldson *et al.*, 1976).

In the *in vitro* rat striatal dopamine (10^{-4} M) stimulated adenylate cyclase system, however, metoclopramide, sulpiride, tigan and the clebopride metabolite had no inhibitory action at 10^{-7}–10^{-4} M. Clebopride caused a small reduction in cyclic AMP production at 10^{-4} M.

Thus, although these substituted benzamides exert pharmacological and biochemical effects consistent with their being dopamine antagonists, they have little effect in the adenylate cyclase model of the dopamine receptor. Their mode of action therefore remains an open question.

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