The order of potency of the various agonists is similar to that previously determined in homogenates of rat striatum (Miller, Horn, Iversen & Pinder, 1974; Munday, Poat & Woodruff, 1976), suggesting a similarity between the dopamine receptors in the two regions of the brain. The high potency of ADTN is consistent with previous behavioural and electrophysiological studies with this compound.

K.J.W. is an MRC student.

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The effects of some indolalkylamines on the uptake and release of 5-hydroxytryptamine in rat striatum

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The mammalian CNS shows a differential anatomical distribution of 5-hydroxytryptamine (5-HT) (Bogdanski, Weissbach & Undenfriend, 1957) and *in vitro* exhibits an active transport system for the uptake of 5-HT which is distinguishable from that of noradrenaline and dopamine (Blackburn, French & Merrills, 1967; Shashkan & Snyder, 1970). In this study we have investigated the effects of various indolakylamines on the uptake and release of [^{3}H]-5-HT *in vitro* providing complementary data to the structure-activity study of Horn (1973) with these compounds on the uptake of 5-HT.

The method of Raiteri, Angeli & Levi (1974) was used; briefly rat striatum tissue was removed, weighed and chopped into cubes 0.1 x 0.1 x approximately 2.0 mm. The tissue was suspended in 10 ml cold incubation medium (containing 5.10^{-5} M pargyline) and pre-incubated for 15 min at 37° and subsequently incubated for 10 min [^{3}H]-5-HT at a final concentration of 1.10^{-8} M (5-[1,2-^{3}H(N)]; S.A. 22.5 Ci/mmol). In uptake experiments the drug was added simultaneously with the radioactive 5-HT and after the incubation the tissue was separated from its incubation medium either on Millipore filters or by centrifugation at 10,000 x g. The tissue, or tissue and filter, was solubilised with PCS (Amersham-Searle) and the amount of radioactivity accumulated determined by liquid scintillation counting. The results were corrected for non-specific uptake by subtraction of a zero time blank. In the release experiments the radiolabelled tissue resting on Millipore filters was superfused with incubation medium at 37°. This was drawn through the tissue bed at 0.5 ml/min and fractions were collected every minute. After 5 min the superfusing medium was replaced by a medium containing the indolakylamine studied and superfusion continued for a further 10 minutes. The percentage of total recovered radioactivity (filter + tissue + fractions) was calculated for each fraction and the combined values for the first 5 fractions subsequent to the initiation of release corrected for basal release, this value was expressed as a percentage of the maximal release of [^{3}H]-5-HT caused by cold 5-HT (1.10^{-4} M).

IC_{50} values were calculated from semi-log plots and in this preparation were found to be $2.6 \cdot 10^{-7}$ M for tryptamine, $2.7 \cdot 10^{-7}$ M for α-methyltryptamine, $5.5 \cdot 10^{-6}$ M for 5-methoxytryptamine and $1.9 \cdot 10^{-8}$ M for chlorimipramine. In the release experiments chlorimipramine (10^{-5} M) caused no release of 5-HT while tryptamine, α-methyltryptamine and 5-methoxytryptamine at the same concentration caused 69%, 71% and 41% release respectively calculated as described above. At a concentration of 10^{-7} M the values for tryptamine, α-methyltryptamine and 5-methoxytryptamine were 36%, 42% and 0% respectively.

In comparison with chlorimipramine, tryptamine and α-methyltryptamine were approximately an order of magnitude less potent as inhibitors of 5-HT uptake, while 5-methoxytryptamine was still less potent. However while chlorimipramine exhibited no ability to release 5-HT, the other indolakylamines investigated showed the same rank order of potency on release as against uptake inhibition.

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Effects of chronic (±)-propranolol on catecholamines and GABA in rat striatum

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Investigations of the effects of (±)-propranolol on central catecholamine concentrations have produced conflicting results (Peters & Mazurkiewicz-Kwilecki, 1975). However we have shown that chronic administration of propranolol to rats increased steady state concentrations of dopamine in the corpus striatum. (Mahon, O'Donnell & Leonard, 1977). In the study reported here we have attempted to extend our previous findings.

Male Sprague-Dawley rats (180–200 g) were given (±)-propranolol (30 mg/kg) daily for 14 consecutive days in a divided dose. Diazepam (5 mg/kg) was similarly administered to another group and controls received saline. All injections were given i.p. Behaviour was assessed on day 12 using a modified form of the hole-board of Davies & Wallace (1976). Twelve h after the final injections the concentrations of γ-amino-n-butyric acid (GABA), noradrenaline (NA) and dopamine (DA) in the midbrain and striatum were estimated following microwave radiation of the skulls. The catecholamines were determined by the method of Leonard & Tonge (1969) and GABA by the method of Uchida & O'Brien (1964). Striatal catecholamine turnover following similar propranolol treatment was measured in a second experiment using the MAO inhibitor, pargyline.

Chronic administration of propranolol caused a significant ($P < 0.005$) decrease in striatal GABA concentration and increases ($P < 0.05$) in striatal DA and midbrain NA levels. Neither chronic diazepam nor an acute dose of propranolol (30 mg/kg) had any effect on the neurotransmitters measured. No effects of propranolol on turnover were detected. The animals' behaviour was unaltered by any of the drug treatments.

An increase in steady state DA concentration in the striatum could be due to direct receptor blockade, and/or to an effect on tyrosine hydroxylase activity in this brain area. Propranolol has been shown to differ from the phenothiazines in that it augments the rotation produced by amphetamine (Fuxe, Bolme, Agnati & Everitt, 1976). Peters & Mazurkiewicz-Kwilecki (1975) have reported a stimulation of striatal tyrosine hydroxylase activity in rats given propranolol for 6 days. Our results are compatible with an action of the drug on this enzyme.

This work was supported by a grant from Organon, B.V. (Netherlands). Propranolol and Pargyline were gifts of I.C.I. Ltd. and Abbot Laboratories respectively.

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