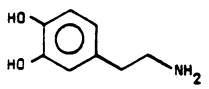
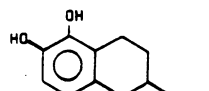
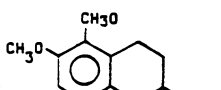
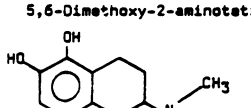
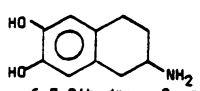
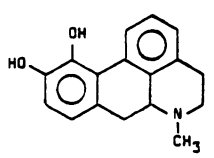
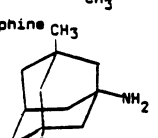
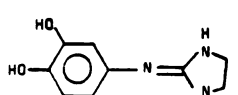
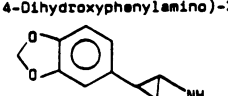
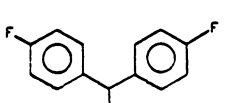
Table 1 Comparison of the pre-synaptic and post-synaptic activities of some dopamine analogues

	Structure	Rabbit ear artery Inhibitory activity negative log. ED_{50} dose (dosing in mol)	Canine renal vasculature Vascular resistance negative log. ED_{50} dose (dosing in mol/kg)
I	 Dopamine	8.91*	7.92*
II	 5,6-Dihydroxy-2-aminotetralin	8.39*	7.95*
III	 5,6-Dimethoxy-2-aminotetralin	<6.00	<6.50
IV	 5,6-Dihydroxy-2-dimethylaminotetralin	9.98*	**
V	 6,7-Dihydroxy-2-aminotetralin	9.84*	8.25*
VI	 Apomorphine	9.63*	7.6* (partial agonist)
VII	 3,5-Dimethyl adamantanamine	<6.00	<6.50
VIII	 (3,4-Dihydroxyphenylamino)-2-imidazoline (DPI)	10.04	<6.50
IX	 trans 2-(3,4-methylenedioxyphenyl)-cyclopropylamine	6.44	<6.50
X	 Flunamine	6.53	<6.5

* Dopamine receptor response

** Dopamine receptor response but insufficient to quantify

Pre- and post-synaptic activities of some dopamine analogues and related compounds

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Structural requirements for peripherally acting dopamine receptor agonists have been reviewed by Goldberg, Volkman & Kohli (1978). We have extended these studies and compared the effects of 10 compounds on the rabbit isolated perfused ear artery preparation and the renal vasculature of the anaesthetised dog.

Rabbit central ear arteries were isolated and perfused with Krebs-Henseleit solution (3 ml/min, 37°C, 95% O_2/5%CO_2) containing cocaine HCl (5×10^{-5} M) and yohimbine HCl (2×10^{-7} M). Vascular sympathetic nerves were stimulated via bipolar platinum ring electrodes for 10 s every 2.5 min (0.5–1 Hz, supramaximal voltage, 0.5 ms pulse width) and compounds were injected intraluminally. Activity at pre-synaptic dopamine receptors was measured as inhibition of stimulation-induced vasoconstriction sensitive to antagonism by metoclopramide (2.5×10^{-6} M).

Renal arterial blood flow measurements were made in pentobarbitone-anaesthetised beagles (McNay & Goldberg, 1966). Renal vascular resistance was also measured. Each animal received phenoxybenzamine HCl (5–10 mg/kg i.v. and 0.1 mg/min i.v.). Compounds were injected (max dose 3×10^{-7} mol/kg) into an intra-renal arterial saline infusion and post-synaptic (vascular) dopamine receptor activity was measured as increases of renal blood flow or falls in renal vascular resistance susceptible to antagonism by haloperidol (0.13 μmol kg^{-1} min^{-1} i.a.).

Compounds were tested in at least 4 ear artery preparations and 2 anaesthetised dogs. Negative log ED_{50} values were estimated from the appropriate dose-response curves. Results obtained are summarised in Table 1.

Our results confirm the potent dopamine receptor activities of certain semi-rigid dopamine analogues, but suggest that structural requirements for pre- and post-synaptic peripheral receptors may differ less than has been previously indicated.

The extended β-rotameric form (V) was a potent agonist in both systems, while pre-synaptic agonists (α-rotamers, II and VI) also show some post-synaptic activity (as measured by vascular resistance changes), a property not previously reported. *N*-alkyl substitution (IV, VI) imparts both potency and relative selectivity for pre-synaptic sites.

DPI (VIII) a potent agonist at dopamine receptors on snail neurones (Struyker-Boudier, Teppema, Cools & Van Rossum, 1975) inhibited neuronal vasoconstriction in the ear artery, but was not dopamine in either test system. Inactivity of VII, IX & X suggests that their central effects may not involve direct interaction with dopamine-like receptors.

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STRUYKER-BOUDIER, H.A.J., TEPPEMA, T., COOLS, A.R. & VAN ROSSUM, J.M. (1975). (3,4-Dihydroxyphenylamino)-2-imidazoline (DPI), a new potent agonist at dopamine receptors mediating neuronal inhibition. *J. Pharm. Pharmac.*, **27**, 882–883.

Further sub-classification of α-adrenoceptors in the cardiovascular system, vas deferens and anococcygeus of the rat

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Observations on pressor effects of agonist drugs in the pithed rat by Bentley, Drew & Whiting (1977) are indicative of two types of post-junctional α-adrenoceptors, one of which is activated by noradrenaline but not by phenylephrine and is resistant to prazosin suggesting similarities with the α_2 receptors previously found only pre-junctionally (Langer, 1974).

We have tested this hypothesis by comparing the pre-junctional and post-junctional effects of 5 α-adrenoceptor agonists i.e. clonidine, guanabenz, oxymetazoline, phenylephrine and xylazine, on four different organ systems in the rat. Arterial blood pressure, heart rate and longitudinal isometric tension of anococcygeus were monitored *in situ* in the pithed