5-Hydroxytryptamine and monoamine oxidase in adult and foetal sheep blood vessels

5-Hydroxytryptamine (5-HT) is a potent constrictor of sheep umbilical blood vessels (Dyer, 1970a). Cocaine potentiated the contractions to 5-HT in sheep isolated umbilical artery and vein and inhibited its uptake into these blood vessels (Dyer, 1970b). We now report the presence of monoamine oxidase and 5-HT in sheep umbilical, foetal and maternal blood vessels. Blood vessels were removed from pregnant sheep at term under pentobarbitone (i.v.) or spinal anaesthesia (lignocaine) (Dyer, 1970a).

Monoamine oxidase activity in 10% tissue homogenates was measured (Kraml, 1965) by the formation of 4-hydroxyquinoline from kynuramine (Century & Rupp, 1968). 5-HT was analysed by the method of Udenfriend, Weissbach & Brodie (1958).

The umbilical vein had about three times the 5-HT concentration of the umbilical artery. Monoamine oxidase activity was found in all blood vessels examined (Table 1). The foetal and umbilical blood vessels contained similar amounts of monoamine oxidase. Although only a limited number of maternal blood vessels were examined, it appears that the maternal monoamine oxidase activity was greater than in foetal or umbilical blood vessels.

Table 1. *5-Hydroxytryptamine concentration and monoamine oxidase activity in sheep tissues.*

	Umbilical vein	Umbilical artery	Foetal portal vein	Foetal aorta	Maternal portal vein	Maternal aorta	Whole cotyledon
	5-HT concentration (μg/g wet tissue)						
N	7	7	5	5	3	2	7
$\bar{X}$	0·38	0·13	0·32	0·17	0·25	0·41	0·22
s.d.±	0·22	0·10	0·06	0·09	0·10	0·18	0·05
	Monoamine oxidase activity (μg 4-hydroxyquinoline/g h^{-1})*						
N	9	8	6	4	4	3	5
$\bar{X}$	13·3	11·5	13·4	11·3	18·0	40·0	4·9
s.d.±	6·7	6·4	6·4	3·3	5·9	15·6	1·5

* Activity expressed as μg 4-hydroxyquinoline formed from kynuramine per gram of wet weight of tissue per hour at 37°, with air as the gas phase.

Our experiments provided evidence for the presence in sheep of endogenous 5-HT and monoamine oxidase in foetal maternal and umbilical blood vessels. Monoamine oxidase may play a role in the termination of the action of 5-HT in sheep umbilical blood vessels as well as the previously described uptake mechanism.

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Potentiation by desipramine of the pressor and depressor effects of dopamine

Imipramine and desipramine are known to potentiate the peripheral effects of noradrenaline and other amines. These facts supported the hypothesis relating the antidepressant action of imipramine to the activation of adrenergic mechanisms in the brain (Sigg, 1959).

The demonstration of the inhibition of catecholamine uptake in peripheral tissues and in the brain by imipramine-like drugs (Dengler & Titus, 1961; Glowinski & Axelrod, 1964) has provided a biochemical basis for the suggested mechanism of their antidepressant effect (Sulser, Bickel & Brodie, 1964) and the interactions with endogenous amines.

Tricyclic antidepressants potentiate the inhibitory effects of noradrenaline at the synaptic level (Cairncross, McCulloch & others, 1967; Kądzielawa, Gawęcka & Kądzielawa, 1967, 1968; Kądzielawa & Widy-Tyszkiewicz, 1969). We have found that imipramine and desipramine activate the depressor action of dopamine and we now report an analysis of this effect.

Male rats, 250–350 g; guinea-pigs, 400–500 g; rabbits, 3–3·5 kg, and cats, 2·8–3·5 kg were anaesthetized with urethane (25% soln) at doses of 0·7 ml/100 g, subcutaneously for rats and 0·9 ml/100 g for guinea-pigs; 1·7 g/kg, intraperitoneally for rabbits and 1·0/kg for cats. Blood pressure was recorded from cannulated carotid common artery by means of a mercury manometer. Drugs were dissolved in normal saline and injected through a polythene cannula in the femoral vein. In rats and guinea-pigs the amount of injected solution did not exceed 0·1–0·2 ml/100 g. Desipramine hydrochloride and dopamine hydrochloride was used in these experiments. The doses refer to the salts. In guinea-pigs, rats and rabbits dopamine (2·5–30 μg/kg) produced an acute fall in blood pressure, with gradual recovery to normal values in few minutes, depending upon the dose used. In cats anaesthetized with urethane, dopamine (10–30 μg/kg) induced a biphasic response; an acute and short lasting increase in blood pressure followed by a decrease in pressure lasting for 2–5

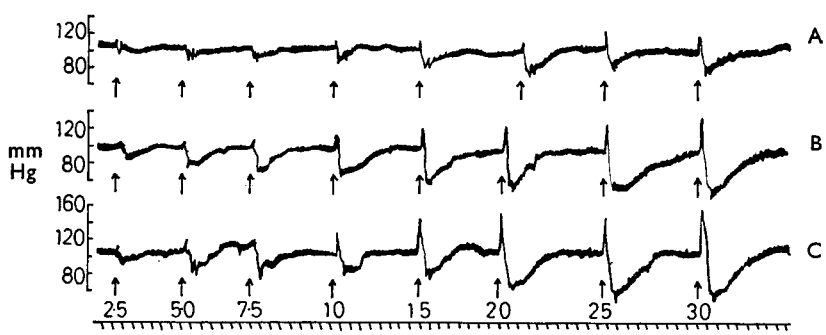

FIG. 1. The influence of a sequence of doses of dopamine (in μg/kg) on the blood pressure in a cat anaesthetized with urethane. A, Before, B, 30 min and C, 90 min after i.v. desipramine (6 mg/kg). Time marker in min.