colonies were unaltered, the xylene responses as well as those to intradermal bradykinin, histamine and 5-hydroxytryptamine, were markedly reduced.

Thus, the response of Wistar rats to chemical and thermal injury varies with the colony used. The present results also show that xylene is capable of releasing kinin. Further experiments are in progress to study the interaction between kinin release by xylene and sensory nerve activation.

REFERENCE

ROCHA, E. SILVA, M. & ANTONIO, A. (1960). Release of bradykinin and the mechanism of production of a thermic oedema in the rat's paw. *Med., exp,*. **3**, 371–382.

STARR, M. S. & WEST, G. B. (1967). Bradykinin and oedema formation in heated paws of rats. *Br. J. Pharmac. Chemother.*, **31**, 178–187.

Drug-induced changes in blood flow in normal and ischaemic regions of the canine myocardium

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Recently it has been shown (Ledingham, McArdle & Parratt, 1972) that carbochromen, an active coronary dilator drug, is incapable of increasing flow in the acutely ischaemic canine myocardium. The purpose of this investigation was to determine whether other drugs, which increase blood flow to the normal myocardium, could improve perfusion in a developing infarct.

Myocardial infarcts were produced in 42 greyhounds, breathing oxygen and 0·5-1·0% trichlorethylene, by acute ligation of the anterior descending branch of the left coronary artery. A catheter inserted distal to the ligature was used to measure peripheral coronary pressure (PCP), retrograde flow (PCF) and infarct flow by the myocardial clearance of ^{133}xenon injected into this catheter. Flow to the normal myocardium was measured with a non-cannulating Nycotron electromagnetic flow probe around the left circumflex artery. The effects, in this experimental model, of five vasoactive substances are summarized in Table 1.

TABLE 1. *Effect of five vasoactive drugs on normal and ischaemic myocardial blood flow in greyhounds, when administered intravenously, 2–3 h after coronary artery ligation (mean ± S.E.)*

Drug	Dose	Normal myocardial blood flow (ml/min) Pre	Normal myocardial blood flow (ml/min) Post	Infarct blood flow (ml/100 g/min) Pre	Infarct blood flow (ml/100 g/min) Post	Effective sub-endocardial driving pressure (mmHg) Pre	Effective sub-endocardial driving pressure (mmHg) Post
Dipyridamole	0·25 mg/kg	68 ±9	132* ±22	20 ±2	15 ±3	8 ±3	5 ±2
Glucagon	50 μg/kg	65 ±11	82* ±16	14 ±1	12 ±3	8 ±2	5 ±4
Isoprenaline	0·4 μg/kg/min	64 ±6	103* ±10	13 ±3	19 ±4	9 ±3	7 ±2
Noradrenaline	1·0 μg/kg/min	79 ±8	145* ±13	18 ±3	40* ±4	3 ±1	16* ±6
Oxyfedrine	0·5 mg/kg	65 ±8	107* ±8	12 ±2	23* ±2	4 ±2	8* ±3

* $P < 0·05$ (paired 't' test)

Neither arteriolar dilatation (dipyridamole) nor myocardial stimulation (glucagon and isoprenaline) increased blood flow in the ischaemic region, although each of these drugs markedly increased flow in the normal myocardium. This is presumably because the vessels in the ischaemic region are near-maximally dilated. Only noradrenaline and oxyfedrine (Ledingham *et al.*, 1972) consistently increased blood flow in the ischaemic region. These were also the only drugs that increased the transventricular perfusion gradient ('effective sub-endocardial driving pressure'; diastolic PCP—left ventricular end-diastolic pressure (LVEDP), Marshall & Parratt, 1973). Noradrenaline achieved this

by increasing DPCP and oxyfedrine by reducing LVEDP. These results suggest that increasing the pressure gradient across the ventricular wall is the important factor determining nutritive flow in the acutely ischaemic myocardium.

We thank the Scottish Hospitals Research Trust for financial support and Dr. J. Domenet (Geigy) for gifts of oxyfedrine and the Nycotron flowmeter.

REFERENCES

LEDINGHAM, I. McA., McARDLE, C. S. & PARRATT, J. R. (1972). Comparison of a coronary vasodilator drug (carbochromen) and a cardiac stimulant (oxyfedrine) on blood flow and oxygen extraction in experimental myocardial infarcts. *Br. J. Pharmac.*, **44**, 323–324P.

MARSHALL, R. J. & PARRATT, J. R. (1973). The effect of noradrenaline on blood flow and oxygen consumption in normal and ischaemic areas of myocardium. *Br. J. Pharmac.*, in press.

Cardiovascular and respiratory effects of cannabis extracts and Δ^1-tetra-hydrocannabinol (Δ^1-THC)

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Studies have been made of the effects of cannabis extract (assay 1·25% Δ^1-THC) and Δ^1-THC on the cardiovascular and respiratory systems of anaesthetized animals. In urethane anaesthetized rats, it was found that cannabis extract (10 and 50 mg/kg I.V.) and Δ^1-THC (0·5 and 1 mg/kg, I.V.) caused hypotension, bradycardia and a reduction in respiratory rate. The hypotensive response induced by the extract was markedly reduced by pretreatment with atropine (1 mg/kg, I.V.). Tolerance to these actions has also been shown to develop in rats which had been treated with the extract for 14 days [(50 mg/kg)/day].

In pentobarbitone anaesthetized cats with autoperfused hindquarters and a delay circuit (Li & Bentley, 1970), both intravenous cannabis extract (10 mg/kg) and Δ^1-THC (0·2 mg/kg) depressed systemic blood pressure, pulse rate, hindlimb perfusion pressure and respiratory rate. The histamine and ACh-induced reflex vasoconstriction as well as the carotid occlusion reflex were markedly reduced following intravenous administration of either the extract or Δ^1-THC. However, these drugs did not diminish the noradrenaline-induced reflex hindlimb vasodilatation.

These studies demonstrate that cannabis has significant effects on the cardiovascular and respiratory systems and that tolerance can develop to these physiological actions of cannabis.

This work was supported by an M.R.C. grant.

REFERENCE

LI, D. M. F. & BENTLEY, G. A. (1970). Reflex vascular responses to vasoactive drugs. *Eur. J. Pharmacol.*, **12**, 203–214.

Inhibition by cromoglycate of histamine release induced by dextran plus phosphatidyl serine

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Dextran produces anaphylactoid reactions in rats (Voorhees, Baker & Pulaski, 1951) and releases histamine from rat peritoneal cells *in vitro* when phosphatidyl serine is added (Goth, Adams & Knoohuizen, 1971). Calcium ions are also necessary (Foreman