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.

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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.

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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

& Mongar, 1972). We have studied the characteristics of the dextran-phosphatidyl serine interaction at 37° C using peritoneal cells from female Canterbury Ash Wistar rats. In our experiments, dextran (mol. wt.=110,000) 6 mg/ml in Tyrode solution (1·8 mM $CaCl_2$) released only 2–3% of total histamine (above the spontaneous release of about 2%). Phosphatidyl serine (0·3–100 μg/ml), which has little releasing activity of its own, when added with 6 mg/ml dextran produces a dose-dependent release of histamine. Maximum release was about 30% of total. In the presence of 10 μg/ml phosphatidyl serine, dextran in the range 0·2–15 mg/ml produced a dose dependent release.

Disodium cromoglycate (DSCG) inhibits the response to dextran in rat skin (Assem & Richter, 1971) and reduces histamine release after injection of dextran into the peritoneal cavity *in vivo* (Hanahoe, Holliman, Gordon & Wieczorek, 1972). We have found that the release of histamine from rat peritoneal cells *in vitro* by a mixture containing 6 mg/ml dextran and 10 μg/ml phosphatidyl serine is inhibited by DSCG, 50% inhibition occurring at a concentration of 10^{-5}M DSCG. At lower concentrations (10^{-7}M) DSCG sometimes increased release (3 out of 4 experiments). DSCG depressed the slope and maximum of the dextran dose-response curve. However, when dextran was kept constant at 6 mg/ml the inhibition by 2×10^{-6}M and 10^{-5}M, but not by 3×10^{-4}M, DSCG was overcome by increasing the concentration of phosphatidyl serine from 10 to 30 or 300 μg/ml. The results suggest a non-competitive inhibition with spare receptors for phosphatidyl serine. The release by the mixture of 6 mg/ml dextran and 10 μg/ml phosphatidyl serine increased as the calcium concentration was raised to 3 mM but was depressed below the optimum by concentrations of 10 and 30 mM $CaCl_2$. Inhibition of release by DSCG was not overcome by increasing the calcium concentration. In fact, inhibition was greater in the presence of higher calcium concentrations.

The inhibition dose-response curve in the dextran system was almost co-linear with that for the inhibition of antigen-induced histamine release *in vitro* from peritoneal cells of rats actively sensitized to ovalbumin using *B. pertussis* as adjuvant (Mota, 1964). This suggests that histamine release by dextran plus phosphatidyl serine may share a common pathway with reaginic hypersensitivity reactions in the rat and may be useful for identifying anti-allergic drugs like DSCG. However, the result sheds no light on whether the dextran reaction is antibody mediated as was suggested by Goth (1967).

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Prostaglandin synthesis by the pregnant rat uterus at term and its possible relevance in parturition

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Indomethacin, an inhibitor of prostaglandin (PG) synthesis (Vane, 1971) abolishes spontaneous contractions and PG release by isolated pregnant uteri of the rat (Vane & Williams, 1972). The present communication extends these findings and demonstrates

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