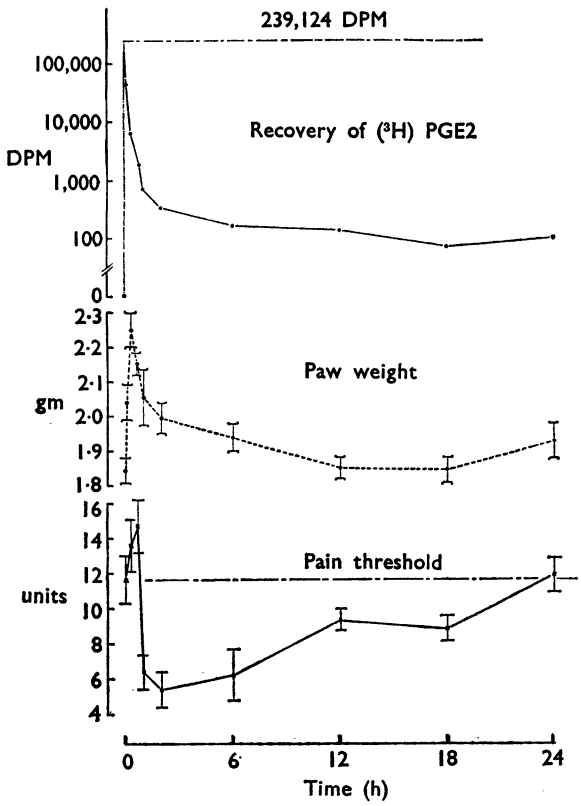

FIG. 1. Temporal relationship between disappearance of injected PGE_2, paw weight and 'pain threshold'. Results shown are means (±S.E.M.) for 16 pairs.

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A method for perfusing the whole rabbit ear with homologous blood

C. NICOL (introduced by A. G. H. BLAKELEY)

Department of Pharmacology, University of Glasgow, Glasgow G12 8QQ

Dutch rabbits of either sex, weighing 1·5–3·0 kg are used. The rabbit is anaesthetized with 4% Halothane in a 2:1 mixture of N_2O/O_2. The trachea, external jugular vein and carotid artery are cannulated. The rabbit is injected with 4,000 I.U. Heparin and 50 μg prostaglandin E_1 to prevent clotting of the blood and aggregation of the platelets, Blakeley, Brown, Dearnaley & Woods (1969). Approximately 30–40 ml of warm oxygenated Krebs' bicarbonate saline is infused into the rabbit and the animal is bled out. The ears are then cut off close to the head, one being used as a control. The skin is shaved over the central artery near the base of the ear. The artery is then exposed by blunt

dissection and a polythene cannula inserted. The ear is then perfused at a flow rate of 1·0 ml/min with the blood collected previously. The resting pressure, usually between 60 and 70 mmHg is measured by a pressure transducer and recorded on a potentiometric recorder. A peristaltic pump draws the blood from a film oxygenator consisting of a polypropylene cylinder 8·5 cm in diameter, 19 cm long, inclined at an angle of 30° from the horizontal and rotated at 30 r.p.m. Moistened 95% oxygen 5% CO_2 is blown down into the base of the cylinder. The blood is pumped through the filter removed from an Avon A10 blood administration set and then runs through a heat exchange coil at 37° C prior to entering the ear through the cannula. The ear is suspended by the tip inside a glass heating jacket which excludes draughts and warms the ear. The venous blood flowing out of the ear is collected by a polythene funnel and either returns to the reservoir or is collected for assay, Injections are made through thick-walled rubber tubing into the blood as it enters the heating-coil.

The advantage of blood perfusion over saline perfusion of the ears is that there is little tissue deterioration. Saline perfusion for 90 min results in a severe oedema ; an 80% weight gain being found. A weight gain of only 20% resulted after blood perfusion for over 3 hours.

With this system records can be made of the perfusion pressure and, after the injection of ^{3}H-noradrenaline, the radioactivity of the venous effluent can be assayed by standard liquid scintillation techniques.

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The isolated perfused rat liver in the study of the metabolism of foreign compounds

A. BOOBIS and G. POWIS

Department of Pharmacology, University of Glasgow, Glasgow G12 8QQ

The use of the isolated perfused rat liver in studies upon the metabolism of foreign compounds is not new (Bahr, Alexanderson, Azarnoff, Sjoqvist & Orrenius, 1970). The present method of perfusion differs from those described previously in certain important respects. The liver was perfused through the portal vein with a semi-synthetic perfusate consisting of aged human cells (packed cell volume 20%) suspended in Krebs bicarbonate buffered saline pH 7·4, containing 3% bovine serum albumin and 0·2% glucose, at a constant flow rate of 1 (ml/g)/min, corresponding to a portal venous pressure of 10 mmHg. The perfusate was gassed with air containing 5% CO_2 to avoid the degenerative changes associated with the use of higher oxygen tensions reported by Abraham, Dawson, Grasso & Goldberg, 1968. The liver was suspended in liquid paraffin maintained at 37° C, this served to support the lobes and allowed an even perfusion.

The preparation remained both macroscopically and histologically normal for up to 6 h. The metabolic criteria of viability adopted, the values of which proved similar to those reported *in vivo* were glucose production, K^+ efflux and the ratio of lactate to pyruvate in the perfusate. Bile production fell from an initial rate of 1 ml/h to 0·1 ml/h at the end of 6 h. Hexobarbitone or aniline was added to the vascular perfusate to give an initial concentration of 1 mM. The disappearance of substrate was followed by extracting the unmetabolized substrate from aliquots of perfusate taken at 15 min intervals, into an organic phase. Hexobarbitone was measured by the method of Remmer (1959) and aniline by the method of Bratton & Marshall (1939).

The half life for the removal of hexobarbitone was 33 min and for the removal of aniline 82 min. Attempts to measure the formation of metabolites from aniline were only partially successful. At the end of 3 h perfusion 22·8% of the aniline remained unmetabolized, whilst aniline conjugates accounted for a further 20%, and conjugates of p-aminophenol for 10%. Free p-aminophenol could not be detected in the perfusate. Thus 61% of the aniline disappearing could not be accounted for in terms of the major