previously constricted vein. These blocking effects of both practolol and ICI-66082 were overcome by increasing the rate of infusion of isoprenaline.

This study has demonstrated that propranolol is effective in blocking both heart rate and peripheral vascular responses to infused isoprenaline, but practolol and ICI-66082 are less effective in blocking peripheral vascular responses.

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Central hypotensive effect of propranolol in the rabbit

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The action of propranolol in the treatment of hypertension is not well understood. The effective dose in chronic oral treatment may be very high (Prichard & Gillam, 1969) and although propranolol induces a rapid fall in cardiac output, the fall in arterial pressure is usually a gradual one. Several antihypertensive drugs exert actions on noradrenergic pathways in the central nervous system (CNS) and this is a possible site of action for propranolol, which achieves high CNS concentrations.

Intracerebroventricular (ICV) injection of (±)-propranolol (500 μg) produced a rapid rise in mean arterial pressure (MAP) in the conscious rabbit, 27·5±6·0 mmHg at 5 min, followed by a prolonged fall, 8·8±3·3 mm Hg at 4 h. A similar early rise in MAP was produced by (+)-propranolol 500 μg ICV, 42·2±4·5 mmHg, but there was no late fall. Procaine (1 mg) ICV produced a similar rise, 51·0±10 mm Hg at 5 min. The pressor effect of both (+)-propranolol and procaine were both abolished by pentobarbitone anaesthesia. This early rise in MAP may be related to the membrane stabilizing action shared by procaine and both isomers of propranolol.

(−)-Propranolol 500 μg ICV raised MAP 20·8±4·1 mm Hg at 5 min, but the subsequent fall was greater than that produced by the racemate (14·6±4·5 mmHg at 4 h). The central hypotensive effect of (−)-propranolol was abolished by pretreatment of rabbits one week previously with intracisternal 6-hydroxydopamine (500 μg/kg), which destroys CNS noradrenergic neurones.

Isoprenaline (50 μg ICV) caused a transient fall in MAP, 10·0±0·4 mmHg at 5 min. In rabbits pretreated with 500 μg (−)-propranolol ICV 2 h previously, this response to central isoprenaline was abolished.

It appears therefore that propranolol can lower arterial pressure in the rabbit by an action on the CNS. This action is dependent on the integrity of noradrenergic neurones and the effect is related to β-adrenoceptor blocking activity and not to local anaesthetic activity.

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Rabbit monoarticular arthritis and synovial prostaglandins

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An immune arthiritis is produced in the rabbit using a modification of the method of Dumonde & Glynn (1962). Essentially, this consists of sensitizing the animals intra-