activity therefore may be of importance in explaining the wide differences in pharmacological effects produced by β-adrenergic blockers represented by MJ-1999 and propranolol, particularly in their cell membrane actions.

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Hypotensive action of ephedrine in cats

SIR,—In the previous report (Maj & Langwiński, 1966) we described a temporary decrease of blood pressure in cats and rats after tachyphylaxis to tyramine. The depressor action of tyramine was regarded as being connected with the process of histamine liberation. Ephedrine belongs to the group of amines which cause tachyphylaxis. The purpose of the present paper was to find whether ephedrine causes a depressor action and if so, its mechanism of action.

The experiments were made on 40 cats anaesthetized with chloralose (80 mg/kg, i.p.) or urethane (1·5 g/kg, i.p.) accompanied by bilateral cervical vagotomy. Blood pressure was recorded from the carotid artery by a mercury manometer, respiration—with Marey's tambour, the kidney volume plethysmographically, and the contraction of the nictitating membrane recorded isotonically. All the substances were injected into a femoral or jugular vein. Ephedrine hydrochloride of specific rotation of $-33°$ to $-35·5°$ was used.

A hypotensive action of ephedrine in doses of 5 and 10 mg/kg was seen after tachyphylaxis was reached. The general dose of ephedrine averaged $8·9 \pm 1·9$ mg/kg. When such an average dose was administered, the additional dose of 5 mg/kg of ephedrine caused the depression of blood pressure of $14·6 \pm 1·4$mm Hg and the dose of 10 mg/kg caused the depression of the pressure $21·4 \pm 2·3$ mm Hg. Such a decreased blood pressure lasted 2–5 min. The depressive action of ephedrine was accompanied by the decrease of the kidney volume. During the hypotensive phase of ephedrine action, the contraction of the nictitating membrane was unchanged.

The type of anaesthesia, vagotomy, atropine (0·5 mg/kg), antazoline (10·0–30·0 mg/kg), cyclizine (2·0 mg/kg), methysergide (0·5–1·0 mg/kg), dichloroisoprenaline (5·0 mg/kg), propanolol (2 mg/kg) did not abolish or decrease the hypotensive action of ephedrine. Dihydroergotamine (1·0–2·0 mg/kg) and phentolamine (0·5–1·0 mg/kg) abolished the hypotensive action and decreased the kidney volume affected by ephedrine (5·0–10·0 mg/kg). Blackwell & Marley (1967) found that the hypotensive action of some amines depends on the values of the blood pressure in rats. Dihydroergotamine and phentolamine depressed the

blood pressure and therefore after their administration, continuous intravenous angiotensin infusion was used to increase the blood pressure to the initial value. In those conditions dihydroergotamine and phentolamine also abolished the hypotensive action of ephedrine. Ganglion blocking agents like chlorisondamine (2 mg/kg) and pempidine (2 mg/kg) only reduced the hypotensive action of ephedrine.

In contrast to tyramine (Maj & Langwiński, 1966), ephedrine in the concentrations used (10^{-5}–10^{-3}) relaxed the isolated jejunum of guinea-pig.

The results of the experiments showed that the depressive responses do not come from the released histamine as is the case with tyramine (Maj & Langwiński, 1966). Paton (1957) found also that ephedrine does not release histamine from the isolated skin preparation of the cat. It is supposed that the depressive action of ephedrine can be explained by the blockade of adrenergic α-receptors because drugs blocking those receptors (dihydroergotamine and phentolamine) abolished the hypotension observed after ephedrine. This supposition is supported by the reports of Valette, Cohen & Huidobro (1960), who discovered that the continuous infusion of noradrenaline in dogs caused the depressive action of the second dose of ephedrine (3 mg/kg) and also by the explanation of Fleckenstein & Burn (1953) who found that ephedrine besides its indirect effect also possesses direct activity.

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