Influence of Guanethidine on the Catecholamine Depleting Effects of Tyramine in the Rat Heart

SIR,—Tyramine showed no pressor action in animals whose noradrenaline stores were depleted with reserpine (Carlsson and others, 1957), but its actions were re-established by prolonged infusion with noradrenaline (Burn and Rand, 1958). It was predominately these facts which led the same authors to advance the hypothesis that the actions of tyramine are mediated through the release of noradrenaline. Studies carried out in this laboratory as well as by Potter and others (1962) have provided direct evidence for this hypothesis in the intact animal.

Since guanethidine has been shown to antagonise the pressor action of tyramine (Maxwell, Plummer, Povalski and Schneider, 1960) and tyramine exerts its effects by liberating noradrenaline, guanethidine would be expected to prevent the depleting action of tyramine. This possibility was examined in the following experiment. Male rats (Holtzman Strain), weighing 200 to 225 g. were given guanethidine sulphate 5 mg./kg. intravenously 20 min. before the intramuscular injection of tyramine hydrochloride (20 mg./kg.). 30 min. after tyramine administration the animals were killed by decapitation. The concentrations of catecholamines in the ventricular myocardium were determined by the trihydroxyindole fluorimetric procedure of Shore and Olin (1959) and are expressed as μg. of noradrenaline per g. of fresh tissue.

TABLE I

EFFECT OF GUANETHIDINE ON THE CATECHOLAMINE DEPLETING EFFECT OF TYRAMINE IN THE RAT HEART

Treatment	Number of animals	Catecholamine concentration μg./g. of fresh tissue. Mean $\pm$ s.e.
None	18	1·06 $\pm$ 0·03
Tyramine	11	0·70 $\pm$ 0·02
Guanethidine	7	0·95 $\pm$ 0·03
Guanethidine + tyramine ..	18	0·67 $\pm$ 0·03

The results, summarised in Table I, show that guanethidine had no effect on the depleting effects of tyramine in the rat heart. The observation of Lindmer and Muscholl (1961) that guanethidine significantly reduces the tyramine-induced release in the isolated, perfused rabbit heart appears to be unrelated to its pharmacological action in the intact animal.

B. BHAGAT*

Department of Pharmacology and Toxicology,
The University of Wisconsin,
Madison, Wisconsin, U.S.A.
December 7, 1962

REFERENCES

Burn, J. H. and Rand, M. J. (1958). *J. Physiol. (Lond.)*, **144**, 314–336.
Carlsson, A., Rosengren, E., Bertler, A. and Nilsson, J. (1957). In *Psychotropic Drugs*, p. 363, Elsevier Publishing Co., Amsterdam.
Lindmar, R. and Muscholl, E. (1961). *Arch. exp. Path. Pharmak*, **242**, 224.
Maxwell, R. A., Plummer, A. J., Povalski, H. and Schneider, F. (1960). *J. Pharmacol.*, **129**, 24–30.
Potter, L. T., Axelrod, J., Kopin, I. J. (1962). *Biochem. Pharmacol.*, **11**, 254–256.
Shore, P. A. and Olin, J. S. (1959). *J. Pharmacol.*, **122**, 295–300.

* Present address: Department of Pharmacology, University of Minnesota Medical School, Minneapolis 14, Minnesota, U.S.A.