(10 mg/kg intravenously) abolished the inhibitory effect of adrenaline on the bronchial muscle but not that of ascorbic acid. Reserpinisation of the animals with four daily doses of reserpine, 2 mg/kg, intraperitoneally, did not modify the action of ascorbic acid on the spasmogen response. Dr. Collier & Mrs. Piper also tell us that adrenalectomy does not reduce the protective effect of ascorbic acid on bradykinin bronchospasm.

The present results show that the inhibition of bronchospasm by ascorbic acid is not mediated by catecholamines, does not involve β-adrenergic receptors since its action is not prevented by pronethalol, and is probably a direct effect.

Department of Pharmacology,
School of Pharmacy,
University of London,
29/39 Brunswick Square,
London, W.C.1.
July 20, 1965

W. DAWSON
G. B. WEST

References

Dawson, W. & West, G. B. (1965). *Brit. J. Pharmacol.*, **24**, 725–734.
Guirgis, H. M. (1965). *J. Pharm. Pharmacol.*, **17**, 387.

Anorexigenic drugs and lipid mobilisation

SIR,—As reported previously (Santi & Fassina, 1964), dexamphetamine, a typical anorexigenic substance, strongly elevated the plasma level of free fatty acids. Effectiveness of anorexigenic sympathomimetic drugs, may thus be considered to be based, not only on modification of psychic function, but mainly related to an interference with the central mechanisms of regulating food intake (Andersson & Larsson, 1961).

TABLE 1. EFFECT OF SOME ANOREXIGENIC DRUGS ON PLASMA FREE FATTY ACIDS (FFA) IN RATS

Treatment and dose	Time of death min	Plasma FFA μequiv./litre mean ± s.e.
Saline	30	424 ± 30 (11)† —
Chlorphentermine hydrochloride 12 mg/kg ..	30	710 ± 10 (4) < 0·001*
Methylphenidate hydrochloride 14 mg/kg ..	30	713 ± 28 (7) < 0·001
Pipradol hydrochloride 16·5 mg/kg	30	847 ± 10 (4) < 0·001
Saline	60	403 ± 33 (19) —
Dexamphetamine sulphate 2 mg/kg	60	672 ± 26 (17) < 0·001

* P versus saline treated controls.
† number of animals.
Adult non-fasted female rats (Wistar strain, 200–250 g) were given drugs or saline intraperitoneally and decapitated under ether anaesthesia. Time of death corresponded to the maximum activity for each drug. Free fatty acids were titrated by the method of Dole (1956). Doses of chlorphentermine, methylphenidate and pipradol are equimolar (54 μmoles/kg); dose of dexamphetamine (10·8 μmoles/kg).

We have now investigated the effects of additional anorexigenic drugs on plasma free fatty acids in rats. The three different classes investigated show a particular pharmacological and structural interest. Chlorphentermine is closely related chemically to dexamphetamine, but is almost completely devoid of the typical central nervous system (CNS) stimulant activity (Holm, Huus, Kopf, Möller Nielsen & Petersen, 1960; Gylys, Hart & Warren, 1962). Methylphenidate and pipradol (Karczmar & Howard, 1959; Spengler & Waser, 1959) are CNS stimulants and differ from amphetamine in structure (piperidine-like compounds) and in adrenergic properties (Krueger & McGrath, 1964).

Finally, desipramine, imipramine and amitriptyline were tested because they have been claimed to have anorexigenic action (Waser & Spengler, 1963).

As shown in Table 1, chlorphentermine, methylphenidate and pipradol, injected in rats in equimolar doses (54 μmoles/kg) all induced an increase of plasma free fatty acids. The amount of such increases was comparable for the three drugs (+ 70–100%). Dexamphetamine was about five times more active (on a molar basis) than the other drugs.

Desipramine (82 μmoles/kg), imipramine and amitriptyline (160 μmoles/kg) strongly increased plasma free fatty acids (60–80%, Table 2). Desipramine was more active than imipramine and amitriptyline. The lipomobilising action of these drugs is less rapid in onset than the action of amphetamine or piperidine-like compounds: the maximum value of plasma free fatty acids was reached 30–60 min after injection by using chlorphentermine, methylphenidate, pipradol or dexamphetamine, and 150 min after desipramine, imipramine or amitriptyline.

TABLE 2. EFFECT OF SOME THYMOLEPTIC DRUGS ON PLASMA FREE FATTY ACIDS (FFA) IN RATS

Treatment and dose	Time of death min.	Plasma FFA μequiv./litre mean ± s.e.	
Saline	150	563 ± 29 (12)†	—
Desipramine hydrochloride 25 mg/kg	150	1044 ± 46 (12)	< 0·001*
Saline	150	521 ± 30 (12)	—
Imipramine hydrochloride 50 mg/kg	150	924 ± 42 (12)	< 0·001
Saline	150	550 ± 15 (12)	—
Amitriptyline hydrochloride 50 mg/kg	150	863 ± 21 (12)	< 0·001

* P versus saline treated controls.
† number of animals.
Drugs and saline were injected i.p. in adult non-fasted male rats (Wistar strain, 200–250 g). Doses correspond to 82 μmoles/kg for desipramine and to 160 μmoles/kg for imipramine and amitriptyline.

These results support the hypothesis that the metabolic action of these drugs is related to their anorexigenic effect (Santi & Fassina, 1964). It may be recalled that the breakdown of a molecule of glucose makes available 24 molecules of adenosine triphosphate, whereas a molecule of a long chain fatty acid (for instance C18) could supply 144 moles of adenosine triphosphate, if completely metabolised. Whatever the mechanism, the test of lipid mobilisation may be regarded as an experimental tool for the further characterisation of some centrally acting drugs.

Institute of Pharmacology,
University of Padua, Italy

R. SANTI
G. FASSINA

July 20, 1965

References

Andersson, B. & Larsson, S. (1961). *Pharmacol. Rev.*, **13**, 1–16.
Dole, V. P. (1956). *J. Clin. Invest.*, **35**, 150–154.
Gylys, J. A., Hart, J. J. D. & Warren, M. R. (1962). *J. Pharmacol.*, **137**, 365–373.
Holm, T., Huus, I., Kopf, R., Möller Nielsen, I. & Petersen, P. V. (1960). *Acta pharm. tox. Kbh.*, **17**, 121–136.
Karczmar, A. G. & Howard, J. H. Jr. (1959). *Proc. Soc. exp. Biol., N.Y.*, **102**, 163–167.
Krueger, G. L. & McGrath, V. R. (1964). *Psychopharmacological Agents*, Editor, Gordon, M. Vol. I, p. 225–250, New York and London: Academic Press.
Santi, R. & Fassina, G. (1964). *J. Pharm. Pharmacol.*, **16**, 130–131.
Spengler, J. & Waser, P. G. (1959). *Arch. exp. Path. Pharmak.*, **237**, 171–185.
Waser, P. G. & Spengler, J. (1963). *Schweiz. med. Wschr.*, **93**, 90–92.