Table 1. Anti-inflammatory ED_{50} Values of Drugs by Various Tests (mg/kg orally)

Drug	Kaolin	
	Blocking	Weighing
Aspirin	220	370
Chlorpromazine	2·5	5·4
Phenylbutazone	64	> 400
Hexadimethrine bromide (polybrene p.o.)	6·2	55
Hydrocortisone	Ineffective	2·6

ments therefore are compatible with the view that kinins are liberated in the inflammatory response, but also show that oedema formation and protein transfer are two separate aspects of this response, kinin formation being associated with the latter aspect.

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[1] Parratt, J. R., and West, G. B., *Brit. J. Pharmacol.*, **13**, 45 (1958); *J. Physiol.*, **139**, 55 (1957).
[2] Northover, B. J., and Subramanian, G., *Brit. J. Pharmacol.*, **18**, 546 (1962); **16**, 103 (1961).
[3] Ginzy, E., and Kato, I., *J. Physiol.*, **132**, 1 (1957).
[4] Wilhelm, D. L., *Pharmacol. Rev.*, **14**, 151 (1962).
[5] Armstrong, D. A., and Stewart, J. W., *Nature*, **194**, 199 (1962).

Pharmacological Activity of Phenylisopropylhydroxylamine and its O-Methyl Ether

The well-known stimulatory action of 2-phenylisopropylamine (amphetamine) and, more recently, the use of 2-phenylisopropylhydrazine as a psychic energizer[2], prompted us to investigate the pharmacology of *N*-(2-phenylisopropyl)hydroxylamine (PIH) and its *O*-methyl ether (PIHE). Little has been published concerning the pharmacology of *N*-substituted hydroxylamines although Jones and Major[1] examined the action of a series of hydroxylamino analogues of certain biologically active amines and Lewin[3] commented on the toxicity of *N*-phenylhydroxylamine.

PIH was prepared from phenylacetone oxime by the procedure of Vavon and Crajinovic[4] and the corresponding *O*-methyl ether was obtained similarly from phenyl-2-propanone oxime-*O*-methyl ether. Both bases were isolated, purified and stored as their stable neutral oxalates, but were injected as freshly prepared solutions of their hydrochlorides.

PIH, at a dose-level of 25 mg/kg (intramuscular), evokes a lower level of rage in healthy adult cats than does amphetamine, but the effects lasted longer. Rage behaviour is judged by changes in pilomotor activity, salivation, pupil dilation, growling, hissing, withdrawal and aggressive behaviour as reported by Norton and deBeer[5]. Cats receiving this compound, in addition to rage, exhibit both a peculiar circular head motion and profuse salivation. Pretreatment of these animals with chloropromazine (intramuscularly at 10 mg/kg) causes blockade of the rage response but fails to inhibit the characteristic head motion. Atropine does not block the salivation. PIH does not significantly increase the rectal temperature of cats, while many amphetamine-like compounds are pyrelogenic. PIHE fails to produce any observable changes in cat behaviour.

Spontaneous motor activity in mice, measured by light beam interruptions[5], indicates that PIH has an ED_{100} = 20 mg/kg (effective dose to double motor activity) where amphetamine has twice this activity, or ED_{100} = 10 mg/kg. Interestingly, PIHE was inactive, at 100 mg/kg, in this test during the usual observation time of 0·5 h, but spontaneous motor activity began to increase 2 h later and finally reached levels seven times that of the control; clonic convulsions and death followed.

PIH decreased hexobarbital sleeping time in mice by about 20 per cent while PIHE increased it by 44 per cent. PIH has 1·3 times the relative pressor activity of β-phenethylamine, while PIHE was almost without effect as measured in the α-chloralose anaesthetized cat.

We are now examining the pharmacology of a number of ring-substituted phenylisopropylhydroxylamines and their corresponding methoxyamines in order further to determine the role of the hydroxylamine group in central and autonomic activity.

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[1] Bhl, J. H., Drukker, A. E., Shott, P. A., Spector, S., and Boelle, B. B., *J. Amer. Chem. Soc.*, **80**, 1519 (1958).
[2] Jones, L. W., and Major, R. T., *J. Amer. Chem. Soc.*, **49**, 1527 (1927).
[3] Lewin, L. Fraenkel, *Arzneimittel-Synthese*, 7th (Julius Springer, Berlin, 1962).
[4] Vavon, G., and Crajinovic, M., *Bull. Soc. Chim.* (4), **43**, 251 (1928).
[5] Norton, S., and deBeer, E. J., *Ann. N.Y. Acad. Sci.*, **66**, 249 (1956).
[6] Weidle, B. A., and Young, E. P. H., *J. Medicinal Chem.*, **5**, 378 (1962).

Effect of Angiotensin on Intraocular Pressure

In a previous report from this laboratory[1], it was observed that injections of noradrenaline, made directly into the vitreous body of the rabbit eye, lowered the intraocular pressure, apparently by reducing the resistance to outflow of aqueous humour from the angle of the anterior chamber of the eye. In order to determine whether such an effect could be related to the vasoconstrictor action of noradrenaline, it was decided to examine the ocular effects of angiotensin, a vasopressor compound which does not stimulate sympathetic alpha receptors. Some preliminary results obtained in this study are presented here.

In all these experiments, albino rabbits of the New Zealand white strain were used. Urethane 1–2 g/kg was used as the anaesthetic. Intraocular pressures were recorded manometrically and the facility of outflow of aqueous humour determined from analysis of pressure decay curves as described previously[1,2]. In the first series of experiments, angiotensin was injected close-arterially to one eye via a polythene cannula inserted into a lingual artery. The mean arterial blood pressure was recorded throughout each experiment by means of a cannula inserted into a femoral artery. The anterior chambers of both eyes were cannulated prior to the injection. The results of such an experiment are shown in Fig. 1. Injection of 5 μg angiotensin over a period of 1 min into a lingual artery resulted in a rise in the mean arterial blood pressure, the pressure returning to normal at the end of the injection. It is interesting to note that in contrast to the pressure in the control eye, which followed the general blood pressure changes, the intraocular pressure of the eye which received most of the angiotensin fell during the injection and then returned to normal. The fall in intraocular pressure in the test eye was accompanied by visible blanching of the iris. The transient change in intraocular pressure seen in the test eye could be due to a constriction of blood vessels in the eye or it could be due to a relaxation of the extraocular muscles. Thus, an indication of a marked change in intraocular pressure under these conditions is not sufficient to indicate that angiotensin can alter aqueous humour dynamics.

It is well known that any change in the steady-state intraocular pressure must be explained in terms of three factors which govern intraocular pressure at equilibrium, namely, rate of formation of aqueous humour, resistance to outflow and episcleral venous pressure. To determine the effect of angiotensin on the steady-state intraocular pressure, injections were made directly into the vitreous body of the rabbit eye as described previously[1]. In each