

zodium, to the medium eliminated the occurrence of the hazy area and also produced larger zones of inhibition.

The in vitro antimicrobial spectrum of the antibiotic (Table) indicates that it has activity primarily against yeasts and some select bacteria and molds.

The trivial name of brassicicolin A is assigned to this antibiotic.

**Zusammenfassung.** Bei Untersuchungen von *Alternaria brassicicola*, die eine antibiotische Komplexverbindung bildet, wurde eine der aktivsten Verbindungen mit Brassicicolin A bezeichnet, isoliert und gereinigt. Die Substanz konnte jedoch nicht kristallisiert werden. In-vitro-

Untersuchungen zeigen primär eine Antiwirksamkeit gegen Hefen.

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### Potassium-Stimulated Respiration of Cerebral Cortex of Rats Poisoned with Phosphamidone

In vitro studies have shown that the rate of oxygen uptake of brain tissue from animals poisoned with organophosphorus anticholinesterases is essentially unchanged even after lethal doses of these compounds<sup>1</sup>.

In the present experiments the brain cortical slices taken from rats poisoned with phosphamidone (2-chloro-2-diethyl-carbamyl-1-methyl-vinyl-dimethyl phosphate)<sup>2</sup> were tested in vitro under conditions in which tissue respiration has been stimulated by potassium ions.

Phosphamidone was given s.c. to adult male rats weighing about 200 g. The animals were killed by decapitation 45 min after administration of 15 mg/kg (LD<sub>50</sub>) and 20–30 min after administration of 30 mg/kg (LD<sub>90–100</sub>). The brains were quickly removed and 2 brain slices from each hemisphere were used. The oxygen uptake of cerebral cortex was determined at 38°C by standard Warburg technique, using Krebs-Ringer phosphate solution with glucose as substrate and oxygen as the gas phase. For potassium stimulation 10 mM KCl was added.

As can be seen from the Table, the oxygen uptake of cortical slices from phosphamidone-treated rats was lower than that of slices from control animals. The reduction in the tissue respiration was statistically significant ( $P < 0.05$ ) and of the order of 20–35%. The doses inhibitory to the tissue respiration are, however, distinctly higher than those required for inhibition of cholinesterase in cortical slices<sup>3</sup>.

The respiratory activity of brain cortex from normal rats is considerably increased by addition of a relatively small concentration of potassium chloride<sup>4</sup>. The addition of the same concentration of potassium chloride to the brain cortex from phosphamidone-treated rats brings about a stronger stimulation of the respiration rate. The increase of respiration augmented as the dose of phosphamidone was increased, amounting to more than 100% at a dose of 30 mg/kg.

It is thus obvious that in phosphamidone-treated rats the respiration of brain cortex is much more sensitive to the stimulant action of potassium chloride than in normal animals. It is interesting, however, that the addition of the same concentration of potassium chloride to the brain cortex taken from animals poisoned with equitoxic doses of paraoxon and TEPP has not such an effect. The true nature of these differences is not quite clear. It is possible, however, that the effect of phosphamidone on the chemically stimulated cellular respiration is due to some of its metabolites, since in concentrations of 10<sup>-6</sup> to 10<sup>-2</sup> M phosphamidone has no influence on the rate of oxygen uptake in cortical slices stimulated by potassium chloride.

In vitro effect of potassium ions on the respiration of cerebral cortex of rats poisoned with some organophosphates

Organo-phosphate	(mg/kg)	KCl (mM)	QO <sub>2</sub> <sup>a</sup>	Change of normal (%)
None	–	–	19.2 ± 1.3 (25)	–
	–	1.0	23.9 ± 1.1 (35)	+ 24 <sup>b</sup>
Phosphamidone	15	–	12.5 ± 0.3 (10)	– 34 <sup>b</sup>
	15	1.0	28.5 ± 1.5 (8)	+ 48 <sup>b</sup>
	30	–	11.4 ± 0.4 (14)	– 40 <sup>b</sup>
	30	1.0	37.2 ± 3.7 (6)	+ 93 <sup>b</sup>
Paraoxon	0.25	–	18.7 ± 1.7 (8)	+ 2
	0.25	1.0	17.3 ± 1.6 (4)	– 9
	0.5	–	21.5 ± 1.7 (6)	+ 11
	0.5	1.0	20.5 ± 3.4 (4)	+ 6
TEPP	0.5	–	21.8 ± 2.4 (5)	+ 13
	0.5	1.0	17.8 ± 1.7 (4)	– 7
	1.0	–	12.4 ± 1.8 (5)	– 35 <sup>b</sup>
	1.0	1.0	17.1 ± 1.3 (4)	– 10

<sup>a</sup> QO<sub>2</sub> = μl O<sub>2</sub>/h/mg dry weight of tissue (mean ± S.E.); the figures in parentheses indicate the number of rats. <sup>b</sup>  $P < 0.05$ .

**Résumé.** Chez le rat intoxiqué par des doses léthales de phosphamidone, la consommation in vitro d'oxygène des tranches du cortex cérébral stimulées par KCl est plus élevée que celles des témoins ou des rats intoxiqués au paraoxon ou au TEPP.

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<sup>1</sup> G. PAULET and P. ANDRÉ, J. Physiol. 49, 335 (1957).

<sup>2</sup> Pure sample of phosphamidone (Dimecron®) was kindly supplied by CIBA A.G., Basel.

<sup>3</sup> D. ANDJELKOVIĆ and M. P. MILOŠEVIĆ, in press.

<sup>4</sup> H. McILWAIN, *Chemical Exploration of the Brain* (Elsevier Publ. Co., Amsterdam, London, New York 1963), p. 55.