LETTERS TO THE EDITORS

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Penicillin-like Antibiotics from Various Species of Moulds

SINCE the demonstration of the biological and chemical properties of penicillin, an antibiotic produced by *Penicillium notatum*[1,2,3,4,5], certain other species of moulds have been shown to produce similar substances—*Aspergillus flavus*[6,7,8,9], *A. giganteus* Wehm[10], and *A. parasiticus*[11].

In the course of an investigation of moulds that have been shown by Wilkins and Harris[12,13,14] to produce antibiotics, we have found that in addition to the above-mentioned species penicillin-like substances are produced by the following :

	National collection of type cultures No.
P. fluorescens	6621
P. rubens Biourge	6643
P. avellaneum Thom and Turesson	3751
P. baculatum Westl.	3956
P. turbatum Westl.	6523

Of these, *P. baculatum* and *P. rubens* are morphologically similar to, and therefore possibly related to, the *chrysogenum-notatum* group, but the others are quite widely separated morphologically from that group and from each other (personal communication from Dr. W. H. Wilkins).

The antibacterial activity developed in a variety of media, including in each instance modified Czapek Dox[2], with and without corn steep liquor.

The penicillin-like nature of the antibiotic was established by the following biological and chemical properties : active against *St. aureus*, not against *B. coli* ; extracted into organic solvents at *p*H 2 and re-extracted with water at *p*H 7 ; inactivated by acid and alkali ; partially inactivated by heating at 100° C. at *p*H 7 for 15 minutes ; completely inactivated by penicillinase and by copper ions ; all except the product of *P. turbatum*, which was not tested, were inactivated by methyl alcohol. (Some of the inactivation tests on the product of *P. baculatum* were carried out by Dr. E. Chain. We are indebted to Dr. E. S. Duthie for preparations of penicillinase.)

Thus it is becoming apparent that many species of moulds produce penicillin-like substances.

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Organic Accelerators for Enzyme Systems

IN order to determine the part played by yeast extracts in the stimulation of the respiration of various cells[1], a study was made on the possible antagonism between this respiratory stimulant and several well-known respiratory depressants. The poisons, potassium cyanide, sodium azide, amyl alcohol and urethane, react reversibly or irreversibly with particular enzyme systems of the respiratory chain. Potassium cyanide and sodium azide depress the activity of the iron oxidation catalysts, while amyl alcohol and urethane react with the dehydrogenating system.

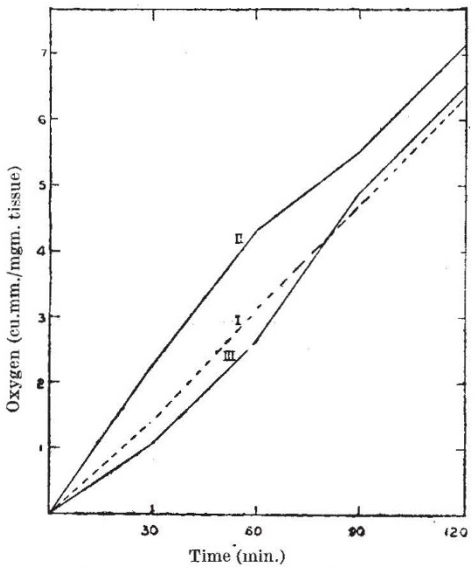

Fig. 1. EFFECTS OF YEAST EXTRACT AND SODIUM AZIDE ON RAT LIVER RESPIRATION
Curve I, control. Curve II, yeast extract initially present and sodium azide added at 60 min. Curve III, sodium azide initially present and yeast extract added at 60 min.

In Fig. 1 is shown the antagonism between yeast extract (6 mgm./ml.) and *M*/1,050 sodium azide on rat liver respiration. The oxygen uptake was determined in Ringer-phosphate glucose solution at a temperature of 37·5° C.[1]. In one set of experiments, 1 ml. of yeast extract (18 mgm./ml.) dissolved in Ringer-phosphate glucose was placed in the flask at the beginning of the experiment. Addition after 60 minutes of 1 ml. of *M*/350 sodium azide in Ringer-phosphate glucose offset the stimulation caused by the extract and brought the rate of oxygen uptake back to that of the control. In the other set of experiments, the depression of respiration due to sodium azide was offset completely when 1 ml. of yeast extract was added from the side arm. Qualitatively similar results were obtained with potassium cyanide. No antagonism could be found between the yeast extract and poisons such as amyl alcohol and urethane. We suggest, therefore, that the yeast extract stimulation occurs at the same part of the chain blocked by cyanide and azide, namely, cytochrome oxidase. Yeast and rat skin have behaved in a manner qualitatively similar to liver.

Since cytochrome oxidase is known to be an iron porphyrin enzyme containing a hæmin-like prosthetic group, it was thought desirable to study more closely the activity of the yeast extracts on simpler systems containing such iron enzymes as horse radish root