NOTES

INHIBITION OF BACTERIAL GROWTH BY PIPRADROL

ERNEST BEERSTECHER, JR. AND ELEANOR J. EDMONDS

Department of Biochemistry, School of Dentistry, University of Texas, Houston, Texas

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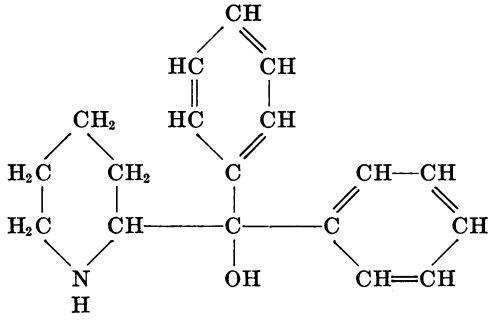
As part of an investigation of the fundamental biochemical mode of action of the recently introduced behavioral drugs, it was decided to test some of these for inhibitory effects upon microorganisms. It was discovered in the course of this study that pipradrol[1] at levels of 500 μg per ml of medium was inhibitory to the growth of *Escherichia coli* grown in mineral salts-glucose medium and to *Lactobacillus plantarum* ATCC strain 8014 grown in a more complex synthetic medium. The inhibition of *E. coli* was studied in some detail. It was not reversed by serotonin or any of the psychopharmacological drugs investigated, and it was not significantly affected by normal growth levels of vitamins, amino acids, or other metabolites. Yeast extract, however, did show competitive reversal properties, as did, to a lesser extent, casein hydrolyzate and urine.



METHODS

Attempts were made to isolate the reversing factor in yeast extract by chromatography, bioautography, and countercurrent distribution techniques, but the results were highly equivocal and suggested that more than a single factor was involved. Since casein hydrolyzate showed considerable activity, and since the activity of yeast extract was destroyed by nitrous acid and to some extent by 1 N NaOH, but not by 1 N HCl, it seemed probable that the activity resided

TABLE 1

Ability of niacin and pantothenic acid to potentiate the amino acid reversal of pipradrol inhibition of Escherichia coli*

Amino Acid Mixture		Top Growth				
		Supplement				
		None	Vitamin mixture†	Niacin (10 μg per ml)	Pantothenic acid (10 μg per ml)	Niacin and pantothenic (10 μg of both per ml)
	μg/ml	%	%	%	%	%
Control	0	0	8	0	5	13
Glutamic acid	441	5	11	5	38	54
Phenylalanine	495	20	20	20	57	67
Phenylalanine and Glutamic Acid	441 + 495	21	20	20	31	85

* All cultures contained 700 μg per ml of pipradrol.
† 5 μg each of 8 other B vitamins per tube.

[1] Generously provided by the Wm. S. Merrell Company under their trade name of Meratran. It is [α-(2-piperidyl) benzhydrol] hydrochloride, a central stimulant, and is water-soluble and thermostable.

in a combination of amino acids. It was subsequently found that a mixture of phenylalanine and cysteine promoted partial reversal of the inhibition, but that in the presence of a B vitamin supplement, the activity of the cysteine was less pronounced, whereas a mixture of phenylalanine and glutamic acid showed even greater activity. The activity of the vitamin supplement resided in its niacin and pantothenic acid content, as shown in table 1, in which the values represent the percentage of the growth obtained in identical cultures lacking the inhibitor. Growth was measured turbidimetrically after incubation for 16 hr at 37 C. Tyrosine and 3,4-dihydroxyphenylalanine were completely inactive. A mixture of pantothenate, niacin, glutamic acid, and phenylalanine gave 85 per cent release of the pipradrol inhibition, and nothing that we have been able to identify in the yeast extract further potentiated this effect.

DISCUSSION

The individual roles in brain metabolism played by the four members of the reversing complex have been so well established in recent years that it is tempting to suggest from the data presented that pipradrol acts pharmacologically by competing for some enzyme system to which the four metabolites are related as precursors. Unfortunately, however, extended further study will be essential before it can be stated with certainty that the bacterial enzyme system blocked in this instance is functionally identical with that affected by pipradrol in mammalian brain tissue.

ISOLATION OF BACTERIOPHAGE ACTIVE AGAINST ALL TYPES OF *MYCOBACTERIUM TUBERCULOSIS*

KENJI TAKEYA AND TETSUYA YOSHIMURA

Department of Bacteriology, School of Medicine, Kyushu University, Fukuoka, Japan

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Bacteriophages active against saprophytic acid-fast bacilli have been reported by several investigators. Recently, Froman *et al.* (Am. J. Public Health, **44**, 1326, 1954) succeeded in isolating phages which lyse *Mycobacterium tuberculosis* of both human and bovine types. No reference, however, to a phage active against *Mycobacterium avium* and *Mycobacterium muris* (Vole bacillus) has been found in the literature. Attempts were made to isolate phages active against these mycobacteria.

Modifications of the soil enrichment technique

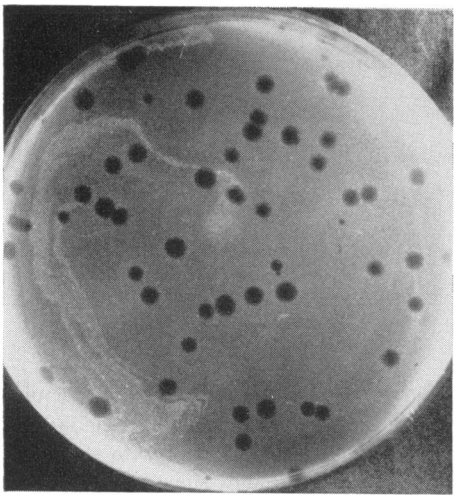

Figure 1. Plaque type of bacteriophage B1 strain on host strain *Mycobacterium avium* (Jucho).

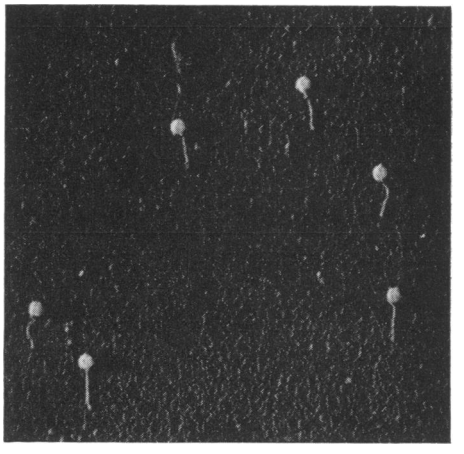

Figure 2. Electronmicrograph of bacteriophage B1 strain. Shadowed with chromium.