TABLE I.
Velocity and Duration of Pulmonic Arterial Waves.

	Avg distance from 1st sound to foot of pulse wave	Distance between foot and peak of the same wave	Transmission time	Speed of the wave
Pulmonary knob	0.08 sec. ± 25% Mx = 0.10 Mn = 0.05	0.14 sec.		
Right hilar shadow	0.12 sec. ± 25% Mx = 0.15 Mn = 0.09	0.24 "	Pulm. knob to rt. hilus 0.04 sec.	2 M/sec.
Right lung (visible base)	0.16 sec. ± 25% Mx = 0.22 Mn = 0.10	0.23 "	Rt. hilus to visible base of rt. lung 0.04 sec.	2.75 M/sec.

Summary. A study of 15 normal subjects has been performed by using fluorocardiography, a method which permits recording on a continuous film of the pulsations of various cardiovascular structures revealed by the x-ray. (a) The tracing of the ascending aorta presents a typical pattern which partly is due to transmission of intraventricular pressure and partly to motions of the aortic root connected with ventricular systole and diastole. (b) It is possible to record in certain cases a tracing of the pulmonary veins. Its most typical feature is a positive wave during presystole. (c) The velocity of the pulse wave in the lesser circulation is much lower than in the greater circulation. It is more rapid in the smaller branches than in the stems of the pulmonary artery. Average figures are given. (d) The tracing of the pulmonary parenchyma is the equivalent of a plethysmogram. While the rise and the ascending branch of the wave are of arterial pulmonary origin, the peak and the descending branch of the wave are probably of venous pulmonary origin.

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Bacillomycin: An Antibiotic from *Bacillus subtilis* Active against Pathogenic Fungi.*

M. LANDY,† G. H. WARREN, S. B. ROSENMAN, AND L. G. COLIO.
From Wyeth Institute of Applied Biochemistry, Philadelphia, Pa.

Since the discovery of *subtilin* by Jansen and Hirschmann,[1] 3 additional antibiotics i.e., *bacitracin, bacillin,* and *eumycin* have been described as products of strains of *Bacillus subtilis* (for an excellent, comprehensive review see Benedict and Langlykke[2]). With the exception of *eumycin,* the antibiotics possess incidental antifungal properties in association with a more specific antibacterial action.

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† Present address: Army Medical Department Research and Graduate School, Washington, D.C.

1 Jansen, E. F., and Hirschmann, D. J., *Arch. Biochem.*, 1944, **4**, 297.

2 Benedict, R. G., and Langlykke, A. F., *Ann. Rev. Microbiol.*, 1947, **1**, 193.

TABLE I.
Antifungal Spectrum of Bacillomycin.

Organism	Source of strain	mg of Bacillomycin per ml of medium									
		0.5	0.25	0.10	0.05	0.025	0.010	0.005	0.0025	0.001	Control
Dermatophytes:											
Epidermophyton floccosum	Univ. of Penn.	—	—	—	—	—	+	+	+	+	+
Microsporum audouini	" " "	—	—	—	—	—	+	+	+	+	+
Microsporum gypseum	" " "	—	—	—	—	—	+	+	+	+	+
Trichophyton mentagrophytes	A.T.C.C.	—	—	—	—	—	+	+	+	+	+
Trichophyton rubrum	"	—	—	—	—	—	+	+	+	+	+
Trichophyton schoenleini	Univ. of Penn.	—	—	—	—	—	+	+	+	+	+
Systemic Fungi:											
Blastomyces dermatitidis (Mycelial)	Duke Univ.	—	—	—	—	—	—	R	+	+	+
*Blastomyces dermatitidis** (Yeast form)	" "	—	—	—	—	—	—	—	—	+	+
Candida albicans	Army Med. Sch.	—	—	—	—	R	+	+	+	+	+
Coccidioides immitis	" " "	—	—	—	—	—	R	+	+	+	+
Torula histolytica	Naval Med. Center	—	—	—	—	R	+	+	+	+	+
Histoplasma capsulatum	Duke Univ.	—	—	—	—	—	R	+	+	+	+
Hormodendrum pedrosoi	Univ. Brazil	R	R	+	+	+	+	+	+	+	+
Monosporium apiospermum	Duke Univ.	—	—	—	—	—	+	+	+	+	+
Nocardia asteroides	Army Med. Sch.	+	+	+	+	+	+	+	+	+	+
Phialophora verrucosa	Nat. Inst. Health	R	+	+	+	+	+	+	+	+	+
Sporotrichum schenckii	Duke Univ.	—	—	—	—	R	+	+	+	+	+
Blastomyces braziliensis	" "	—	—	—	—	—	+	+	+	+	+

Cultures were incubated at 30°C for 15-17 days. Medium was Sabouraud maltose agar.
* Inoculated from a culture in "yeast" phase and incubated at 37°C for 20 days.
Key: + = growth, R = growth restricted; — = no growth.

In the course of a program designed to find antibiotics active against *Torula histolytica* infections, there was isolated from a contaminated *Actinomyces griseus* culture a strain of *Bacillus subtilis* which possessed negligible antibacterial activity and striking fungistatic properties. Although concentrates of this antibiotic and *eumycin*[3,4] showed a spectrum similar in many respects, the limited available data on the chemistry of *eumycin* as well as its specific action on *Corynebacterium diphtheriae* and acidfast bacilli appeared to differentiate it from our antibiotic and warranted further study. The antibiotic substance has been designated *bacillomycin*.

Bacillomycin occurs in the cell-free fermentation liquor after cultivation of the organism for 2 to 3 days in shake culture or 5 to 6 days in surface culture at 24-28°C in a synthetic medium composed of 20 g glucose, 5 g l-glutamic acid, 0.5 g $MgSO_4$, 0.5 g KCl, 1 g KH_2PO_4, 0.15 mg $FE_2(SO_4)_3 \cdot 6H_2O$, 5.0 mg $MnSO_4 \cdot H_2O$, 0.16 mg $CuSO_4 \cdot 5H_2O$ and 1000 ml distilled water; final pH is 6.0. Maximal yields of the product are obtained with a rise in pH of the medium to 7.0-7.6.

Crude filtrates are assayed against a standardized spore suspension of *Trichophyton mentagrophytes* by the agar cup method on Sabouraud's maltose agar. Standard solutions and experimental samples are tested in duplicate on each plate and the latter incubated at 30°C for 72 hours. The unit of activity is equivalent to the zone produced by 0.1 mg of a standard preparation of *bacillomycin*. This represents a zone of 20 to 25 mm.

The antifungal activity of partially purified *bacillomycin* was measured by the agar plate-dilution method. The results are reported in terms of the smallest amount of the antibiotic in a constant volume of test medium (10 ml) which will give complete inhibition of the test organism. Incubation of the tests (with one exception) was at 30°C for 15-17 days. A summary of the inhibition experiments on a spectrum of pathogenic fungi is compiled in Table I.

Bacillomycin is precipitated from the broth by acidifying to pH 2.5 with hydrochloric acid solution. The precipitate is extracted with ethanol, washed with ether and dried *in vacuo* over phosphorus pentoxide. (The ether step assumes importance in the extraction since an additional antibiotic elaborated by the organism and active against gram positive bacteria is also precipitated at pH 2.5. However, whereas the antifungal product is largely ether insoluble, the antibacterial activity is soluble.) The activity averages 5 units/mg and the yield is approximately 0.3 g/liter broth with a 35 to 50 % recovery.

Bacillomycin is soluble in methanol, ethanol, n-butanol and acetone. It is precipitated by concentrated neutral ammonium sulfate solution. The active substance is readily adsorbed on activated charcoal but is difficult to elute. The antibiotic will not dialyze through cellophane membranes.

Bacillomycin is not destroyed by trypsin or pepsin. The product is stable in dried form. Samples stored at room temperature have retained their activity for months. Solutions adjusted in pH to include acid (3.0) neutral and alkaline (9.0), may be autoclaved (120°C-20 minutes) with no appreciable loss of activity.

Summary. A strain of *Bacillus subtilis* has been isolated which elaborates a previously undescribed antibiotic "Bacillomycin." This antibiotic possesses striking antifungal activity and almost complete lack of antibacterial action. The fungus spectrum of "Bacillomycin" includes practically all of the important dermatophytes and systemic fungi. A satisfactory bioassay employing the agar cup plate technic and a spore suspension of *Trichophyton mentagrophytes* is described. Some physical and chemical properties of the antibiotic are given together with a simple procedure for its concentration from culture broths.

[3] Johnson, E. A., and Burdon, K. L., *J. Bact.*, 1946, **51**, 591.

[4] Burdon, K. L., and Johnson, E. A., Conference on Antibiotic Research, Antibiotics Study Sect., Nat. Inst. Health, 1947.