

on the sterilization of swimming pools, has been made to the Michigan State College at East Lansing.

PLANS have now been completed whereby the American Society for Metals will provide an annual fund of \$1,000 for the support of research in the field of corrosion. The American Coordinating Committee on Corrosion has been designated to receive and approve applications for grants from this fund. A subcommittee on research has been appointed under the chairmanship of Dr. R. M. Burns, assistant chemical director of the Bell Telephone Laboratories, New York, N. Y. Other members are T. S. Fuller, of the General Electric Company; Dr. F. W. Adams, of the Pittsburgh Plate Glass Company, and Dr. H. L. Maxwell, of the E. I. du Pont de Nemours Experiment Station. The committee will select such research projects as appear worthy of support, will approve the qualifications of applicants for grants-in-aid from the research fund, and will certify to the American Society for Metals the names of successful applicants. The grants-in-aid will vary from \$250 to \$1,000.

THE Williams and Wilkins Company has announced the establishment of the Passano Foundation "for

scientific and educational purposes, particularly to provide for scientific research and to publish the results of scientific research and to make awards for meritorious achievements in scientific research." By the terms of the charter the board of directors may inaugurate the establishment of "an annual award not to exceed \$5,000 for an outstanding contribution by an American citizen to the advancement of medical science made within the year." The directors include Dr. Emil Novak, associate in gynecology at the Johns Hopkins University Medical School, and Dr. George Corner, director of the Embryological Laboratory of the Carnegie Institution of Washington. E. B. Passano is chairman of the board and Robert S. Gill is president.

It is planned to establish at the University of Oxford a center for research and postgraduate study for the prevention of blindness and the better treatment of diseases of the eye. The Ophthalmological Research Endowment Committee, of which Sir William Goodenough is chairman, plans to raise £250,000 for the purpose. So far about £26,000 towards the founding of a department of ophthalmology has been collected.

DISCUSSION

PURIFICATION AND ANTIBACTERIAL ACTIVITY OF FUMIGACIN AND CLAVACIN

THE rapid progress that is being made at the present time in the study of antibiotic substances produced by microorganisms can best be illustrated by an examination of the results of recent investigations of two mold products, fumigacin and clavacin. In the eighteen months that have elapsed since the first announcement¹ of the production of these two substances by two groups of fungi, *Aspergillus fumigatus* and *Aspergillus clavatus*, respectively, they have been crystallized and their chemical nature determined. Moreover, each has been described under different names, and one has been found to be produced by several different groups of fungi. In order to avoid further confusion in the characterization of these two chemical compounds, a brief summary of the results thus far obtained is justified.

Fumigacin was originally described² as a substance produced by a number of strains of *A. fumigatus*, as containing a small amount of nitrogen, as active largely against gram-positive bacteria and as characterized by appreciable toxicity to animals. Menzel,

Wintersteiner and Hoogerheide³ demonstrated that fumigacin prepared from *A. fumigatus* by the method of Waksman, Horning and Spencer² contained 20 per cent. gliotoxin, a substance high in nitrogen and in sulfur⁴ and appreciably toxic to animals; when the gliotoxin fraction was removed, the purified fumigacin was found^{3,5} to retain its original antibacterial activity, was free from nitrogen, and possessed only a limited toxicity to animals. Unaware of these findings, a group of British workers⁶ isolated the same substance from a strain of *A. fumigatus* and described it as helvolic acid. This preparation proved to be identical with the purified fumigacin in chemical composition, in antibacterial activity and *in vivo* activity. Helvolic acid must, therefore, be considered as identical with fumigacin.

Clavacin was originally prepared² only in crude form. It was reported to be active against a variety of bacteria found among both the gram-positive and the gram-negative groups, and was highly toxic when

³ A. E. O. Menzel, O. Wintersteiner and J. C. Hoogerheide, *Jour. Biol. Chem.* In press.

⁴ J. R. Johnson, W. F. Bruce and J. D. Dutcher, *Jour. Amer. Chem. Soc.*, 65: 2005-2009, 1943.

⁵ S. A. Waksman and W. B. Geiger, *Jour. Bact.* In press.

⁶ E. Chain, H. W. Florey, M. A. Jennings and T. I. Williams, *Brit. Jour. Exp. Path.*, 24: 108-119, 1943.

¹ S. A. Waksman, E. Horning and E. L. Spencer, *SCIENCE*, 96: 202-203, 1942.

² S. A. Waksman, E. Horning and E. L. Spencer, *Jour. Bact.*, 45: 233-248.

injected into the animal body, 3.5 mg being lethal per kilogram of body weight.⁷ Recently, two contributions appeared dealing with the isolation and crystallization of clavacin from two kinds of fungi, *Penicillium patulum*⁸ and *A. clavatus*;⁹ both preparations proved to be identical chemically. A comparison of the respective antibacterial spectra, as announced for the crude clavacin¹⁰ and for patulin⁸ (the name given to the substance isolated from *P. patulum*), and as found for crystalline clavacin¹¹ further established the fact that the two substances are identical. The crystalline clavacin was found to be less toxic to animals than crude clavacin,¹¹ its activity being in this respect, as well, identical with that reported for patulin.⁸

As this note was being written, an article appeared¹² dealing with the identity not only of clavacin and patulin, but also of claviformin, a substance produced by *P. claviforme*;¹³ the authors,¹² believing that they were the first to crystallize clavacin, proposed a new name for this substance, namely, clavatin. It may be of interest to record here that clavacin, as first

These results definitely indicate that the five preparations are identical in their chemical nature and antibacterial activities (slight quantitative differences in activity may be due to the use of different strains of test organisms). Whatever may be the final decision concerning the proper designation of this substance, the fact remains that three different organisms, *A. clavatus*, *P. claviforme* and *P. patulum*, produce the same antibiotic substance.

It is thus important to record here that considerable confusion has arisen from the fact that various microorganisms are capable of producing the same type of antibiotic substance. This has already been demonstrated for the following: citrinin is formed by *P. citrinum* and *A. candidus*; penicillic acid, by *P. puberulum* and *P. cyclopium*; penicillin, by *P. notatum*, *P. chrysogenum* and *A. flavus*; gliotoxin, by *Trichoderma*, *Gliocladium* and *A. fumigatus*; spinulosin, by *P. spinulosum* and *A. fumigatus*; and clavacin by *P. claviforme*, *A. clavatus* and *P. patulum*.

For the sake of completeness, it should also be mentioned that much confusion in the study of anti-

TABLE 1

Name of preparation	When announced	Empirical formula	Melting point °C	Antibacterial activities	
				<i>E. coli</i> units	<i>S. aureus</i> units
Clavacin, non-crystalline	Aug. 20, 1942 ¹			165,000–230,000 ¹⁰	100,000–200,000 ¹⁰
Claviformin	Aug. 1942 ¹³	C ₇ H ₆ O ₄	110	80,000	160,000
Patulin	1943 ⁸	C ₇ H ₆ O ₄	111	33,000–50,000	33,000–50,000
Clavacin, crystalline	Jan. 7, 1944 ⁹	C ₇ H ₆ O ₄	109–110	200,000–250,000 ¹¹	200,000 ¹¹
Clavatin	Dec. 25, 1943 ¹²	C ₇ H ₆ O ₄	109.5–110.5		64,000–128,000

announced,¹ possessed quantitatively all the antibacterial properties of the crystalline preparation, thus pointing to the fact that it was in a nearly pure, even though non-crystalline, state. The isolation of claviformin was announced simultaneously with that of clavacin. Furthermore, the claviformin preparation contained a small amount of sulfur, and the wrong chemical formula was suggested for it (C₉H₈O₅). Comparative data for the various preparations are brought out in Table 1.

⁷ H. Robinson, Some toxicological, bacteriological and pharmacological properties of antimicrobial agents produced by soil microorganisms. Thesis. Rutgers Univ., 1943.

⁸ H. Raistrick, J. H. Birkinshaw, S. E. Michael, A. Bracken, W. E. Gye and W. A. Hopkins, *Lancet*, 245: 625–635, 1943.

⁹ I. R. Hooper, H. W. Anderson, P. Skell and H. E. Carter, *SCIENCE*, 99: 16, 1944.

¹⁰ S. A. Waksman and A. Schatz, *Proc. Nat. Acad. Sci.*, 29: 74–79, 1943.

¹¹ Unpublished data.

¹² F. Bergel, A. L. Morrison, A. R. Moss, R. Klein, H. Biderknecht and J. L. Ward, *Nature*, 152: 750, 1943.

¹³ E. Chain, H. W. Florey and M. A. Jennings, *Brit. Jour. Exp. Path.*, 23: 202–205, 1942; see also recent note in *Lancet*, 246: 112–114, 1944.

biotic substances has arisen from the fact that many organisms are capable of producing more than one type of substance. It is sufficient to call attention to the confusion that has arisen from the designation of the second antibacterial factor produced by *P. notatum*, namely, the glucose-oxidase, which has been designated as *E. coli* factor, penatin, notatin and penicillin B, and which has often been confused with the true penicillin. *A. fumigatus*, however, apparently tops the list, since it has the capacity of forming four different antibacterial compounds, spinulosin, fumigatin, fumigacin and gliotoxin, the first two of which are closely related.

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A LAST WORD ON "STARRING"

I HAVE read with interest Dr. F. C. Whitmore's remarks in *SCIENCE* for November 26, 1943, on "starring," but was somewhat surprised to note how far he has strayed from the original meaning of this distin-