CHEMISTRY

Penicillin Made by Man

Better penicillins even than the mold makes are expected to come from laboratories. Only a small quantity for research has been made.

➤ NEW AND BETTER penicillins are expected as a result of the duplication in the laboratories of this mold chemical announced by chemists of Cornell Medical College in the journal, *Science,* (Nov. 8).

The scientists who synthesized penicillin and are now at work synthesizing new penicillins are Prof. Vincent du Vigneaud and associates, Frederick H. Carpenter, Robert W. Holley, Arthur H. Livermore and Julian R. Rachele.

Chemical remedies for such still-unconquered diseases as tuberculosis, the common cold, influenza and infantile paralysis may be forthcoming, now that chemists have learned how to synthesize penicillin and to change and perhaps improve its chemical make-up. That is something the mold itself could not do.

Laboratory Product

Synthetic penicillin is still a laboratory product. The very small amount of 10 milligrams is all that has been made so far. It takes over 30,000 milligrams to make an ounce. There is no chance whatsoever of commercial production of synthetic penicillin at the present time, stated Prof. du Vigneaud. He pointed out, however, that throughout the history of chemistry it has usually been the case that if a substance can be synthesized at all, the method can be improved and commercial production becomes possible.

An unusual feature of the synthesis of penicillin is that it was done without knowing the exact architecture of the penicillin molecule. Ordinarily, chemists start with knowledge of this architecture, called a structural formula, and proceed to build up the molecule.

All during the war American and British chemists, working in the secrecy demanded by military security, tried to learn the architecture of the mold chemical that was saving battle-wounded and, later, civilian victims of deadly infections.

In the early stages, the majority of chemists working on the problem favored an oxazolone-thiazolidine structure. Scientists at Oxford University in England and at Merck and Company in the United States independently and almost simultaneously in the first months of 1944 obtained a chemical of this architecture which had anti-germ activity like penicillin's. But they had such minute amounts of material that some of the scientists collaborating on this war research thought the antibiotic activity might be due to something other than penicillin.

Structure Not Right

The architecture of the compound they were working with, it then turned out, was probably not correct for penicillin. That was the situation in January, 1946, when the OSRD contracts terminated. Up to that time, 38 groups of scientists, 17 in Britain and 21 in the United States, had been working on the problem under OSRD and British Medical Research Council auspices.

In the first few months of 1946, Prof. du Vigneaud and his associates succeeded in isolating crystalline penicillin and proving its identity with the natural product.

One of the first things they did to prove their synthetic white crystals really were penicillin was to compare their activity against seven different bacteria with that of natural penicillin. The two penicillins had the same action against the bacteria.

Synthetic Passes Test

Having passed this bacterial spectrum test, synthetic penicillin was next put through a really tough one. This was the excretion test in which the same amounts of natural and synthetic penicillins were given to rabbits and the amounts of each which the animals excreted were measured. The ratio of excreted penicillin to the dose was the same for both penicillins.

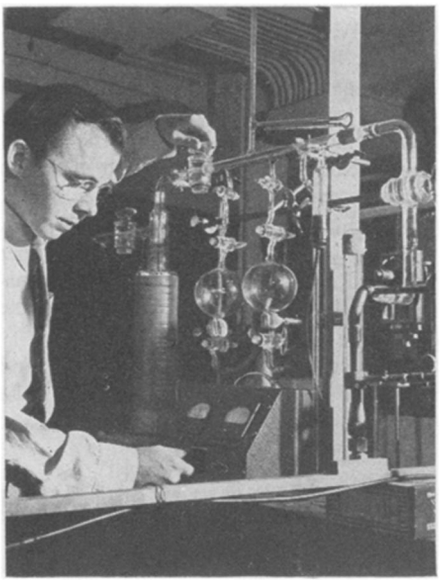
Radioactive sulfur was used in preparing another batch of synthetic penicillin. Natural penicillin was added and then isolated as a triethylammonium salt. This salt contined radioactive sulfur and held it through two recrystallizations and through conversion to two derivatives.

When the enzyme, penicillinase, which rapidly inactivates natural penicillin was added to the synthetic, this was inactivated in the same way. Synthetic penicillin also showed the absorption band in the infrared region characteristic of natural penicillin.

Part of the battle to prove that the synthetic material actually was penicillin consisted in fractionations to "fish out the active material in higher and higher concentrations," Prof. du Vigneaud explained. His group finally succeeded in obtaining synthetic penicillin at a concentration of 270 units per milligram.

"Particularly noteworthy," he points out, is the fact that the synthetic penicillin finally obtained is the same optical isomer as natural penicillin although there could be about eight isomers of penicillin.

Science News Letter, November 16, 1946



MOLECULE TARGETS—Apparatus reveals by microwave the kind of gas molecules present and the behavior of their atoms. The ammonia is contained in the glass bulb on the left. It passes into the long rectangular "barrel" or waveguide which extends across the lower part of the picture. When the vibrations of the gas are "in tune" with the vibrations of the microwaves, the microwaves are absorbed and a study of the absorption can be made. Research is being done at Westinghouse laboratories.