Selman Waksman: the Father of Antibiotics

The Chemical Nature of Actinomycin, an Anti-microbial Substance Produced by Actinomyces Antibioticus


Selman Abraham Waksman (1888–1973) was born in the rural Ukrainian town of Novaya Priluka. The town and its nearby villages were surrounded by a rich black soil that supported abundant agricultural life. Although Waksman did not do much farming as a child, the chemistry of the fertile soil incited a curiosity in him that would eventually influence the direction of his future endeavors.

In 1910, after completing his matriculation diploma, Waksman followed the example of several relatives and migrated to the United States. He worked for a few years on a family farm in New Jersey and then enrolled in Rutgers College. There he studied bacteria in culture samples from successive soil layers, which resulted in his introduction to the actinomycetes. These bacteria became an enduring interest that Waksman studied for both his Master’s and Doctorate degrees and on which he would eventually become a major expert.

After receiving his doctorate from the University of California, Berkeley, in 1918, Waksman secured a position at the Rutgers Bacteriology Department where he continued his research on soil microflora. Several years later, a young French biologist named Rene Dubois joined his laboratory. By 1927, Dubois was studying the one-on-one effects of soil organisms in decomposing cellulose and was beginning an approach that would lead to modern antibiotics. In collaboration with Oswald Avery at the Rockefeller Institute Hospital, Dubois isolated a soil bacterium that could attack the capsular polysaccharide of Streptococcus pneumoniae (1). This discovery inspired Waksman to look for more pre-existing antibacterial organisms in soil samples.

By 1940, Waksman and H. Boyd Woodruff had devised a technique for identifying natural substances with antibacterial properties (2). The screening was done by looking for growth inhibition zones around single colonies of systematically isolated soil microbes, grown under a variety of culture conditions, and then testing the inhibition on specifically targeted pathogenic bacteria.

The first true antibiotic Waksman identified was from Actinomyces antibioticus, a member of the actinomycetes family (3). The microbe produced a substance, actinomycin, that had both bacteriostatic and bactericidal properties. Waksman and Woodruff determined that actinomycin could be separated with petroleum ether into two constituents, an orange-red colored actinomycin A and a colorless actinomycin B. Actinomycin A had strong bacteriostatic and bactericidal properties whereas actinomycin B displayed only bactericidal characteristics.

In the Journal of Biological Chemistry (JBC) Classic reprinted here, Waksman and Max Tishler, who was featured in a previous JBC Classic (4), describe the nature and properties of actinomycin A. The pair found that actinomycin is a quinine-like pigment with a molecular formula of either C_{41}H_{56}N_{8}O_{11}, C_{37}H_{50}N_{7}O_{10} or C_{36}H_{49}N_{7}O_{9} \cdot \frac{1}{2} H_{2}O. The compound is highly active against various gram-positive bacteria but less active against gram-negative organisms. Unfortunately, Waksman and Tishler also discovered that actinomycin is extremely toxic to experimental animals and thus of little therapeutic value.

Waksman followed this initial failure with a comprehensive program of screening actinomycetes for their ability to produce antibacterials. He identified more than 20 new natural
inhibitory substances, including streptomycin and neomycin, and proposed the now standard term “antibiotics” for this class of natural growth inhibitors.

With his discovery of streptomycin in 1944, Waksman initiated a collaboration with Merck and Company. Tishler led the microbiological group that developed the fermentation process for producing bulk quantities of streptomycin. As a result of his success in developing manufacturing processes for products such as streptomycin, riboflavin, cortisone, vitamin B_{12}, and penicillin, Tisher eventually became the first president of the Merck Sharp & Dohme Research Laboratory Division of Merck & Co. Inc. and remained there until 1970, running the research programs.

Waksman patented and licensed his promising antibiotics, but rather than keeping the money for himself, he gave 80% of his patent earnings to Rutgers University. In 1951 he established an Institute of Microbiology in association with Rutgers, the construction of which was completed in 1954. The institute was endowed and supported by the generous assignment of 80% of Waksman’s streptomycin patent royalties to Rutgers. Waksman’s philanthropic nature was further evident when he established the Foundation for Microbiology in 1951 and assigned one-half of his 20% personal royalties for its support.

During his lifetime, Waksman received some 66 awards and 22 honorary degrees for his scientific work. He was elected to the National Academy of Sciences in 1942. However, Waksman’s greatest honor came when he won the Nobel Prize in physiology or medicine in 1952 “for his discovery of streptomycin, the first antibiotic effective against tuberculosis.” This distinction earned him the title of “Father of Antibiotics” and gained him well deserved recognition for his philanthropy and contributions to science and medicine.¹

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REFERENCES


¹ All biographical information on Selman Waksman was taken from Ref. 5.
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