



HISTORY OF TETRACYCLINES

The tetracycline class of antibiotics comprises a distinct family of substituted hydronaphthalene compounds produced by strains of *Streptomyces aureofaciens* and *Streptomyces rimosus*. The first member of the group to be discovered was chlorotetracycline (Aureomycin) in the late 1940s by Dr. Benjamin Duggar, a scientist employed by Lederle Laboratories, who derived the substance from a soil-dwelling bacterium named *Streptomyces aureofaciens*. Two years later, Finlay and coworkers reported the isolation of Terramycin produced by *Streptomyces rimosus*. Nobel laureate Robert B. Woodward determined the structure of oxytetracycline enabling Pfizer chemists, led by Lloyd H. Conover, to successfully produce tetracycline itself as a synthetic product.

Few new tetracycline antibiotics have been developed and approved in recent years. The most recently approved tetracycline derivative, Tygacil® (tigecycline, Pfizer), was introduced in 2005 to treat infections resistant to other antimicrobials. Prior to this, the last time a tetracycline derivative gained approval from the U.S. Food & Drug Administration was 1971.

To date, chemically modified tetracycline analogs have invariably been prepared by semi-synthesis, a process in which isolated natural products are chemically transformed.

Tetracyclines are proven antibacterial agents and represent one of the most trusted classes of antibiotics. Tetraphase's use of its synthetic chemistry platform allows its researchers to build polyfunctional tetracycline molecules with previously inaccessible structural variability, going beyond the limitations of current traditional methods to build diverse, potent, and novel compounds.