Upjohn Sitosterol Transformation Team (Wovcha Team)

Discovered use of a *Mycobacterium fortuitum* mutant to convert sterols, even those with saturated sidechains like sitosterol and campesterol, to 9α-hydroxyandrostendione. Discovery allowed the use of nearly all of the soy sterols as starting material for manufacture of steroid medicines. Further, the oxidation at the key 9-position, along with further innovative chemistry development, enabled more direct and efficient conversion to products.

Here's what happened:

Late 1950's: Upjohn's Greiner developed process for recovering stigmasterol (~20%) from soy sterols, which concurrently recovers the remaining sterols (predominately sitosterol & campesterol)

late1950's – 1970's: Upjohn stockpiles the recovered sterols from the Greiner process

1970's: Upjohn initiates the sitosterol utilization project, investigating chemical and microbiological approaches for converting the recovered sterols to an intermediate compatible with steroid manufacturing processes.

1974: Wovcha Team discovers mutant strain of *Mycobacterium fortuitum* that converts nearly all of the recovered sterols to 9α-hydroxyandrostendione, which can be used as an intermediate for steroids manufacture more efficiently because of the 9-oxidation.

What has been said about the significance of this discovery

"Wovcha discovered a mutant of *Mycobacterium fortuitum*, a potent sterol degrader, which lacked the enzymes to go beyond 9α-hydroxyandrostendione in sitosterol degradation. In a single microbiological step, both the sterol side-chain degradation and 9α-hydroxylation of ring C were accomplished, the latter usable for the required 11-oxygenation.
The exercise of sound strategy and a bit help from the luck of the draw enabled Upjohn to be favored by [another] microbiological breakthrough."

from: J.A. Hogg. Steroids, the steroid community, and Upjohn in perspective: a profile of innovation. *Steroids*, 1992, 57, 593-616

Team Published Paper

M.G. Wovcha, F.J. Antosz, J.C. Knight, L.A. Kominek, T.R. Pyke. **Bioconversion of sitosterol to useful steroid intermediates by mutants of mycobacterium fortuitum.** *Biochim. Biophys. Acta*, 1978, 531, 308-320.

Team Patents

M.G. Wovcha. **Process for Preparing 9α-Hydroxyandrostenedione.** U.S. Patent 4,035,236. Filed 25 Oct 1975, granted 12 Jul 1977.

M.G. Wovcha, C.B. Biggs. ***Mycobacterium Phlei* Mutants Convert Sterols to Androsta-1.4-diene-3,17-dione and Androsta-4-ene-3,17-dione.** U.S. Patent 4,345,029. Filed 8 September 1980, granted 17 August 1982.