

The Origins of Drugs

I. INTRODUCTION

Drugs have a number of origins, as outlined by the bullet points:

- Natural products, for example, chemicals from plants and microorganisms
- Analogues of naturally occurring chemicals, where these chemicals reside in the biosynthetic pathways of mammals
- Antibodies that bind to naturally occurring targets in the body
- Discovery that an existing drug, established as effective for a first disease, is also effective for treating an unrelated second disease
- Drugs identified by screening libraries of chemicals.

Some drugs are based on natural products, where the natural products were known to have pharmacological effects. The term “natural products” is a term of the art that generally refers to chemicals derived from plants, fungi, or microorganisms. Drugs that are derived from natural products, or that actually are natural products, include warfarin (1) penicillin (2,3) cyclosporin (4) aspirin (5,6) paclitaxel (7) fingolimod (8) and reserpine (9). Many other drugs have structures based on chemicals that occur naturally in the human body, that is, where the drugs are analogues of these chemicals. These include analogues of intermediates or final products of biosynthetic pathways. Drugs that are analogues of chemicals in biosynthetic pathways include methotrexate, cladribine, and ribavirin.

Still other drugs originated by first identifying a target cell, or target protein, and then by preparing antibodies that bind to that target. Once a target protein is identified, this target protein (or a derivative of it) can be used as a vaccine. Moreover,

¹ Wardrop D, Keeling D. The story of the discovery of heparin and warfarin. *Br J Haematol*. 2008;141:757–763.

² Diggins FW. The true history of the discovery of penicillin, with refutation of the misinformation in the literature. *Br J Biomed Sci*. 1999;56:83–93.

³ Fleming A. On the antibacterial action of cultures of a penicillium, with special reference to their use in the isolation of *B. influenzae*. 1929. *Bull World Health Organ*. 2001;79:780–790.

⁴ Heusler K, Pletscher A. The controversial early history of cyclosporin. *Swiss Med Wkly*. 2001;131:299–302.

⁵ Lafont O. From the willow to aspirin. *Rev Hist Pharm*. (Paris). 2007;55:209–216.

⁶ Mahdi JG, Mahdi AJ, Mahdi AJ, Bowen ID. The historical analysis of aspirin discovery, its relation to the willow tree and antiproliferative and anticancer potential. *Cell Prolif*. 2006;39:147–155.

⁷ Socinski MA. Single-agent paclitaxel in the treatment of advanced non-small cell lung cancer. *Oncologist*. 1999;4:408–416.

⁸ Adachi K, Chiba K. FTY720 story. Its discovery and the following accelerated development of sphingosine 1-phosphate receptor agonists as immunomodulators based on reverse pharmacology. *Perspect Medicin Chem*. 2007;1:11–23.

⁹ Rao EV. Drug discovery from plants. *Curr Science*. 2007;93:1060.