Discoveries in Pharmacological Sciences

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Popat N. Patil

The Ohio State University, USA

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Dedication

*To my Grandchildren:
Mikah, Allie, Jack, George, Grace, Alec, Josephine, Conner,
Mason and the younger generation of Bedse-Patils,
Chinchkhede, M.S., India.*

Popat N. Patil
November 29, 2011

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Preface

Human diseases existed long before the discoveries of drugs. With human migration from Africa nearly 150,000 years ago, human curiosity, intellect and creativity began to flourish — as did disease and treatment. The first recorded use of medicine appears 5,000 years ago when the multicultural societies of Mesopotamia introduced herbal medicine and the code of Hammurabi into medical practice. Later, lists of prescriptions appeared on Egyptian Papyrus, in Indian Ayurvedic medicine, in Chinese herbal documents, and in Greco-Roman Dioscorides' *Materia Medica*. Discovery is a cumulative process. The information in ancient society, however, was scattered. In many cases, the utility of medicines was understood, but the logistics of sharing discoveries proved difficult. Developments in treatments progressed slowly. In 160 AD, based on his observation of functional anatomy of laboratory animals, Galen promoted medical treatments that lasted over a thousand years. Galen's dogma was not challenged until the beautiful and anatomically accurate drawings of Andreas Vesalius were published in 1543. The discovery of circulation by William Harvey was reported in 1628 AD and provided a better foundation for the medical practice of the day. After 1700 AD, starting with hospital bedside observations of patients by Herman Boerhaave, physicians discovered many pathologies: Bright's disease, Grave's disease, Addison's disease, Angina, Glaucoma, Parkinson's disease, Asthma, Cancer, Alzheimer disease, Schizophrenia and other Neurological diseases. Thus, diseases known through ancient times are still current challenges. The Nobel achievements of James Watson, Francis Crick, Francis Collins, J. Craig Venter and Elizabeth Blackburn created new refined molecular targets for the drug discovery.

It is important to note that plants containing morphine, quinine, physostigmine, pilocarpine, (–)-hyoscyamine, (+)-tubocurarine, reserpine, tetrahydrocannabinol, cardiac glycosides, ephedrine and colchicine were used by various cultures for centuries. In 1805 AD, the German pharmacist, Friedrich Sertürner isolated pure morphine (Morpheus) from poppy capsules. French pharmacists, P.J. Pelletier and J.B. Caventau in 1820 AD isolated quinine and other alkaloids. For the study of drug action, the Parisian pharmacists collaborated with Francois Magendie, a famous physiologist who correctly discovered dorsal (sensory) and ventral (motor) nerves of the spinal cord. Thus, Magendie is considered the founder of modern experimental pharmacology. Parallel to these developments, Charles Darwin, Gregore Mendel and Louis Pasteur added spectacular discoveries in evolution, laws of heredity and biologic specificity of (+) and (–)-tartrates. Anesthetic properties of ether were discovered.

The growth in drug discovery continued to be aided by advances in other sciences. The U.S. army physician, Fredrick Beamont first published the nature of gastric digestion by observing a patient with a bullet wound to the stomach. A pupil of Michael Foster, Charles Sherrington coined the term synapse and recognized the reciprocal (activation and active inhibition) control of the skeletal muscle. John N. Langley not only outlined the nervous system but used nicotine and curare alkaloids to postulate the pharmacologic receptors at the neuroeffector junction. The chemical structures of natural products were elucidated. Based on the template of alkaloidal structures, hundreds of synthetic analogues were prepared and tested to improve the therapeutic index. J.H. Gaddum, H.O. Schild and E.J. Ariens introduced better methods to quantitate drug receptor interactions. R.P. Stephenson recognized functional receptor reserve for the potent agonists in organs. Hormones and neurotransmitters were characterized. After the 1820s, Merck, Wyeth, Lilly, Merrell, Abbott, and Upjohn pharmaceutical companies had their specialty products marketed through the innovative research. The era of antibiotics, sulfa drugs, vitamins and psychotropic medication emerged and soon the distinction between basic academic and applied research disappeared.

An understanding of the history of drugs and toxic chemicals is essential for the proper utility of these substances. It is also an invaluable aid to future innovation. Thus the educational need became eminent. This book provides a critical analysis of the major discoveries in pharmacology, including time, places and scientists involved. The title *Discoveries in Pharmacological Sciences* includes biochemical, morphological aspects of neuroscience, pharmaceutical, physiological, and toxicological sciences. The book contains the following topics: Evolution, human migration, diseases and treatments; ancient medicine and the discovery of natural therapeutic agents; history of anesthesia, acupuncture, hypnosis, mesmerism, anesthetics and hypnotics; emergence of modern medicine; contributions of anatomists and physiologists to the neurofunctional outline of the nervous system; pharmacology comes of age; discovery of receptors and related events, a century of receptors and transduction; development of drug laws and quantitation; drug discoveries; and growth of the drug industry, research institutions and universities. There is some overlap in chapter topics. Summaries for each chapter are added. The book is written for graduate students, scientists and faculty with the purpose to familiarize the investigators about the discoveries in chemical, pharmaceutical, pharmacological, clinical and biomedical sciences. Brief profiles of scientists are included. Their discoveries are fascinating.

I had fun in finding connecting stories of drug discoveries through the ages; it has been a rewarding research, teaching and writing experience. During my academic career, either on the campus or at other locations, I was fortunate to get exceptional help and meet many distinguished scientists interested in pharmacological sciences, namely: Chauncey D. Leake, Arther Tye, Emil Bozler, Eric Ogden, Robert Gardier, Melvin Newman, Prabir Dutta, K.K. Chen, Irvine Slater, E.J. Ariens, J.M. Van Rossum, A.M. Simonis, Richard Shultes, Robert Furchgott, Ullrich Trendelenburg, William Fleming, Solomon Langer, Norman Weiner, Michael Rand, Robert Maxwell, David Trigg, Philip Portoghese, Jules LaPidus, Ulf S. von Euler, L. Terenius, Eric Muscholl, Hermann Blaschko, Julius Axelrod, Solomon Snyder, Robert Lefkowitz, A.G. Gilman, Jr., J.C. Venter, Edith Bülbirg, Marthe Vogt, B.N. Dhawan,

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Popat N. Patil

August 15, 2011