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Essentials of Foye's Principles of Medicinal Chemistry

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Dedication to William O. Foye

William O. Foye, Sawyer Professor of Medicinal Chemistry at the MCPHS University (formerly Massachusetts College of Pharmacy), Boston, MA, was born in 1923 in western Massachusetts. He received his BA (1944) in chemistry from Dartmouth College and PhD in Organic Chemistry (M. Cormack) from Indiana University in 1948. He served in the U.S. Navy during World War II as a chemical warfare instructor. He joined DuPont (Delaware) as a research scientist, then in 1950 joined the School of Pharmacy at the University of Wisconsin as assistant professor of pharmaceutical chemistry. In 1955, he moved to MCPHS University, Boston as Professor of Chemistry, where he brought a new vision of pharmaceutical chemistry (medicinal chemistry) to the pharmacy curriculum. As department chair, he advocated for organic medicinal chemistry in the pharmacy curriculum.

The impetus for a new text in medicinal chemistry, grounded on Alfred Burger's two-volume Medicinal Chemistry, came from Dr. Norman Doorenbos, College of Pharmacy University of Maryland (Baltimore), who had made arrangements with Lea & Febiger (forerunner of Lippincott Williams and Wilkins) for publishing a companion text to Wilson & Gisvold's *Textbook of Organic Medicinal and Pharmaceutical Chemistry*. Because Dr. Doorenbos was moving to chair the new Pharmacognosy Department at the School of Pharmacy, University of Mississippi, he relinquished the job of editing this text to Dr. Foye. During this time, a number of teachers and researchers in medicinal chemistry felt that a text on drugs that included biochemical modes of action, aimed primarily for undergraduates, should be written. Although other pharmaceutical and medicinal chemistry books had been written during this time [*The Chemistry of Organic Medicinal Products*, Jenkins and Hartung, and *Textbook of Organic Medicinal and Pharmaceutical Chemistry*, Wilson and Gisvold), these authors organized their books according to the accepted scheme of chemical classification of the more important organic medicinal compounds, their methods of synthesis, properties and descriptions, and their uses and modes of administration. Therefore, this "Principles" text provided a contemporary basis for the biochemical understanding of drug action that included the principles of structure – function relationships and drug metabolism. Dr. Foye assembled authors who were experts in their respective fields and published the first edition of *Principles of Medicinal Chemistry* in 1972.

The current authors of the 7th edition *Foye's Principles of Medicinal Chemistry* uphold the original concept for an undergraduate medicinal chemistry principles textbook to assist its readers to pull together the chemical understanding of drug action and to appreciate its practical relevance to contemporary pharmacy practice. Because medicinal chemistry students have often expressed the desire for a short and "to the point" text that clearly summarizes the most important chemical elements of therapeutically relevant drug classes, the *Essentials of Foye's Principles of Medicinal Chemistry* book was constructed to meet this need. The authors hope this Essentials book not only meets your short-term need for focused medicinal chemistry education, but also stimulates a lifelong desire to know more about how the chemicals we call drugs work.

Dr. Foye had a long and creative career in medicinal chemistry with more than 150 refereed scientific publications, book chapters, and editor of Cancer Chemotherapeutic Agents ACS Monograph Series. His research focused on numerous areas especially the SAR of antiradiation organosulfur compounds, anticancer agents,

and chelation as mechanism of drug action. He was elected Fellow of the AAPS, Fellow of APhA, received the APhA Foundation Research Achievement Award in Medicinal Chemistry, and was an emeritus member of AAAS, ACS, APhA, and AAPS. He was one of the founding members of the Medicinal Chemistry Group of the Northeast Section of the American Chemical Society (1968). He retired in 1995. In addition to being Chair of the Department of Chemistry, he was also the Dean of Faculties and Dean of Graduate Studies at the MCPHS University. Dr. Foye traveled widely and was an invited participant at numerous meetings.

Not only was Dr. Foye a distinguished scientist, he was an avid fly-fisherman, outdoorsman, and environmentalist. He published several books about the western Massachusetts wilderness, *Trout Waters: Reminiscence with Description of the Upper Quabbin Valley* (1992) and *North Quabbin Wilds: A populous Solitude* (2005). He was a dedicated supporter of the arts in Boston. He married Lila Siddons in 1974 and has a son Owen and stepson Kenneth. Dr. Foye died in 2014.

David A. Williams, PhD

William O. Foye (1923–2014)

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Contents

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Essentials of *Essentials*

The authors of the *Essentials* text want readers to glean the most from this abbreviated and focused medicinal chemistry resource. In this first chapter, we share the rationale behind the development of the book and provide guidance for its optimal use to advance chemical understanding and appreciate its practical relevance to contemporary pharmacy practice.

Why an Essentials *Text?*

Students have often expressed the desire for a short and "to the point" text that clearly summarizes the most important chemical elements of therapeutically relevant drug classes. The *Essentials* book was constructed to meet this need.

Chapter Content and Format

Each chapter of *Essentials* captures the key "take-home" chemical points of its companion chapter in *Foye's Principles of Medicinal Chemistry*, 7th edition. "Essential" concepts are bulleted to get to the heart of the chemical message with a limited amount of text.

Sections related to mechanism of action (MOA), structure–activity relationships (SAR), physicochemical and pharmacokinetic properties, metabolism, and clinical applications (most commonly, therapeutic use) are found consistently in all chapters. Additional sections appropriate to specific topics are sometimes incorporated (e.g., resistance mechanisms in the Antimicrobial Agents and Cancer Chemotherapy chapters). Figures and tables are commonly used in lieu of words to illustrate concepts. Complementary information on adverse effects, drug–drug or drug–food interactions, chemical points of interest, and unique aspects of clinical use are often captured in side boxes or summarized in Chemical Note side bars.

Each chapter concludes with a section emphasizing the clinical relevance of the content covered in the chapter, and five review questions to allow self-assessment of learning and identification of areas for further study.

Getting the Most From Each Chapter

The in-depth understanding of medicinal chemistry that underpins therapeutic decision-making requires more than memorizing facts and diagramming pathways. The authors recommend that learners first read the appropriate chapter in *Foye* to get the full chemical picture of the drug classes under discussion. The *Foye* chapters are written to be descriptive and comprehensive narratives that educate about all aspects of therapeutically relevant drug chemistry.

Armed with that significant level of understanding, the *Essentials* text can then be used to prompt recollection of crucial chemical concepts and allow assessment of the ability to summarize central aspects of, among others, chemical mechanism, SAR, and metabolic pathways. Areas of deficient understanding uncovered by a review of the *Essentials* chapter can be addressed by revisiting the appropriate chapter in *Foye*.

The section on clinical relevance that concludes each chapter was crafted to stimulate reflective thinking on how understanding of drug chemistry allows practitioners to scientifically approach patient care. Drugs are chemicals, and they behave as such in the environments encountered in vitro and in vivo. Pharmacists are the only health care professionals educated in the chemical behavior of drug molecules and are in a unique position to predict therapeutic