

Polymers and Fighting Cancer

Chemistry and Pharmacology of Anticancer Drugs

By David E. Thurston.

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Chemistry and Pharmacology of Anticancer Drugs is a noteworthy survey of the pharmacology of most anticancer agents presently in clinical use and of many agents still under development. The overview is unique in comparison with others provided by similar books on the market.

The book comes out at a peculiar time in the practice of clinical oncology, when classical cytotoxic chemotherapy approaches are rapidly going out of date despite their current widespread use. Drug therapies developed over the last 50 years have markedly improved the management of some cancer types, especially hematological malignancies, but the outcomes and side effects for treatment of the most common types of cancers remain unacceptable. Currently one out of three people in the western world still develop cancer sometime in their lives, and one in four die from the disease.

Nowadays, after 50 years of feverish cancer research efforts worldwide, the discovery of distinct biological pathways in cancer cells has led to improved therapies that are based on more specific targeting. Most of the current efforts of pharmaceutical companies is aimed at the clinical development of so-called target therapies. The author, a renowned scientist in cancer research and drug development, clearly does not fail to provide up-to-date information on this trend in today's pharmacology.

A book that covers such a large number of anticancer drugs, ranging from those in clinical use to those under basic research, is nearly impossible to write. Dr. Thurston has done so, howev-

er, thanks to his expertise in the field. Notably, within only ~300 pages, he additionally covers new research directions and fundamental concepts in the emerging areas of personalized medicine, such as oncogenomics and chemoprevention.

Dr. Thurston summarizes all these various topics with a mastery of balance. The fundamental causes of cancer, modes of its treatment, and the philosophy of cancer drug discovery are covered in the first chapter. Subsequent chapters deal specifically with anticancer drugs, classified by their common mechanism of action. The book provides molecular structures for each agent and discusses its history, chemistry, mechanism of action, structure–function relationships, relevant pharmacology, cytotoxicity, side effects, and formulation and dose-scheduling issues. Even drug failures and hazards are openly discussed. Warnings and simple but fundamental golden rules for clinicians are disseminated throughout all the chapters. A precise analytical index at the end makes all this information easily accessible.

The final few chapters are mostly dedicated to the future. The author is well aware of the fact that a book on cancer research could easily risk becoming outdated before its publication. He has thoroughly done his best to avoid this pitfall with the wit of a researcher, proposing open questions for upcoming research. I truly found these research hints a helpful distillation of experience in cancer pharmacology. A number of novel approaches and strategies for cancer targeting are analyzed. Promising agents under development are presented, and even natural compounds and biological agents are not forgotten. Dealing with aspects of cancer research currently en vogue, the book covers, quite appropriately, epigenetics. However, the immunology of tumors and immunotherapy is rather poorly covered. In this case only an overview is given, but it fails to

depict crucial points that have emerged very recently in the field. Tumor micro-environment cell diversities, stem cells, and cell subpopulations coming from the immune system of the host are continuing to be identified as strong contributors to carcinogenesis, and improved anticancer strategies should probably attempt to target all of them differentially.

The author claims his intention with this book is to contribute to the education of future generations of researchers, who will go on to discover more effective drugs and therapies. In fact, easy readability and directness make the book ideal for students. Its breadth of coverage makes it suitable for undergraduate and postgraduate courses in medicine, pharmacy, and related disciplines. The book is also an excellent starting point for cancer researchers, medicinal chemists, and other biomedical scientists. *Chemistry and Pharmacology of Anticancer Drugs* should also be an indispensable resource for the libraries of research institutes, universities, and hospitals.

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Dendrimers in Medicine and Biotechnology

By U. Boas, J. B. Christensen, and P. M. H. Heegaard.

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Dendrimers are a new class of polymers comprising hyper-branched compounds with diverse features. They are well-defined, have high degrees of molecular

uniformity and monodispersity, and are highly functionalised at their surfaces. Despite the fact that dendritic architectures were first described in 1978 (the term *dendrimer* was coined in the early 1980s), efficient methods for their synthesis were not developed until the 1990s; commercially available dendrimers soon followed. Dendrimers have since been used as catalysts, optical sensors, and light-harvesting devices, among other applications.

This book is devoted to dendrimer applications in medicine and biotechnology. The book, which comprises six chapters, can be divided into two clear parts. The first, which encompasses chapters 1 and 2, introduces readers to the field, preparing them to better understand the second part, chapters 3–6, each of which is dedicated to a specific biomedical application of dendrimers. Although each chapter can be considered as an independent review, reading the entire book gives a global view of the field.

The first chapter is a brief and clear introduction to dendrimers, defining the relevant nomenclature (e.g. *dendrimer generation*, *inner* and *outer shells*, *end group* and *terminal group*). The most common dendrimer types (PAMAM, PPI, MAP) and general synthetic approaches (convergent and divergent strategies) are also briefly described. Moreover, this chapter describes the physicochemical properties of various dendrimer classes and the effects of factors such as pH, solvent, molecular growth, salt, and concentration on the conformational behaviour of dendrimers.

Chapter 2 describes the *in vitro* and *in vivo* properties of dendrimers in biological systems, including biocompatibility, toxicity, biopermeability, immunogenicity, and biodistribution, as well as the molecular features that affect them. All of these properties are important for the development of any delivery system or drug. The authors make a remarkable

effort here, establishing general rules for the behaviour of dendrimers that interact with biological systems, by drawing on a rich body of literature. For example, the effects of surface modification, dendrimer generation, global and/or surface charges, and dendrimer integrity are outlined. Moreover, these traits are correlated with the capacity of dendrimers to cross cell membranes and tissue barriers (epithelia/endothelia crossing), as well as with their *in vitro* and *in vivo* toxicity.

Chapter 3 summarises the use of dendrimers as drug-delivery vehicles. The authors describe the numerous dendrimer types that have been designed to entrap and release drugs via different mechanisms, including host–guest complexes, covalently bound drug–dendrimer conjugates, and self-immolative systems. The host–guest-based systems are largely covered, as they are the most studied type, and are classified here according to the interaction between the host (dendrimer) and the guest (drug). Additionally, targeted drug-delivery-based systems are described, and the use of dendrimers as gene-transfer reagents is outlined.

The application of dendrimers as drugs and therapeutic systems is the topic of chapter 4. A general introduction explains the advantages of dendrimer drugs (multivalent presentation and, consequently, the *dendritic effect*) and requirements for their design. Dendrimer drugs, which vary widely in their respective multivalent surface modifications, are described for antiviral or antibacterial indications. The use of dendrimers as antitumour or anticancer drugs is also illustrated with examples based on the *multivalent surface effect* or a *core/drug* shielded by the dendritic branches. Another part of this chapter is devoted to dendrimer-based vaccines. It explains the basic principles of the immune system and then reviews the use of dendrimers as scaffolds for vaccines and/or immune-stimulating or immune-sup-

pressing compounds. Moreover, the ability of dendrimers to interact with proteins and lipid membranes and their application to the solubilisation of protein aggregates, such as the misfolded prion aggregates responsible for prion-associated diseases (such as Alzheimer's), are explained.

Chapter 5 covers diagnostic applications of dendrimers, including their use as contrast agents for imaging and as bioassay reagents. The book ends with chapter 6, which is dedicated to the use of dendrimers as functional mimics of natural macromolecules such as proteins, protein-based receptors, enzymes, antigens, cell surfaces, and antibodies. The study of dendritic mimics is a growing field, as they offer marked improvements over their respective parent systems (for example, higher stability and more predictable conformational behaviour). Although some applications of these dendrimer mimics are mentioned in previous chapters, the authors have made an effort to point out common trends without being redundant.

Overall, this book provides a good introduction to dendrimer applications in medicine and biotechnology, and would be useful to experts in dendrimer research as well as to those interested in polymer-based therapeutic agents. The book provides a complete overview of the field, while offering an interesting view to the future. The chapters are accessible to non-specialists without renouncing any details. The text is well written, easy to follow, and lively. The authors are especially adept anticipating and clarifying potential points of confusion. In conclusion, *Dendrimers in Medicine and Biotechnology* is recommended for anyone interested in therapeutic applications of dendrimers and of polymers in general.

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