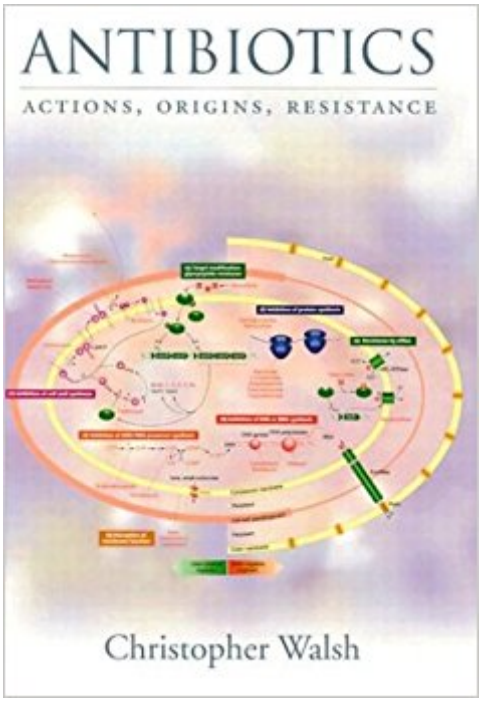
Antibiotics: Actions, Origins, Resistance



Synopsis

This is the first comprehensive book on antibiotics since the 1981 classic by Gale et al. It focuses on the increased interest in antibiotics due to emerging bacterial diseases and resistance. It shows how antibiotics work on targets; gives new insights into antibiotic modification and design; and reviews strategies for finding novel antibiotics.

Book Information

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Customer Reviews

Walsh's `Antibiotics' is a great introduction to the major classes of antibiotics and how each works, or doesn't, against cells, including not only bacteria but fungi and cancer cells. Each class of antibiotic is described, with step-by-step explanations of the chemical mechanics of the antibiotic on its target. The author discusses the growing problem of bacterial resistance to antibiotics and what steps are being taken, in terms of new drug development and new schemes for existing drug use, to overcome this problem.This was a very satisfying read. The information is dense but the author's style is reader-friendly and concise. The text is supported by many illustrations of the mechanics being described and these illustrations are detailed and explicit. I wanted an up-to-date, fairly technical book about antibiotic function and this book fit the bill better than I could have hoped. I look forward to going back to Walsh's book again for an even better understanding.

Legendary among natural product chemists, Christopher Walsh takes us through the detailed mechanisms of the biosynthetic pathways which common classes of antibiotics target. This is a

valuable reference book because it allows us to see why antibiotics work on an atom-by-atom basis--something which most microbiology texts are incapable of doing. A strong background in organic chemistry is required to really understand the mechanisms outlined in the text, but coupled with an undergraduate organic textbook, this book is superior introduction to the overlapping worlds of medicinal, organic, and biosynthetic chemistry.

Christopher Walsh is a great chemist and a great writer alike; Dr. Timothy Wencewicz was also my favorite professor, and he collaborated on it. Really made me appreciate antibiotic chemistry.

When I bought this book it was listed as a first edition 2013, whilst in fact it is a reprint of a 2003 hardcover book. I'm unhappy having spent nearly $100 on a ten year old book that is in fact badly out of date. The one star rating does not represent the quality of the book, simply that on it was misrepresented as a new book.

This book was written by the eminent biochemist Christopher Walsh, whose broad research interests include the study of antibiotic action and resistance. It is extremely well written and organized, with an abundance of excellent illustrations. The approach is to give the reader an in depth but not exhausting coverage of several key topics in modern antibiotic research. Both novice and seasoned researcher will find much of value within the pages of this modest sized book. This important work is published at a period in time in which the resistance of a broad range of pathogenic bacteria to antibiotics has grown to alarming levels. At the same time, many pharmaceutical companies have recently abandoned research and development of new antibiotic agents.Walsh starts the book with a brief chapter on fundamental antibiotic concepts. Where do antibiotics come from? How do they work? How does resistance develop? He next launches into a thorough review of the main classes of antibiotics, interweaving antibiotic chemical structures and targets of the drugs with the underlying microbial physiology processes that are targeted. He begins with the various classes of bacterial cell wall inhibitors, emphasizing the members of the large beta-lactam class, as well as glycopeptides and moenomycin. Next he delves into the multiple classes of protein synthesis inhibitors. He makes full use of the latest structural data emerging from X-ray crystallography of ribosomal subunits, to illustrate the mechanisms of drug action. He covers the macrolides, tetracyclines, and aminoglycosides, as well as the new glycylcyclines and oxazolidinones. The DNA topoisomerases are next featured as targets, and the interactions of quinolone antibiotics with DNA gyrase and topoisomerase. This chapter was a bit short and sparse

in some details as compared to the preceding chapters, but does hit the main highlights. A final chapter in this section addresses other antibiotic classes such as the folate metabolism antagonists (sulfa drugs and trimethoprim), as well as peptide antibiotics.The next section addresses the many mechanisms of antibiotic resistance. These four chapters examine different types of mechanisms employed by bacteria to evade antibiotics. Succinct coverage of the broad range of beta-lactamases and the aminoglycoside modifying (inactivating) enzymes are found in a chapter on enzymatic destruction or modification of antibiotics. This is followed by a very nice summary chapter around antibiotic efflux pumps, which again incorporates some structural biology. Unfortunately, the book was published just prior to the latest crystallographic studies of the RND class AcrB pump, which has added much to our understanding of efflux pumps. The final resistance chapter highlights target modification or replacement. The methicillin resistance story in Staphylococcus, mediated by PBP2a, is detailed, as is the resistance mediated by the mosaic PBP genes in pneumococci. Macrolide resistance by ribosomal methylation and the fascinating story of vancomycin resistance by the restructuring the terminal D-alanine dipeptide target is covered (Walsh's laboratory was a major contributor to the vancomycin story).The next section of the book deals with the biosynthesis of antibiotics by producing organisms, primarily Streptomyces species. These chapters interweave the genetics and biochemistry of secondary metabolism. The signaling pathways used among producer organisms, as well as the gene regulation of the individual antibiotic biosynthetic genes, which are clustered on the chromosome are discussed. There is a chapter on each on polyketide antibiotic synthesis (erythromycins and tylosin) and non-ribosomal synthesis of peptide antibiotics (penicillins, bacitracin, vancomycin).The book ends with 3 chapters on identifying new antibiotics. A survey of targets, both "old" and new is presented, and several suggestions for novel ways to interfere with bacterial function are briefly reviewed. Another chapter examines identifying new chemical entities with antibacterial properties. The initial part of the chapter emphasizes combinatorial chemistry approaches. Unfortunately, this process to date has led to only sparse results, with some inhibitors identified. As Walsh notes, the conversion of a chemical inhibitor of an antibacterial enzyme target to a lead compound that can be subsequently endowed with all the myriad pharmacological properties necessary to be a drug is an extremely daunting task. The vast majority of compounds identified cannot be successfully modified to possess the properties necessary to be a drug. A second approach that he covers, the modification by genetic means of antibiotic producing organisms to synthesize new antibiotics (combinatorial biosynthesis), may be more promising.Walsh closes out the book with some thought provoking chapters around the proper use of antibiotics, and strategies to minimize resistance development. He highlights the antibiotic

resistant pathogens of the 21st century, and the continued problem of methicillin resistant staphylococci and vancomycin resistant enterococci. He makes it abundantly clear that there has been no victory in the fight against infectious diseases, and the reports from the front lines are less than encouraging for the future.