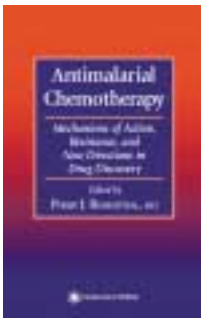

Antimalarial Chemotherapy: Mechanisms of Action, Resistance and New Directions in Drug Discovery

Edited by Philip J. Rosenthal, Humana Press 2001, Price $125.00, 400 pages in hardback, ISBN 0-896-03670-7

In many ways this is a timely book. The rapid progress in the *Plasmodium falciparum* genome sequencing project and the recognition, at both international and government levels, of the inadequacy of control measures have helped to renew interest in the chemotherapy of malaria. The improving situation is reflected in the establishment in 2000 of a public–private partnership, the Medicines for Malaria Venture (MMV), which brings together expertise in academia and the pharmaceutical industry in the search for new antimalarials. It is this return of the pharmaceutical industry to the search and development of new drugs for malaria, coming after recent decades of neglect, that is crucial to the future treatment and control of this widespread and often fatal disease.

Of the antimalarial drugs that have emerged in the past three decades only atovaquone, which was developed by Wellcome, can be claimed to have its origins in the research base of the pharmaceutical industry. Most of the others came either from the work of the Walter Reed Army Institute for Research (Washington, DC, USA), such as mefloquine, halofantrine and tafenoquine, or from the Chinese research community (artemisinin and its derivatives, pyronaridine and lumefantrine). Fortunately, during these 'dry' years a few individuals in the pharmaceutical industry helped to turn these drugs into products.

Putting together a monograph on a subject that is moving as rapidly as biochemistry and molecular biology related to the chemotherapy of *Plasmodium* is no easy task. Not only do you risk missing research areas revealed by the advancing genome sequence, but you also have to compete with more immediate and up-to-date reviews and the ease that most individuals have to access primary literature through databases.

The most recent references in the majority of the chapters of the book are to papers published in 1999 thus missing some significant advances on isoprenoid and fatty acid biosynthesis inhibitors. The book aims, as stated in the introduction, to provide a review for those in malaria and an entry point for those new to the field. For both groups it is worth noting that the book's subtitle is more relevant than the title; there is little here on treatment or clinical aspects. However, the book does bring together a body of knowledge about anti-malarial drug targets and drug design that will ensure that this book is a well-used addition to library shelves.

The book is divided into introductory, established drug and new drug sections. Relevant background is provided in chapters on transporters in *Plasmodium*-infected erythrocytes and on the food vacuole, although other areas of biochemistry, for example, energy metabolism, are omitted and genomic approaches are not included. A chapter on the clinical aspects of drug resistance concludes this least satisfactory section of the book.

Things improve in *Section Two*, which includes incisive reviews on the mechanisms of action of 4-amino-quinolines (Tilley *et al.*), 8-amino-quinolines (Brueckner *et al.*) and folate antagonists (Crowe). However, the organization of the book itself leads to two problems. There are overlaps in chapters, for example, those on 8-aminoquinolines, folate inhibitors and artemisinins that are found within the second and third sections, and there is a separation of biology and chemistry, the interface of which is at the core of drug discovery. Therefore, the Tilley and Brueckner chapters should ideally be read back-to-back with the clearly explained chemistry in the chapter on novel quinolines (Stocks *et al.*). Similarly, the chapter on artemisinin in *Section Two* (Meshnick) is best read back-to-back with the chemistry on trioxanes and endoperoxides in *Section Three* (Posner *et al.*). The chapters on transport at the beginning and end of the book are also best considered together. At least the chapter on mechanisms of quinoline resistance is placed adjacent to those on the action of these drugs. Chapters on naphthoquinones (Vaidya) and iron chelators (Loyevsky and Grodeuk) are more stand-alone.

In addition to the chemistry, the third section includes excellent chapters on novel drug targets, those on the potential of antibiotics and targets in the plastid organelle (Clough and Wilson) and the unravelling of targets and inhibitors of phospholipid metabolism (Vial and Calas) being particularly enjoyable. Although Rathod's chapter, entitled *Fresh Paradigms for Curative Antimetabolites*, has some overlaps with that of Crowe, it also provides a provocative reminder of some of the dangerous simplifications that have formed part of many drug discovery strategies, as well as including constructive directions for the future. It would have made a good ending to the book.

Simon Croft
Department of Infectious and Tropical Diseases
London School of Hygiene and Tropical Medicine
Keppel Street
London, UK
WC1E 7HT
tel: +44 20 7636 8636
fax: +44 20 7636 8739
e-mail: simon.croft@lshtm.ac.uk

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