Antimalarial Drugs II

Current Antimalarials and New Drug Developments

Editors:
W. Peters and W. H. G. Richards

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Preface

The construction of this volume has been guided by two personal convictions.

Experience in the field of experimental chemotherapy, both in the pharmaceutical industry and academia, has convinced us that recent quantum technological advances in biochemistry, molecular biology, and immunology will permit and, indeed, necessitate an increasingly greater use of rational drug development in the future than has been the custom up to now. In Part 1, therefore, we asked our contributors to provide detailed reviews covering the biology of the malaria parasites and their relation with their hosts, the experimental procedures including culture techniques that are necessary to take a drug from primary screening to clinical trial, and an account of antimalarial drug resistance.

Our second conviction is that many research workers are all too loath to learn from the lessons of the past. For this reason we asked the contributors to Part 2 of this volume to review very thoroughly the widely scattered but voluminous literature on those few chemical groups that have provided the antimalarial drugs in clinical use at the present time. Much can be learned from the history of their development and the problems that have arisen with them in man. Some indeed may still have much to offer if they can be deployed in better ways than they are at present. This question has been taken up by several authors.

From about 1963 the threat posed by the increasing failure of chloroquine to cure people infected with *Plasmodium falciparum* led to a rapidly rising crescendo of drug development. Largely under the auspices of the US Army's Walter Reed Army Institute of Research and, latterly, the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases, this research has led, through well over a quarter of a million compounds in primary screen, to a small handful of more or less new drugs that may help to control the problem for a few years. Paradoxically one of the best new drugs, mefloquine, is a close analogue of that ancient remedy quinine, while a second is another plant derivative known in traditional medicine five times longer than quinine itself, the Chinese compound Qinghaosu or artemisinine. The plant itself, *Artemisia annua* L., was first described as an antipyretic agent 2,000 years ago. Attention is currently being focused, too, on the search for new and better tissue schizontocides for the radical cure of relapsing vivax malaria, a second major problem in many tropical and subtropical areas. Neither mefloquine nor artemisinine possess tissue schizontocidal properties.

The final chapters of this work summarise the intensive research that has been carried out, especially over the past decade, in a number of particularly promising chemical groups from one or more of which, we hope, will emerge the next generation of antimalarials. Once these become available it is vital that we should,

for once, try to learn from the lessons of the past and obtain the maximum use possible from them. We have concluded, therefore, with some suggestions concerning the prevention of drug resistance. A major step in this direction, we believe, will be the deployment of rationally selected combinations of antimalarial drugs. While this principle has long been accepted in other antimicrobial fields, e.g., tuberculosis, it has still to prove its value and become accepted (if proven) in the chemoprophylaxis and treatment of malaria.

History has shown that malaria parasites have an uncanny ability to survive in spite of man's best endeavours to eliminate them by drugs or to interrupt their transmission by the use of insecticides to which the vectors become resistant. It is our firm conviction that malaria will be with us for many decades to come, and that we will constantly need to look back to see what has been done before, in order that we can try to do better in the future. That, we believe, fully justifies the considerable effort of all those colleagues who have so generously helped us in the production of this work, including the editorial staff of Springer-Verlag, to all of whom we express our deep gratitude.

Wallace Peters
William H.G. Richards

Contents of Companion Volume 68, Part I

Contents

Antimalarial Drugs in Current Use

CHAPTER 1

CHAPTER 2

Quinine and Quinine Analogues. W. HOFHEINZ and B. MERKLI
With 2 Figures

CHAPTER 3

8-Aminoquinolines. P. E. CARSON. With 3 Figures

Novel Methods of Drug Development

CHAPTER 8

Cell Targeting of Primaquine

A. TROUET, P. PIRSON, R. BAURAIN, and M. MASQUELIER

Recent Developments in Antimalarials

CHAPTER 9

Drugs with Quinine-like Action. T.R. SWEENEY. With 12 Figures

CHAPTER 10

8-Aminoquinolines. T.R. SWEENEY. With 14 Figures

CHAPTER 11

Lapinone, Menoctone, Hydroxyquinolinequinones and Similar Structures
A.T. HUDSON. With 12 Figures

CHAPTER 12

4-Aminoquinolines and Mannich Bases. T.R. SWEENEY and R.O. PICK
With 20 Figures

CHAPTER 13

Triazines, Quinazolines and Related Dihydrofolate Reductase Inhibitors
P. MAMALIS and L.M. WERBEL. With 33 Figures