

Antimalarial Drugs II

Current Antimalarials
and New Drug Developments

Editors:

W. Peters and W. H. G. Richards



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Current Antimalarials and New Drug Developments

Contributors

R. Baurain · P.E. Carson · R. Ferone · C.D. Fitch · W. Hofheinz
A.T. Hudson · R. Leimer · P. Mamalis · M. Masquelier
E.W. McChesney · B. Merkli · W. Peters · R.O. Pick · P. Pirson
R. Richle · K.H. Rieckmann · H.J. Scholer · T.R. Sweeney
A. Trouet · D. Warburton · L.M. Werbel · D.F. Worth

Editors

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WALLACE PETERS, M.D., DSc, FRCP, DTM & H
Professor of Medical Protozoology,
London School of Hygiene and Tropical Medicine,
Keppel Street,
London WC1E 7HT,
Great Britain

WILLIAM H.G. RICHARDS, BSc, Ph. D.
Manager, Scientific Advisory Services,
Wellcome Research Laboratories,
Ravens Lane,
Berkhamsted, Herts. HP4 2DY,
Great Britain

With 150 Figures

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List of Contributors

- R. BAURAIN, Laboratoire de Chimie Physiologique, Faculté de Médecine, Université Catholique de Louvain and International Institute of Cellular and Molecular Pathology, UCL 7539, Avenue Hippocrate, 75, 1200 Bruxelles, Belgium
- P. E. CARSON, Professor and Chairman, Department of Pharmacology, Rush-Presbyterian – St. Luke's Medical Center, 1753 West Congress Parkway, Chicago, IL 60612, USA
- R. FERONE, Group Leader, Department of Microbiology, The Wellcome Research Laboratories, Burroughs Wellcome Co., 3030 Cornwallis Road, Research Triangle Park, NC 27709, USA
- C. D. FITCH, Professor, Department of Internal Medicine, Division of Endocrinology, School of Medicine, St. Louis University Medical Center, 1402 S. Grand Blvd., St. Louis, MO 63104, USA
- W. HOFHEINZ, F. Hoffmann-La Roche & Co. Ltd., Pharmaceutical Research Division, 4002 Basel, Switzerland
- A. T. HUDSON, Department of Therapeutic Chemistry, Wellcome Research Laboratories, Langley Court, Beckenham, Kent BR3 3BS, Great Britain
- R. LEIMER, F. Hoffmann-La Roche & Co. Ltd., Department of Clinical Research, 4002 Basel, Switzerland
- P. MAMALIS, Research Associate, Beecham Pharmaceuticals, Research Division, Walton Oaks, Dorking Road, Tadworth, Surrey KT20 7NT, Great Britain
- M. MASQUELIER, Laboratoire de Chimie Physiologique, Faculté de Médecine, Université Catholique de Louvain and International Institute of Cellular and Molecular Pathology, UCL 7539, Avenue Hippocrate, 75, 1200 Bruxelles, Belgium
- E. W. MCCHESENEY, Research Professor of Toxicology (Ret.), Albany Medical College, private: 14 Alden Court, Delmar, NY 12054, USA
- B. MERKLI, F. Hoffmann-La Roche & Co. Ltd., Pharmaceutical Research Division, 4002 Basel, Switzerland
- W. PETERS, Professor of Medical Protozoology, London School of Hygiene and Tropical Medicine, Keppel Street, London, WC1E 7HT, Great Britain

- R. O. PICK, Chief, Department of Medicinal Chemistry, Division of Experimental Therapeutics, Walter Reed Army Institute of Research, Walter Reed Army Medical Center, Washington, DC 20012, USA
- P. PIRSON, Laboratoire de Chimie Physiologique, Faculté de Médecine, Université Catholique de Louvain and International Institute of Cellular and Molecular Pathology, UCL 7539, Avenue Hippocrate, 75, 1200 Bruxelles, Belgium
- R. Richle, F. Hoffmann-La Roche & Co. Ltd., Pharmaceutical Research Division, 4002 Basel, Switzerland
- K. H. RIECKMANN, 70 Pinion Mill Place, Albuquerque, NM 87131, USA
- H. J. SCHOLER, F. Hoffmann-La Roche & Co. Ltd., Pharmaceutical Research Division, 4002 Basel, Switzerland
- T. R. SWEENEY, 1701 N. Kent Street, Apartment 1106, Arlington, VA 22209, USA
- A. TROUET, Professor, Laboratoire de Chimie Physiologique, Faculté de Médecine, Université Catholique de Louvain and International Institute of Cellular and Molecular Pathology, UCL 7539, Avenue Hippocrate, 75, 1200 Bruxelles, Belgium
- D. Warburton, May and Baker Limited, Dagenham, Essex RM10 7HS, Great Britain
- L. M. WERBEL, Pharmaceutical Research Division, Warner-Lambert Company, 2800 Plymouth Road, Ann Arbor, Michigan 48105, USA
- D. F. WORTH, Pharmaceutical Research Division, Warner-Lambert Company, Plymouth Road, Ann Arbor, Michigan 48105, USA

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 artemisinin. 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 artemisinin 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

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