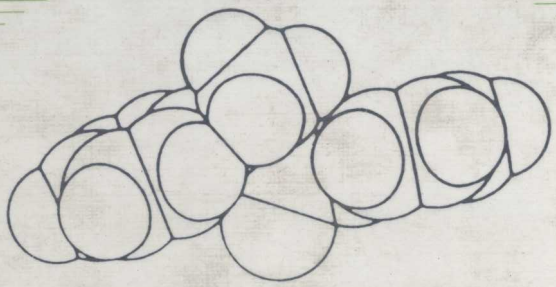
Drug Metabolism~ from Molecules to Man



Edited by
D. J. Benford, J. W. Bridges and G. G. Gibson

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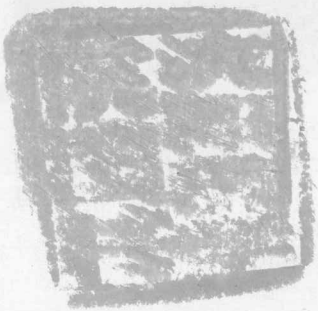

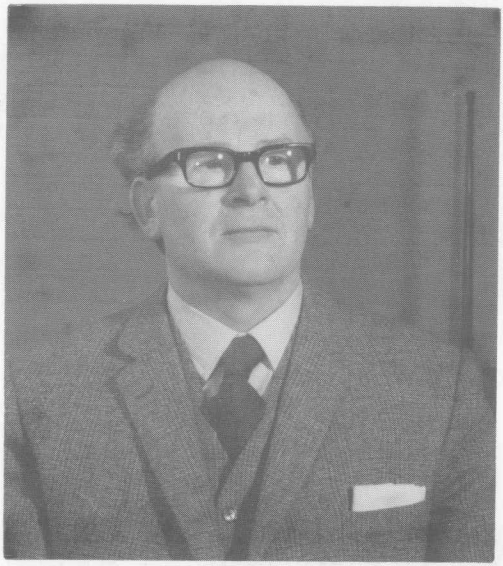

Dedicated to Professor Dennis Parke in recognition of his extensive contributions to the field of drug metabolism

PREFACE

The European Drug Metabolism Workshops began at the University of Surrey, Guildford, UK, in 1970. Since then Workshops have been held in Guildford (1971), Tubingen (1972), Mainz (1974), Stockholm (1976), Leiden (1978), Zurich (1980), Liege (1982), Nancy (1984). From the moment the concept of a workshop was proposed Professor Dennis Parke who was Head of the Biochemistry Department at Surrey, provided the strong encouragement and practical support which was crucial in getting it underway. It was therefore particularly appropriate that the Tenth European Drug Metabolism Workshop should be held at Guildford in honour of Professor Parke.

Professor Parke's contributions to the field of drug metabolism are immense. In addition to his many important research contributions (which number over 300 publications) and the key role he played in the Drug Metabolism Workshops he founded the first journal dedicated to drug metabolism, Xenobiotica, of which he remains the Editor. He also started the still thriving section of Pharmacological Biochemistry of the Biochemical Society (UK) and began the first taught postgraduate degree course in the world in Toxicology. This course lays strong emphasis on the molecular basis of toxicity and incorporates a major element of instruction on the principles of drug metabolism.

Professor Parke's career in drug metabolism began when he joined Professor R. T. Williams' Department at St Mary's Hospital Medical School in 1949 as a Research Assistant. He was one of the earliest workers to use radiolabelled substrates to study the metabolic fate of chemicals, in this case benzene and aniline. During the fifties and early sixties he was involved in establishing with others a firm scientific basis both in the technical and structure activity aspects of *in vivo* drug metabolism studies. As a natural outcome of his increasing interests in biochemistry during the sixties and early seventies the emphasis of his research shifted progressively to *in vitro* based investigations of drug metabolism pathways and particularly to the identification of the role of cytochrome P450 in chemical toxicity and the influences on factors which modify P450 activity. In the last few years he has initiated an entirely new phase of drug metabolism studies namely computer modelling of substrate enzyme interactions again using cytochrome P450 as the model. A consistent hallmark of Dennis Parke's work has been his outstanding ability to link fundamental discoveries to practical human

medicine and to communicate to scientists and laymen alike the excitement of his subject.

He has been a true visionary for his subject, never afraid to challenge existing dogma or to adopt new techniques and approaches to investigate problems. Dennis Parkes' very positive approach, enormous span of knowledge and willingness to discuss research ideas and to help others has never faltered and has been an inspiration to all who have been involved with him. The large number of his PhD students who have gone on to hold senior positions in academia, industry and govenment departments all over the world is a continuing record of his great achievements as a teacher. He has dedicated much time to helping developing countries both in establishing research activities and in practical advice on chemical safety. Some measure of the respect in which his judgement is held is reflected in the very impressive list of major national and international committees on which he has served. These include:

Member of the Committee of Safety on Drugs, U.K., 1968-70; Committee on Safety of Medicines, U.K., 1970-83. Member of Committee on Medical Aspects of Chemicals in Food and the Environment, Department of Health and Social Security, U.K., 1972-. Member of the Biology committee, 1970-76, and Life Sciences Committee, Ministry of Defence, U.K., 1978-1984. Member of Food Additives and Contaminants Committee, Ministry of Agriculture, Fisheries and Food, 1972-78. Member of the Council and Medical and Scientific Committee, Marie Curie Memorial Foundation 1970-. WHO Expert Panel on Food Additives, 1975- ;Joint FAO/WHO Committee on Pesticide Residues, Geneva, 1975- ; WHO Scientific Group on Toxicity Evaluation of Chemicals, 1975-76; WHO Consultant on Industrial Toxicology, Poland, 1974, 1978, 1980, 1982; WHO Consultant on Environmental Health, Vienna, 1983; British Council Consultant on Toxicology DSIR, India, 1976; Member of Advisory Committee for Center of Toxicology, Ontario, Canada; U.K., 1977; Member of the British National Committee on Pharmacology 1976-81; Member of SGOMSEC (WHO and SCOPE), 1978- ; Member of the Expert Committee of Pathologists and Toxicologists, ILSI, Washington, 1978-1982.

Although Dennis Parke is stepping down from the Headship of the Biochemistry Department of the University of Surrey in 1987, no one should presume that this means a lessening of commitment to drug metabolism research. Although his research into computer modelling of the drug metabolising enzymes is still at an early stage his determination to open another new and exciting chapter in

drug metabolism is as strong as ever.

We look forward to Dennis' continued involvement with drug metabolism for many years to come.

We hope that this volume will make a worthy and fitting tribute to Professor Dennis Parke. In addition to identifying recent advances in specific aspects of drug metabolism we believe that the book will be useful in providing an overview of the growing importance of the subject and give valuable pointers to likely future developments.

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The editors would like to thank the other members of the DMW '86 Organising Committee for their assistance in compiling the scientific programme which has resulted in a rather comprehensive analysis of the 'state of the art' from both theoretical and practical viewpoints.

In addition we would particularly like to express our sincere gratitude to the typists - Michele Brookes and Sally Coel - for their long hours spent producing the final copy for this volume and the great care they have taken with it.

D.J. Benford
J.W. Bridges
G.G. Gibson

CONTENTS LIST