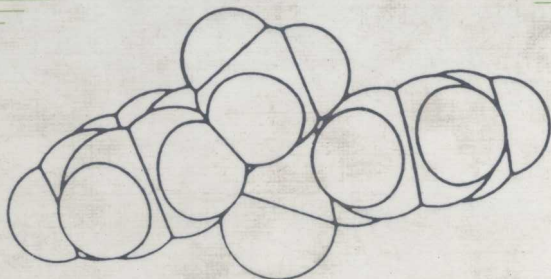


Drug Metabolism~ from Molecules to Man



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



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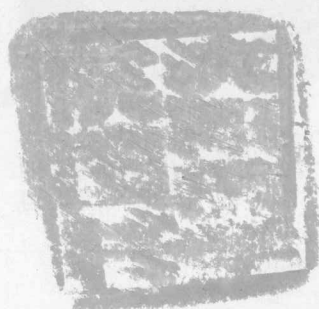
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Drug Metabolism — from Molecules to Man





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 government 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.

D. J. Benford	J. W. Bridges
M. D. Burke	G. M. Cohen
C. R. Elcombe	G. G. Gibson
J. D. Houston	M. J. Humphrey
L. J. King	B. G. Lake
C. R. Wolf	

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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

Preface	xiv
---------	-----

1. Drug metabolizing enzymes at the molecular level

Similarities and differences in properties between constitutive forms of cytochrome P-450 <i>J.B. Schenkman, L.V. Favreau, I. Jansson and J.E. Mole</i>	1
--	---

Molecular aspects of cytochrome P-450 monooxygenases: Characterization of some constitutively expressed forms <i>C.R. Wolf, R. Meechan, M.D. Burke, D.J. Adams, F. Oesch, T. Friedberg, M. Adesnik and N. Hastie</i>	14
---	----

Glutathione transferase <i>B. Mannervik</i>	30
--	----

Molecular characterization of hepatic UDP - glucuronyl transferases <i>B. Burchell, M.R. Jackson, M.W.H. Coughtrie, D. Harding, S. Wilson and J.R. Bend</i>	40
--	----

The regulation of rat liver epoxide hydrolases in relation to that of other drug-metabolizing enzymes <i>C. Timms, L. Schladt, L. Robertson, P. Rauch, H. Schramm and F. Oesch</i>	55
---	----

2. Human drug metabolizing enzymes

Human P-450 enzymes <i>P. Kremers and P. Beaune</i>	71
--	----

Human glutathione S-transferase <i>J.D. Hayes, L.I. McLellan, P.K. Stockman, J. Chalmers, A. Forbes-Howie, A.J. Hussey and G.J. Beckett</i>	82
--	----

Polymorphisms of human drug metabolizing enzymes <i>U.A. Meyer</i>	95
A human isozyme of glutathione transferase activity in different organs and its relation to lung cancer <i>J. Siedegard, R.W. Pero, G.G. Jonsson, S.-A. Olsson, L. Stavenow and K.-F. Aronsen</i>	106
Studies with monoclonal antibodies against a highly purified anticonvulsant-induced human liver cytochrome <i>T.S. Barnes, P.M. Shaw, M.D. Lobban, W.T. Melvin and M.D. Burke</i>	111
Oxidation of quinidine by human liver cytochrome P-450 <i>D. Muller-Enoch and F.P. Guengerich</i>	115
 3. Conjugating enzymes	
Interrelationship between conjugating enzymes <i>in vivo</i> <i>G.J. Mulder</i>	121
Subcellular localization of drug metabolizing enzymes in relation to their function <i>B. Antoine, G. Siest, S. Fournel, A. Visvikis and M.-M. Wellman-Bednawska</i>	135
The role of conjugating enzymes in toxic metabolite formation <i>P.J. van Bladeren, I.M. Bruggeman, W.M.F. Jongen, A.G. Scheffer and J.H.M. Temmink</i>	151
Characterization of the inherited deficiency of UDP-glucuronyl transferase activities in the Gunn rat <i>M.W. Coughtrie, B. Burchell and J.R. Bend</i>	171
Stereoselective glucuronidation of orciprenaline and fenoterol in rat intestinal and hepatic cells and microsomes <i>A.S. Koster, A.C. Frankhuijzen-Sierevogel, P.A.L. Goossens and A. Mentrup</i>	176

Pharmacokinetics of glutathione conjugation
in the rat *in vivo*
*J.M. te Koppele, E.J. van der Mark and G.J.
Mulder* 180

The spontaneous and enzymic reaction of
N-acetyl-benzoquinone-imine with glutathione:
A stopped-flow kinetic study
*B. Coles, I. Wilson, J. Hinson, S. Nelson, P.
Wardman and B. Ketterer* 185

4. Techniques in drug analysis

The detection of drug metabolites in biological
samples by high resolution proton NMR
spectroscopy
J.K. Nicholson and I.D. Wilson 189

Rapid metabolic profiling using thermospray
LC-MS/MS
P. Rudewicz and K. Straub 208

HPLC procedures for drug metabolism studies:
The potential of column switching
J. Schmid and W. Roth 213

N-methyiacetamide, unlike N-methylformamide,
is not a hepatotoxin in the mouse: The role
of metabolism
P. Kestell, M.D. Threadgill and A. Gescher 217

5. Probes for drug metabolizing enzymes

Substrates and inhibitors as probes of
individual forms of drug metabolizing systems
M.D. Burke and C.R. Wolf 219

Biological activities of modifiers of
cytochrome P-450 activities
H. Vanden Bossche and P.A.J. Janssen 244

Antibodies as probes for drug metabolizing
enzymes
*P. Bentley, W. Staubli, F. Bieri and
F. Waechter* 263

Quantitative cytochemistry <i>J. Chayen and L. Bitensky</i>	275
<i>In vivo</i> probes for drug metabolizing enzymes <i>B.K. Park</i>	285
cdNA and complete amino acid sequence of rat 3-methylcholanthrene-inducible NAD(P)H: Menadione oxidoreductase <i>J.A. Robertson and D.W. Nebert</i>	297
Kinetics of drug inhibition: use of metabolite concentration-time profiles to assess relative importance of inhibitor potency and inhibitor pharmacokinetics <i>P.N. Shaw and J.B. Houston</i>	300
Nitroimidazole inhibition of mouse and human cytochrome P-450 mediated hydroxylation of the chloroethylnitrosourea, CCNU <i>P. Workman, F.Y.F. Lee, M.I. Walton, J.T. Roberts and N.M. Bleehen</i>	303
 6. Extrapolations	
Comparison of model systems for metabolism <i>P. Moldeus</i>	309
Comparison of foetal and adult drug metabolizing enzymes <i>K.J. Netter</i>	317
Species variations in pharmacokinetics <i>D.A. Smith</i>	330
Extrapolation from measurement <i>in vitro</i> to drug metabolism <i>in vivo</i> in man <i>A.R. Boobis, S. Murray, C.J. Speirs, C.E. Seddon, G.C. Harries and D.S. Davies</i>	352

7. Biological models for metabolism

The use of structure-activity relationships <i>D.F.V. Lewis, T.J.B. Gray and B.G. Lake</i>	369
---	-----

Purified enzymes as biological models for drug metabolism <i>G.G. Gibson</i>	379
Intact cells as a biological model for metabolism <i>D.J. Benford</i>	392
Diazepam metabolism in cultured hepatocytes from rat, rabbit, dog, guinea-pig and man <i>R.J. Chenery, A. Ayrton, H.G. Oldham, P. Standring, S.J. Norman, T. Seddon and R. Kirby</i>	401
Xenobiotic biotransformation enzymes are present in rat liver Kupffer and endothelial cells <i>P. Steinberg, W.M. Lafranconi, T. Friedberg and F. Oesch</i>	404
The stereoselective formation of benzo(a)pyrene dihydrodiols by purified rat liver cytochromes P-450 <i>M. Hall, D.K. Parker, M. Christou, C.R. Jefcoate and P.L. Grover</i>	411
Galactosamine/endotoxin-induced hepatitis in mice: A model for peptido-leukotriene mediated toxicity <i>A. Wendel and G. Tiegs</i>	415
Reconstitution of the liver drug oxidation system in a soluble monomeric state <i>G.I. Bachmanovo, E.D. Skotselyas, I.P. Kanaeva, E.V. Petrachenko, D.R. Davydov, S.A. Gordeev, V.A. Karyakin, G.P. Kuznetsova, E.N. Korneva and A.I. Archakov</i>	419
8. Biological techniques and drug metabolism	
Preservation of human liver cells and their function <i>A. Guillouzo, C. Chesne, D. Ratanasavanh, J.-P. Campion and C. Guguen-Guillouzo</i>	423

DNA cloning: Technology and applications to drug metabolism <i>I.R. Phillips, E.A. Shephard and A. Ashworth</i>	436
The interferon mediated loss of cytochrome P-452 <i>K.W. Renton, S.M. Moochhala, G.G. Gibson and R.J. Makowski</i>	448
The suicidal reductive activation of carbon tetrachloride by protohaem <i>M. Manno, L.J. King and F. De Matteis</i>	452
The <i>in vitro</i> metabolism of amino azaheterocycles <i>J.W. Gorrod</i>	456
Interaction of potential quinone cytostatic drugs with DNA <i>N.J. de Mol, I.L. Groothuis-Pielage, K. Lusthof and J. Decuyper</i>	462
Influence of cytochrome b ₅ on electron flow from NADPH-cytochrome c(P-450) reductase to cytochrome P-450 <i>I. Golly and P. Hlavica</i>	468
Multiplicity of cytochrome P-450 activities: Stoichiometrical approach <i>A.I. Archakov and A.A. Zhukov</i>	473
9. Metabolism and kinetics in safety evaluation	
Metabolism and toxicokinetics studies in the safety evaluation of drugs and other chemicals <i>D.V. Parke</i>	477
Relation of drug metabolism to drug design <i>J.W. Faigle</i>	493
Significance of measuring blood levels of drugs <i>S. Garattini</i>	507

Single versus chronic dosing in the safety evaluation of xenobiotics: Pharmacokinetic considerations <i>M. Danhof</i>	531
Effect of exposure route on metabolism and kinetics <i>J.B. Houston</i>	548
10. Metabolic fate of particular classes of compound	
Recently discovered routes of metabolism <i>B. Testa</i>	563
Metabolism of sulphur-containing drugs <i>L.A. Damani</i>	581
Delivery, distribution, clearance and degradation: Key factors in the design and development of peptide and protein drugs <i>C. McMartin</i>	604
Stereoselectivity in the enzymatic biotransformation of drugs and other xenobiotics <i>N.P.E. Vermeulen</i>	615
Oral bioavailability of the LLL and LDL diastereomers of pyroglutamyl-(2-pyridylalanyl)-prolineamide in rat and dog <i>G.D. Bowers, B. Kaye and D.J. Rance</i>	640
Cytochrome P-450 dependent denitrosation of diphenylnitrosamine: A possible bioactivation pathway <i>K.E. Appel, S. Gorsdorf, T. Scheper, H.H. Ruf, M. Schoepke, C.S. Ruhl and A.G. Hildebrandt</i>	644
Metabolic acetal splitting of budesonide - A novel inactivation pathway for topical glucocorticoids <i>S. Edsbacker, P. Andersson, C. Lindberg, J. Paulson, A. Ryrfeldt and A. Thalen</i>	651

11. Metabolism and Toxicity

- Metabolism and mechanisms of toxicity - An overview
L.J. King 657
- A chemical approach to reactive metabolites
D. Mansuy 669
- Free radical mechanisms in relation to cell injury and cell division
T.F. Slater, K.H. Cheeseman, M.J. Davies and J.S. Hurst 679
- Tissue distribution of drug metabolizing enzymes in relation to toxicity
G.M. Cohen and E.J. Moss 690

12. Active metabolites and extrahepatic metabolism

- Active oxygen species and toxicity
H. Sies 709
- The renal metabolism and toxicity of cysteine conjugates
T. Green 722
- Metabolic activation by the foetus and placenta
O. Pelkonen, M. Pasanen and K. Vahakangas 734
- Cytochrome P-450 of the olfactory epithelium and its degradation by suicide substrates *in vivo*
C.J. Reed, F. De Matteis and E.A. Lock 747
- Subcellular effects of haloalkenes in the kidney
A. Wallin, T.W. Jones, A.E. Vercesi and K. Ormstad 751
- Strong inhibition of lipid peroxidation *in vitro* and *in vivo* by dithiolthione derivatives
P. Dansette, A. Sassi, M. Plat, M.-O. Christen and D. Mansuy 755

Methods in drug metabolism - Future prospects 761
J.W. Bridges

Index 773