Drug Metabolism and Disposition:
the biological fate of chemicals

January/February 1987

CONTENTS

Bromobenzene Metabolism in the Rat and Guinea Pig. K. LERTRATANANGKOON and M. G. HORNING


Mechanisms of Lidocaine Kinetics in the Isolated Perfused Rat Liver. II. Kinetics of Steady State Elimination. BRADLEY A. SAVILLE, MURRAY R. GRAY, and YUN K. TAM


The Series-Compartment Model for Hepatic Elimination. MURRAY R. GRAY and Y. K. TAM

Microsomal Metabolism of Pyrrolizidine Alkaloids from Senecio jacobaea: Isolation and Quantification of 6,7-Dihydro-7-Hydroxy-1-Hydroxymethyl-5H-Pyrrrolizine and N-Oxides by High Performance Liquid Chromatography. HOWARD S. RAMSDELL, BOGDAN KEDZIERSKI, and DONALD R. BUHLER

The Formation of Procainamide Hydroxylamine by Rat and Human Liver Microsomes. ROBERT A. BUDINSKY, STEPHEN M. ROBERTS, EUGENE A. COATS, LOUIS ADAMS, and EVELYN V. HESS

Studies on the Pharmacokinetics and Metabolism of 4-Chlorodiphenyl Ether in Rats. Y. C. CHUI, R. F. ADDISON, and F. C. P. LAW

Effect of Diffusional Barriers on Drug and Metabolite Kinetics. INÉS A. M. DE LANNY and K. SANDY PANG

Cytochrome P-450 Isozymes 2 and 5 in Rabbit Lung and Liver: Comparisons of Structure and Inducibility. ZAHRA PARANDOOSH, VALERIE S. FUJITA, MINOR J. COON, and RICHARD M. PHILPOT

Extrahepatic Expression of N-Acetyltransferase Genotype in the Inbred Hamster. DAVID W. HEIN, WARD G. KIRLIN, FREDERICK O'GOLLA, and ALMA TRINIDAD

Metabolism of the β-Carbolines, Harmine and Harmol, by Liver Microsomes from Phenobarbital- and 3-Methylcholanthrene-Treated Mice: Identification and Quantitation of Two Novel Harmin Metabolites. D. J. TWEEDIE and M. D. BURKE

Stereochemical Aspects of the Glutathione S-Transferase-Catalyzed Conjugations of Alkyl Halides. RICHARD E. RIDGELL and MAHMOUD M. ABD-DEMONEH

Comparative Metabolism and Disposition of 1-Chloro- and 3-Chloro-2-methylpropene in Rats and Mice. BURHAN I. GHANAYEM and LEON T. BURKA

Microbial Transformation of the Antihistamine Pyrilamine Maleate: Formation of Potential Mammalian Metabolites. EUGENE B. HANSEN, JR., CARL E. CERNIGLIA, WALTER A. KORFMACHER, DWIGHT W. MILLER, and ROBERT H. HEFLICH

Disposition and Biotransformation of Quinpirole, a New D-2 Dopamine Agonist Antihypertensive Agent, in Mice, Rats, Dogs, and Monkeys. N. G. GALLICK WHITAKER and T. D. LINDBERG

Characterization of the Induction of Cytosolic and Microsomal Epoxide Hydrolases by 2-Ethylhexanoic Acid in Mouse Liver. BO LUNDGREN, JOHAN MEIJER, and JOSEPH W. DEPIERRE

Deacetylation of Diltiazem by Rat Liver. ELIZABETH LÉBOEUF and ODETTE GRECH-BÉLANGER

Plasma Concentration-Response Relationship for Cimetidine Inhibition of Drug Metabolism in the Rat. ADEYADO ADEDOYIN, LEON AARONS, and J. BRIAN HOUSTON

SHORT COMMUNICATIONS

Comparison of Adenosine 3'-Phosphate 5'-Phosphosulfate Concentrations in Tissues from Different Laboratory Animals. ELIZBETA A. BRZEZNICKA, GEORGE A. HAZELTON, and CURTIS D. KLAASSEN

Influence of Age on Intrinsic Clearance of Bupivacaine and Its Reduction by Cimetidine in Elderly Male Rats. GARY A. THOMPSON, JANE A. MYERS, PATRICIA A. TURNER, DENNIS E. COYLE, WOLFGANG A. RITSCHEL, and DONALD D. Denson

Effect of Surgery on Serum α-Acid Glycoprotein Concentration and Serum Protein Binding of DL-Propanolol in Phenobarbital-Treated and Untreated Rats. TSU-HAN LIN, YUICHI SUGIYAMA, YASUFUMI SAWADA, YASUYUKI SUZUKI, TATSUJI IGA, and MANABU HANANO

Books Received

Vol. 15, No. 1

37
44
51
59
68
74
82
91
97
107
114
122
127
133
136
138
141
CONTENTS

Relationship between Sulfotransferase Activity and Susceptibility to Acetaminophen-induced Liver Necrosis in the Hamster. MARION G. MILLER AND DAVID J. JOLLOW .......................... 143

Dose-dependent Pharmacokinetics of Ibuprofen in the Rat. A. SHAH AND D. JUNG .................. 151

Nomenclature

Nonenzymatic Bioreduction in Rat Liver and Kidney of Nitroxy1 Spin Labels. Potential Contrast Agents in Magnetic Resonance Imaging. ULF G. ERIKSON, ROBERT C. BRASCH, AND THOMAS N. TOZER 155

In Vitro Microsomal Metabolism of the Leukotriene Receptor Antagonist, 5-(2-Dodecylphenyl)-4,6-dithianonanedioic Acid (SK&F 102,081). JOHN F. NEWTON, KENNETH M. STRAUB, RICHARD H. DEWEY, CARL D. PERCHONOCK, THOMAS B. LEONARD, MARY E. McCARTHY, JOHN G. GLEASON, AND REGINA D. ECKARDT ...... 161

In Vivo Metabolism of the Leukotriene Receptor Antagonist, 5-(2-Dodecylphenyl)-4,6-dithianonanedioic Acid (SK&F 102,081) in the Guinea Pig. JOHN F. NEWTON, KENNETH M. STRAUB, GEORGE Y. KUO, CARL D. PERCHONOCK, MARY E. McCARTHY, JOHN G. GLEASON, AND ROBERT K. LYNN .... 168

Alterations in Biliary Excretory Function by Streptozotocin-induced Diabetes. JOHN B. WATKINS III AND THOMAS P. DYKSTRA .......... 177

Uptake, Metabolism, and Secretion of 3'-Methyl-N,N-dimethyl-4-aminooazobenzene by Isolated Perfused Rat Liver. AUDREY R. SAMUELS, LORENZ THEILMANN, YACOV R. STOLLMAN, ALLAN W. WOLKOFF, AND MADHU M. BHARGAVA .... 184

Uptake and Disposition of Putrescine, Spermidine, and Spermine by Rabbit Lungs. SHRINIVAS B. RAO AND HARIHARA M. MEHENDALE .......... 189

Conversion of Melphalan to 4-(Glutathionyl)phenylalanine. A Novel Mechanism for Conjugation by Gluthathione-S-transferases. DEANNE M. DULIK AND CATHERINE FENSELAU ........................................... 195

Conversion of N,N-Dimethylaniline to N,N-Dimethylaniline-N-oxide by a Cytosolic Flavin-containing Enzyme from Trypanosoma cruzi. MOISES AGOSIN AND GERALD T. ANKLEY .......... 200

Pharmacokinetic Interaction between Theophylline and Chloramphenicol in Rats. M. BUSBY AND L. J. LESKO .......................... 204


Urinary Excretion Kinetics of Famotidine in Rats. JIUNN H. LIN, LAYNE E. LOS, EDGAR H. ULM, AND DANIEL E. DUGGAN .... 212

In Vivo and in Vitro Biotransformation of Theobromine by Phenobarbital- and 3-Methylcholanthrene-inducible Cytochrome P-450 Monoxygenases in Rat Liver. Role of Thiou Compounds. CAROL A. SHIVELY AND ELLIOT S. VESELL .......... 217

Effects of Aging on the Properties of Rhesus Monkey Liver Microsomal NADPH-Cytochrome c (P-450) Reductase. DOUGLAS L. SCHMUCKER AND ROSE K. WANG .......... 225


Biotransformation of Caffeine, Paraxanthine, Theophylline, and Theobromine by Polycyclic Aromatic Hydrocarbon-inducible Cytochrome(s) P-450 in Human Liver Microsomes. MONICA E. CAMPBELL, DENIS M. GRANT, TADANOBU INABA, AND WERNER KALOW .......... 237

Pharmacokinetics of Tetrabenazine and Its Major Metabolite in Man and Rat. Bioavailability and Dose Dependency Studies. REZA MEHVAR, FAKHREDIN JAMALI, MICHAEL W. B. WATSON, AND DAVID SKELETON .......... 250


Metabolism of Ethyl 2-(4-Chlorophenyl)-5-(2-furyl)-oxazole-4-acetate, a New Hypolipidemic Agent, in the Rat, Rabbit, and Dog. Glucuronidation of Carbonyl Group and Cleavage of Furan Ring. TSU-TOMU KOBAYASHI, HIDEHIRO ANDO, JUKO SUGIHARA, AND SHOICHI HARIGAYA .......... 262

Continued on next page
Contents (cont’d.)

SHORT COMMUNICATIONS

Mitotane (1-(o-Chlorophenyl)-1-(p-chlorophenyl)-2,2-
dichloroethane) Metabolism in Perfusion Studies
with Dog Adrenal Glands. J. E. SINSHEIMER AND
CORINNE J. FREEMAN ............................................ 267

Comparison of Hepatic and Renal Metabolism of Ac-
etaminophen in Male and Female Miniature
Swine. JAMES O. PEGGINS, TIMOTHY F. McMAHON,
WILLIAM P. BEIERSCHMITT, AND MYRON WEINER 270

In Vivo Inhibition of Phenacetin Oxidation by Suicide
Substrate 1-Aminobenzotriazole. BRUCE A. MICO,
DEBRA ANN FEDEROWICZ, ERIC BURAK, AND
JAMES E. SWAGZDIS ............................................. 274

Pharmacogenetic Association between the Formation
of 4-Hydroxymephenytoin and a New Metabo-
lite of S-Mephenytoin in Man. P. J. WEDLUND,
B. J. SWEETMAN, G. R. WILKINSON, AND R. A.
BRANCH .......................................................... 277
CONTENTS

Hepatic UDP-glucose and UDP-glucuronic Acid Synthesis Rates in Rats during a Reduced Energy State. RUSSELL L. DILLS, STANLEY R. HOWELL, and CURTIS D. KLAASSEN 281

Metabolism and Distribution of 14C- and 35S-Labeled Carbon Disulfide in Immature Rats of Different Ages. ELIZABETH GREEN SNYDERWINE AND ANDREA HUNTER 289

In Vivo and in Vitro 1-Methylxanthine Metabolism in the Rat. Direct Evidence That the Dehydrogenase Form of Xanthine Oxidase Predominates in Intact Perfused Liver. LESTER A. REINKE, MITSUTAKA NAKAMURA, LANCE LOGAN, H. DX CHRISTENSEN, and JOHN M. CARNEY 295

Pharmacokinetic and Deuterium Isotope Effect Studies on the Metabolism of Formaldehyde and Formate to Carbon Dioxide in Rats in Vivo. LARRY K. KEEFER, ANTHONY J. STREETER, LOUIS Y. LEUNG, WILLIAM C. FERRY, HENRY S.-W. HU, and THOMAS A. BAILLIE 300

3,4-Dichlorobenzyloxyacetic Acid Is Extensively Metabolized to a Taurine Conjugate in Rats. RICHARD C. PEFFER, DONALD J. ABRAHAM, MICHAEL A. ZEMAITIS, LAN K. WONG, and JOHN D. ALVIN 305


Disposition of 8-Methoxypsoralen in the Rat. Induction of Metabolism in Vivo and in Vitro and Identification of Urinary Metabolites by Thermospray Mass Spectrometry. DENNIS C. MAYS, STEPHEN G. HECHT, STEVE E. UNGER, CHRISTINE M. Pacula, JEANETTE M. CLIMIE, DALE E. SHARP, and NICHOLAS GERBER 318

Effects of Cisplatin-induced Nephrotoxicity on Gentamicin Pharmacokinetics in Rats. MEHER S. ENGINEER, GERALD P. BODEY, SR., ROBERT A. NEWMAN, and DAH-HSI W. HO 329

Induction and Inhibition of Rat Hepatic Drug Metabolism by N-Substituted Imidazole Drugs. JOSEPH K. RITTER and MICHAEL R. FRANKLIN 335

Influence of Cytochrome b5 on the Stoichiometry of the Different Oxidative Reactions Catalyzed by Liver Microsomal Cytochrome P-450. INGELA JANSSON and JOHN B. SCHENKMAN 344

The Formation of a Glutathione Conjugate Derived from Propranolol. H. A. SASAME, D. J. LIBERATO, and J. R. GILLETTE 349

The Oxidation of Acrolein by Rat Liver Aldehyde Dehydrogenases. Relation to Allyl Alcohol Hepatotoxicity. LORA E. RIKANS 356

The Disposition and Elimination of Two Sequential Doses of 2,4,5,2',4',5'-Hexachlorobiphenyl. LORI A. GALLENBURG AND MARY JO VODNICK 363

Absorption, Distribution, Metabolism, and Excretion of 1,2-Dihydro-2,4,4-trimethylquinoline in the Male F344 Rat. Y. M. IOANNOU, L. T. BURKA, J. M. SANDERS, M. P. MOORMAN, AND H. B. MATTHEWS 367

Pharmacokinetics of Griseofulvin in Blood and Skin Suction Blister Fluid of Rats. M. SCHÄFER-KORTIN 374

Tissue Distribution, Disposition, and Metabolism of Cyclosporin in Rats. O. WAGNER, E. SCHREIER, F. HEITZ, AND G. MAURER 377

Metabolism of Cyclosporin A. I. Study in Freshly Isolated Rabbit Hepatocytes. GÉRARD FABRE, PIERRE BERTAULT-PERES, ISABELLE FABRE, PATRICK MAUREL, SYLVAIN JUST, AND JEAN-PAUL CANO 384

Metabolism of Cyclosporin A. II. Implication of the Macrolide Antibiotic Inducible Cytochrome P-450 3c from Rabbit Liver Microsomes. PIERRE BERTAULT-PERES, CLAUDE BONFILS, GÉRARD FABRE, SYLVAIN JUST, JEAN-PAUL CANO, AND PATRICK MAUREL 391

Urinary Metabolites in Busulfan in the Rat. MOUSTAPA HASSAN AND HANS EHRSSON 399

Liver Metabolism of Budesonide in Rat, Mouse, and Man. Comparative Aspects. S. EDSSBÄCKER, P. ANDERSSON, C. LINDBERG, J. PAULSON, A. RYRFELDT, and A. THALEN 403


Continued on next page
Contents (cont'd.)

Glutathione Conjugation of 1,2-Dibromo-1-phenylethane in Rats in Vivo. C. E. M. Zoetemelk, W. van Hove, W. L. J. van der Laan, B. van Meeteren-Wälchli, A. van der Gen, and D. D. Breimer ........................................... 418

N-Hydroxymethyl Metabolites of 450191-S, a 1H-1,2,4-Triazolyl Benzophenone Derivative, in Dog Plasma. M. Koike, R. Norikura, S. Futaguchi, T. Yamaguchi, K. Sugeno, K. Iwatani, Y. Ikenishi, and Y. Nakagawa ........................................... 426

SHORT COMMUNICATIONS

Plasma Concentration Profiles of Human Recombinant Interleukin-2 (HrIL-2) in the Rat following Administration by Various Systemic Routes. W. A. Colburn, J. Hakimi, and I. Bekersky ............................. 429

Dose- and Time-dependent Effect of Levamisole on the Elimination of Antipyrine in the Rat. Craig K. Svensson and Li-Ling Liu ........................................... 432

Announcements ........................................... 435
CONTENTS

Commentary: Renal Transport Processes and Glutathione Conjugate-mediated Nephrotoxicity. TERENCE J. MONKS and SERRINE S. LAU ................. 437

Species Differences in Disposition of Benz[a]pyrene. ERIC H. WEYAND and DAVID R. BEVAN .......... 442

Uptake, Toxicity, and Distribution of Benz[a]pyrene and Monoxygenase Induction in the Topminnows Poeciliopsis monacha and Poeciliopsis lucida. KATHRYN A. GOODARD, R. JACK SCHULTZ, and JOHN J. STEGEMAN ................. 449

Determination of Metabolite Pharmacokinetics for Orally Administered Prodrugs. GREGORY M. KOCHAK and ASHOK RAKHIT ................. 456

The Metabolism and Elimination of Pyrilamine Maleate in the Rat. DANIEL W. KELLY and WILLIAM SLIKKER, JR. .......... 460

N-Debenzylation of Pyrilamine and Tripelennamine in the Rat. A New Metabolic Pathway. S. Y. YEH ................. 466

Species-dependent Glucuronidation of Drugs by Immobilized Rabbit, Rhesus Monkey, and Human UDP-glucuronyltransferases. DEANNA M. DULIK and CATHERINE FENSELAU ................. 473

Metabolism and Disposition of Ethylene Glycol Mono-butyl Ether (2-Butoxyethanol) in Rats. BURHAN I. GHANAYEM, LEO T. BURKA, J. M. SANDERS, and H. B. MATTHEWS ................. 478

Phencyclidine Iminium Ion. NADPH-dependent Metabolism, Covalent Binding to Macromolecules, and Inactivation of Cytochrome(s) P-450. M. K. P. HOAG, A. J. TREVOR, A. KALIR, and N. CASTAGNOLI, JR. ................. 485

Stereoselectivity of Naphthalene Epoxidation by Mouse, Rat, and Hamster Pulmonary, Hepatic, and Renal Microsomal Enzymes. A. R. BUCKPITT, N. CASTAGNOLI, JR., S. D. NELSON, A. D. JONES, and L. S. BANSON ................. 491

Comparative Defluorination and Cytochrome P-450 Loss by the Microsomal Metabolism of Fluoro- and Fluorochloroethenes. MAX T. BAKER, JAMES N. BATES, and SUSAN V. LEFF ................. 499

Noncovalent Binding of 3'-Methyl-N,N-dimethyl-4-aminoazobenzene and Its Metabolites to Liver Cytosolic Proteins and Its Role in Their Nuclear Translocation. KRISHNAPURA SRINIVASAN, WALTER G. LEVINE, and MADHU M. BHARGAVA ................. 504

Effect of Cytochrome P-450 and Flavin-containing Monooxygenase Modifying Factors on the in Vitro Metabolism of Amiodarone by Rat and Rabbit. ROBERT A. YOUNG and HARIHARA M. MEHENDALE ................. 511

An Investigation of the Antigenic Determinants on Chloroperoxidase and Purified Rat Liver Microsomal Cytochrome P-450. RAMENDRA N. PANDEY, STEVEN C. KUENEMERLE, and PAUL F. HOLLENBERG ................. 518

Effects of Genetic or Chemically Induced Diabetes on Impairment of Monooxygenase. Respective Involvement of Flavin Monooxygenase and Cytochrome P-450-dependent Monooxygenases. E. ROUER, A. LE-MOINE, T. CRESTEIL, P. ROUET, and J. P. LEROUX ................. 524

Stereoselective Metabolism of 2-Phenylpropionic Acid in Rat. I. In Vitro Studies on the Stereoselective Isomerization and Glucuronidation of 2-Phenylpropionic Acid. YUTAKA NAKAMURA and TOSHIRO YAMAGUCHI ................. 529

Stereoselective Metabolism of 2-Phenylpropionic Acid in Rat. II. Studies on the Organs Responsible for the Optical Isomerization of 2-Phenylpropionic Acid in Rat in Vivo. TOSHIRO YAMAGUCHI and YUTAKA NAKAMURA ................. 535

Physiologically Based Pharmacokinetics of Radiodinated Human β-Endorphin in Rats. An Application of the Capillary Membrane-limited Model. HITOSHI SATO, YUICHI SUGIYAMA, YASUFUMI SAWADA, TATSUJI IGA, and MANABU HANANO ................. 540

The Metabolism of Roxatidine Acetate Hydrochloride. Liberation of Deuterium from the Piperidine Ring during Hydroxylation. SEIJIRO HONMA, SATOSHI IWAMURA, REIKO KOBAYASHI, YOSHIHITO KOBAYASHI, AND KEN'YU SHIBATA ................. 551

6-Fluoro-2-methylspiro(chroman-4, 4'-imidazolidine)-2,5'-dione and Related Compounds as Inducers of Monooxygenase in Rat Liver Microsomes. TOHRU HORIE, MITSUKAZU KITADA, HIDEHUMI YOSHIOKA, YOSHIKO KANAKUBO, and TSUNEKO OMURA ................. 560

Disposition of Nafimidone in Rats. D. J. M. GRAHAM, K. M. HAMA, S. A. SMITH, L. KURZ, M. D. CHAPLIN, and D. J. HALL ................. 571

Inhibition and Induction of Hepatic Drug Metabolism in Rats and Mice by Nafimidone and Its Major Metabolite Nafimidone Alcohol. W. R. RUSH, S. A. SMITH, J. H. MULVEY, D. J. M. GRAHAM, and M. D. CHAPLIN ................. 571

Continued on next page
Contents (cont’d.)

SHORT COMMUNICATIONS

Burke, Keith R. Huckle, David H. Hutson, and Peter Millburn .......................... 581
A Phenolic Metabolite of Phencyclidine: The Formation of a Pharmacologically Active Metabolite by Rat Liver Microsomes. Shigeru Ohta, Hiroshi Masumoto, Kaoru Takeuchi, and Masaaki Hirobe .......................... 583
Books Received ........................................ 585
Announcement .......................................... 586

The Metabolic Fate of Oxazepam in Mice. S. F. Sisenwine, C. O. Tio, A. L. Liu, and J. F. Politowski ........................................ 579

Formation of the Taurine Conjugate of Benzoic Acid in Rainbow Trout, Salmo gairdneri. Alison B.
CONTENTS

Letter to the Editor: Criteria for the Acceptability of Experimental Evidence for the Enantiomeric Composition of Xenobiotics and Their Metabolites. JOHN CALDWELL AND BERNARD TESTA .......................... 587

The Metabolism of the Abortifacient Terpene, (R)-(++)-Pulegone, to a Proximate Toxin, Menthofuran. W. PERRY GORDON, ALAIN C. HUITRIC, CYNTHIA L. SETH, ROBERT H. McCLEAN, AND SIDNEY D. NELSON .......................................................... 589

The Disposition and Metabolism of 2',3'-Dideoxycytidine, an in Vitro Inhibitor of Human T-Lymphophotropic Virus Type III Infection, in Mice and Monkeys. JAMES A. KELLEY, CHARLES L. LITTERST, JERI S. ROTH, DAVID T. VISTICA, DAVID G. POPLACK, DAVID A. COONEY, MOHAN NADKARNI, FRANK M. BALIS, SAMUEL BRODER, AND DAVID G. JOHNS ........................................... 595

Influence of a Purified Diet and Route of Administration on the Metabolism and Disposition of Estradiol in B6C3F1 Mice. FLOYD R. FULLERTON, DAVID L. GREENMAN, AND JOHN F. YOUNG ............................. 602

Distribution of trans-4-Hydroxy-2-hexenal and Tandem Mass Spectrometric Detection of Its Urinary Mercapturic Acid in the Rat. CARL K. WINTER, H. J. SEGALL, AND A. DANIEL JONES ................................................. 608

The Role of the Liver in Mediating the Acute Toxicity of the Pesticide Methyl Parathion in the Mouse. LESTER G. SULTATOS .............................................................. 613

Ketorolac Tromethamine Absorption, Distribution, Metabolism, Excretion, and Pharmacokinetics in Animals and Humans. EDWARD J. MROSZCZAK, FRANK W. LEE, DANIEL COMBS, FRANK H. SARQUIST, BEE-LIAN HUANG, ANNE T. WU, LASZLO G. TOKES, MICHAEL L. MADDOX, AND DIANE K. CHO .............................................. 618

Pharmacokinetics and Pharmacodynamics of Physostigmine in the Rat after Intravenous Administration. SATU M. SOMANI AND ABDUL KHALIQUE ........................................ 627

Oxidation of the Alcohol Dehydrogenase Inhibitor Pyrazole to 4-Hydroxyprazolyl by Microsomes. Effect of Cytochrome P-450 Inducing Agents. DENNIS E. FEIERMAN AND ARTHUR I. CEDERBAUM ........................................ 634

Disposition of the Monoclonal Antibody-Vinca Alkaloid Conjugate, KS1/4-DAVLB (LY256787), in Fischer 344 Rats and Rhesus Monkeys. MARSHALL E. SPEARMAN, R. MICHAEL GOODWIN, AND DONALD KAU ........................................................................... 640

Mechanism-based Inhibition of Cytochrome P-450 by Heterocyclic Analogues of Phenycyclidine. JOHN F. BRADY, JOON DOKKO, EMMA W. DI STEFANO, AND ARTHUR K. CHO .............................................. 648

Relationship between the Murine Ah Phenotype and the Hepatic Uptake and Metabolism of 2,3,7,8-Tetrachlorodibenzo-p-dioxin. EMILY S. SHEN AND JAMES R. OLSON ....................................................... 653

The in Vitro Activity, Radioimmunoassay Cross-reactivity, and Molecular Weight of Thirteen Rabbit Cyclosporine Metabolites. N. R. HARTMAN AND I. JARDINE ................................................................. 661

In Vivo and in Vitro Renal Metabolism and Excretion of Benzoic Acid by a Marine Teleost, the Southern Flounder. MARGARET O. JAMES AND JOHN B. Pritchard ........................................... 665

The Disposition of N-(4,6-Dimethyl-2-pyrimidinyl)benzenesulfonamide in the Rat. G. D. PAULSON AND V. J. FEIL .......................................................... 671

The Development of Hepatic Drug-metabolizing Enzyme Activity in the Neonatal Calf and Its Effect on Drug Disposition. SUSAN E. SHOF, WAYNE S. SCHWARK, CHARLES L. GUARD, AND JOHN G. BABISH ......................................................... 676

The Metabolism of 7-Ethylbenz[a]anthracene by Rat Liver Microsomal Preparations. S. MCKAY, P. B. FARMER, P. D. CARY, AND P. L. GROVER ............................................ 682

Physiologically Based Pharmacokinetic Model for the Renal Clearance of Salicylic Acid and the Interaction with Phenolsulfonphthalein in the Dog. FRANS G. M. RUSSEL, ALFONS P. D. FARMER, AND PAULSON AND V. J. GUARD, AND JOHN G. BABISH ......................... 695

Bioactivation of Tetrachloroethylene. Role of Glutathione S-Transferase-catalyzed Conjugation versus Cytochrome P-450-dependent Phospholipid Alkylation. WOLFGANG DEKANT, GISELA MARTENS, FRANZ SCHÄFFER, ALFONS P. D. FARMER, AND DIETRICH HENSCHLER .................. 702

Glucuronidation in Vitro and in Vivo. Comparison of Intestinal and Hepatic Conjugation of Morphine, Naloxone, and Buprenorphine. M. MISTRY AND J. BRIAN HOUSTON ....................................................... 710

Direct Detection of New Fluorocytosine Metabolites in Human Biofluids by 19F Nuclear Magnetic Resonance. JEAN P. VIALANEIX, MARIE C. MALET-MARTINO, JEAN S. HOFFMANN, JACQUES PRIS, AND ROBERT MARTINO ........................................... 718

Continued on next page
Contents (cont'd.)

SHORT COMMUNICATIONS

M. B. Bailie, D. A. Federowicz, K. Dolce, C. Kahn, B. A. Mico, and M. S. Landi........... 729

Influence of Gonadal Hormones upon Rat Hepatic Acetaminophen Sulfotransferases. Robert E. Kane and Lee J. Chen ....................... 725

Effect of Cyclosporine on Hepatic Oxidative and Conjugative Metabolism in Rats. Raymond E. Galinsky, Donald P. Alexander, and Michael R. Franklin ....................... 731

Pharmacokinetics of Acetaminophen, Vancomycin, and Antipyrine in the Hanford Miniature Swine.
Drug Metabolism and Disposition:
the biological fate of chemicals

November/December 1987  Vol. 15, No. 6

CONTENTS

The Disposition and Pharmacokinetics of Ketocona-zole in the Rat. RORY P. REMMEL, KWAME AMOH, AND MAHMUD M. ADEL-MONEM 735

Metabolism and Disposition of Cyproheptadine and Desmethylcyproheptadine in Pregnant and Fetal Rats. SAMSON A. CHOW AND LAWRENCE J. FISCHER 740

Effects of Model Traumatic Injury on Hepatic Drug Metabolism in the Rat. VI. Major Detoxification/Toxicification Pathways. LANDIS K. GRIFFETH, GER-ALD M. ROSEN, AND ELMER J. RAUCKMAN 749

Metabolite Profile in Milk of Lactating Rats after Treatment with a Carcinogen, N-2-Fluorenylacacetamide. DANUTA MALEKA-GIGANTI, WELSONIA J. MAGAT, ANNETTE M. ADELTEIN, AND RICHARD W. DECKER 760

Species-dependent Enantioselective Glucuronidation of Three 2-Arylpionic Acids: Naproxen, Ibuprofen, and Benoxaprofen. MOHAMED EL MOUELHI, B. HAMED, ELIZABETH SUWITA, AMIN A. ABOU-DONIA, F. AIBUT, AND RASHMI BARBHAIYA 767


Disposition, Pharmacokinetics, and Metabolism of a Dermal Dose of [14C]2,5-Hexanedione in Hens. ELIZABETH SIVITA, AMIN A. NOMEIR, AND MOHAMED A. ABOU-DONIA 779

Monooxygenase-mediated Activation of Chlorotriani-sene (TACE) in Covalent Binding to Rat Hepatic Mitochondrial Proteins. MARLENE J. JUDEK, WILLIAM H. BULGER, AND DAVID KUPFER 786

The Pharmacokinetics of Pentane, a By-product of Lipid Peroxidation. SANDRA R. B. ALLERHEILIGEN, THOMAS M. LUDDEN, AND RAYMOND F. BURK 794

Co-oxidation of 2-Bromohydroquinone by Renal Prostaglandin Synthase. Modulation of Prostaglandin Synthesis by 2-Bromohydroquinone and Glutathione. SERRINE S. LAU AND TERRENCE J. MONKS 801

N-Oxidation of N-Methyl Pyrrolidine Released in Vivo from Cefetamine. S. THOMAS FORGUE, PRASAD KARI, AND RASHMI BARBHAIYA 808

Isolation and Characterization of 4'-Hydroxy T-2 Toxin, a New Metabolite of the Trichothecene Mycoxin T-2. CATHERINE A. KNUPP, DAVID G. CORLEY, MICHAEL S. TEMPESTA, AND STEVEN P. SWANSON 816

Metabolism and Excretion of Dinitrobenzenes by Male Fischer-344 Rats. DEBRA D. NYSROM AND DOUGLAS E. RICKERT 821

Cryopreservation of Rat and Dog Hepatocytes for Studies of Xenobiotic Metabolism and Activation. G. POWIS, K. S. SANTONE, D. C. MELDER, L. THOMAS, D. J. WILKE, AND T. J. FEIL 826

Oxidative Metabolism of Butylated Hydroxytoluene by Hepatic and Pulmonary Microsomes from Rats and Mice. JOHN A. THOMPSON, ALVIN M. MALKINSON, MICHAEL D. WAND, SUSAN L. MASTOVICH, ELLIOTT W. MEAD, KATHLEEN M. SCHULLEK, AND WADE G. LAUDENSCHLAGER 833


Mechanism-based Inactivation of the Major β-Naphthoflavone-inducible Isozyme of Rat Liver Cytochrome P-450 by the Chloramphenicol Analog N-(2-p-Nitrophenethyl)chloroacetamide. NATALIE E. MILLER AND JAMES R. HALPERT 846

Selective Inactivation by Chloramphenicol of the Major Phenobarbital-inducible Isozyme of Dog Liver Cytochrome P-450. PAUL J. CIACCIO, DAVID B. DUIGNAN, AND JAMES R. HALPERT 852

Conversion of Bromobenzene to 3-Bromophenol. A Route to 3- and 4-Bromophenol through Sulfur-Series Intermediates Derived from the 3,4-Oxide. K. LERTRATANANGKOON, E. C. HORNING, AND M. G. HORNING 857


Mechanism of Metabolic Cleavage of a Furan Ring. TSUTOMU KOBAYASHI, JUKO SUGIHARA, AND TERRENCE INSON 877

Continued on next page
Contents (cont'd.)

Phenolic Metabolites of Amitriptyline and Nortriptyline in Rat Bile. Ursula Breyer-Pfaff, A. Prox, H. Wachsmuth, and PeiPei Yao .......... 882

Amitriptyline Metabolites in Human Urine. Identification of Phenols, Dihydrodiols, Glycols, and Ketones. A. Prox and Ursula Breyer-Pfaff ... 890

19F NMR Analysis of the Carbamate Reaction of α-Fluoro-β-alanine (FBAL), the Major Catabolite of Fluoropyrimidines. Application to FBAL Carbamate Determination in Body Fluids of Patients Treated with 5'-Deoxy-5-fluorouridine. R. Martino, M. C. Malet-Martino, C. Vialaneix, A. Lopez, and M. Bon ........ 897

Excretion and Biotransformation of Alfentanil and Sufentanil in Rats and Dogs. W. Meuldermans, J. Hendrickx, W. Lauwers, R. Hurkmans, E. Swysen, J. Thussen, Ph. Timmerman, R. Weestenboeck, and J. Heykants ................. 905

Metabolism of (+)-trans-Δ4-Tetrahydrocannabinol in the Mouse in Vitro and in Vivo. D. J. Harvey and H. J. Marriage .................. 914

SHORT COMMUNICATIONS

Identification of the Etodolac Metabolite, 4-Ureidoetodolac, in Mouse, Rat, Dog, and Man. E. S. Ferdinandi, D. Cochran, and R. Gedamke ... 921

[\(^{3}H\)]Chloramphenicol Metabolism in Human Volunteer: Oxamic Acid as a New Major Metabolite. D. E. Corpet and G. F. Bories .......... 925

Author Index ......................................................... 928

Subject Index ....................................................... 930