Drug Metabolism and Disposition: the biological fate of chemicals

January/February 1987

CONTENTS

Bromobenzene Metabolism in the Rat and Guinea Pig. K. LERTRATANAKHOON and M. G. HORNING .......................... 1


The Series-Compartment Model for Hepatic Elimination. MURRAY R. GRAY and Y. K. TAM .................. 27

Microsomal Metabolism of Pyrrolizidine Alkaloids from Senecio jacobaea: Isolation and Quantification of 6,7-Dihydro-7-Hydroxy-1-Hydroxymethyl-5H-Pyrrolizine and N-Oxides by High Performance Liquid Chromatography. HOWARD S. RASMDELL, BODGAN KEDZIERSKI, and DONALD R. BUHLER .......... 32

The Formation of Procainamide Hydroxylamine by the Inbred Hamster. DAVID W. HEIN, NANDA K. KIRLIN, FREDERICK OGOLLA, AND ALMA TRINIDAD .......... 59

Extrahepatic Expression of N-Acetylator Genotype in the Inbred Hamster. DAVID W. HEIN, WARD G. KIRLIN, FREDERICK OGOLLA, and ALMA TRINIDAD ............ 68

Metabolism of the β-Carboline, Harmine and Harmol, by Liver Microsomes from Phenobarbital- or 3-Methylcholanthrene-Treated Mice: Identification and Quantitation of Two Novel Harmine Metabolites. D. J. TWEEDE and M. D. BURKE .......... 74

Stereocchemical Aspects of the Glutathione S-Transferase-Catalyzed Conjugations of Alkyl Halides. RICHARD E. RIDGEBILL and MAHMOUD M. ABD-EL-MONEM .......... 82

Comparative Metabolism and Disposition of l-Chloro- and 3-Chloro-2-methylpropene in Rats and Mice. BURHAN I. GHANAYEM and LEO T. BURKA ......... 91


Disposition and Biotransformation of Quinpirole, a New D-2 Dopamine Agonist Antipsychotropic Agent, in Mice, Rats, Dogs, and Monkeys. N. G. GALILC WHITAKER and T. D. LINDSTROM ......... 107

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 .......... 114

Deacetylation of Diltiazem by Rat Liver. ELIZABETH LEBOEUF and ODETHE GRECH-BÉLANGER ......... 122

Plasma Concentration-Response Relationship for Cimetidine Inhibition of Drug Metabolism in the Rat. ADEDOYIN, LEON AARONS, and J. BRIAN HOUSTON .......... 127

SHORT COMMUNICATIONS

Comparison of Adenosine 3'-Phosphate 5'-Phosphosulfate Concentrations in Tissues from Different Laboratory Animals. ELIZBETA A. BRZEFICKA, GEORGE A. HAZELTON, and CURTIS D. KLAESEN ......... 133

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. DENSCH ......... 136

Effect of Surgery on Serum α,-Acid Glycoprotein Concentration and Serum Protein Binding of DL-Propranolol in Phenobarbital-Treated and Untreated Rats. TSU-HAN LIN, YUICHI SUGIYAMA, YASUFUMI CHU, R. F. RAMOS, and M. D. BURKE ......... 138

Books Received .................. 141

DRUG METABOLISM AND DISPOSITION (ISSN 0090-9556) is published bimonthly by the American Society for Pharmacology and Experimental Therapeutics, 428 E. Preston St., Baltimore MD 21202. Second class postage paid at Baltimore, MD and at additional mailing offices. Postmaster send address changes (Form 3579) to the Williams & Wilkins Co., 428 E. Preston St., Baltimore MD 21202. Price per volume: USA individual rate $60; all other countries $70 surface mail. USA institutional rate $95; all other countries $105 surface mail and $95 to $105 air mail depending upon location, single copy $15.00 ($17.00 foreign). Prices subject to change. Copyright © 1987 by the American Society for Pharmacology and Experimental Therapeutics.
Drug Metabolism and Disposition: 
the biological fate of chemicals

March/April 1987
Vol. 15, No. 2

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

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-dithiophanenonedioc 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. ECKAR T .......................................................... 161

In Vivo Metabolism of the Leukotriene Receptor Antagonist, 5-(2-Dodecylphenyl)-4,6-dithiophanenonedioc 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-aminooxazobenzene by Isolated Perfused Rat Liver. AUDREY R. SAMUELS, LORENZ THEILMANN, YACOV R. STOLLER, ALLAN W. WOLF KOFF, 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 Melphanal to 4-(Glutathionyl)phenylalanine. A Novel Mechanism for Conjugation by Glutathione-S-transferases. DEANNE M. DULIK AND CATHERINE FEN SELAU .......................................................... 195

Conversion of N,N-Dimethylalanine to N,N-Dimethylalanine-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

The Pharmacokinetics of All-trans-retinoic Acid and N(2)-Hydroxyethylretinamide in Mice as Determined with a Sensitive and Convenien Procedure. Solid-phase Extraction and Reverse-phase High Performance Liquid Chromatography. D. MUNSELL, MCPhILLIPS, JACK R. KALIN, AND D. L. HILL .......................................................... 207

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 Monooxygenases in Rat Liver. Role of Thiol Compounds. CAROL A. SHIVELY AND ELLIO T. VESEL .......................................................... 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, Theo phylline, 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 Met abolite in Man and Rat. Bioavailability and Dose Dependency Studies. REZA MEHRAR, FAHKREDIN JAMALI, MICHAEL W. B. WATSON, AND DAVID SKELTON .......................................................... 250


Metabolism of Ethyl 2-(4-Chlorophenyl)-5-(2-furyl)-oxoazole-4-acetate, a New Hypolipidemic Agent, in the Rat, Rabbit, and Dog. Glucuronidation of Carboxyl Group and Cleavage of Fur an Ring. TSUTOMU KOBAYASHI, HIDEHIRO ANDO, JUKO SUGIHARA, AND SHOICHI HIRAGA .......................................................... 262

Continued on next page

DRUG METABOLISM AND DISPOSITION (ISSN 0090-9556) is published bimonthly by the American Society for Pharmacology and Experimental Therapeutics, 428 E. Preston St., Baltimore MD 21202. Second class postage paid at Baltimore, MD and at additional mailing offices. Postmaster send address changes (Form 3579) to the Williams & Wilkins Co., 428 E. Preston St., Baltimore MD 21202. Price per volume: USA individual rate $60; all other countries $70 surface mail. USA institutional rate $95; all other countries $105 surface mail and $95 to $105 air mail depending upon location, single copy $15.00 ($17.00 foreign). Prices subject to change. Copyright © 1987 by the American Society for Pharmacology and Experimental Therapeutics.
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

<table>
<thead>
<tr>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatic UDP-glucose and UDP-glucuronic Acid Synthesis Rates in Rats during a Reduced Energy State.</td>
<td>281</td>
</tr>
<tr>
<td>Metabolism and Distribution of 14C- and 35S-Labeled Carbon Disulfide in Immature Rats of Different Ages.</td>
<td>289</td>
</tr>
<tr>
<td>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.</td>
<td>295</td>
</tr>
<tr>
<td>Pharmacokinetic and Deuterium Isotope Effect Studies on the Metabolism of Formaldehyde and Formate to Carbon Dioxide in Rats in Vivo.</td>
<td>300</td>
</tr>
<tr>
<td>3,4-Dichlorobenzoyloxyacetic Acid Is Extensively Metabolized to a Taurine Conjugate in Rats.</td>
<td>305</td>
</tr>
<tr>
<td>Diazepam Metabolism in Cultured Hepatocytes from Rat, Rabbit, Dog, Guinea Pig, and Man.</td>
<td>312</td>
</tr>
<tr>
<td>Disposition of 8-Methoxypsoralen in the Rat. Induction of Metabolism in Vivo and in Vitro and Identification of Urinary Metabolites by Thermospray Mass Spectrometry.</td>
<td>318</td>
</tr>
<tr>
<td>Effects of Cisplatin-induced Nephrotoxicity on Gentamicin Pharmacokinetics in Rats.</td>
<td>329</td>
</tr>
<tr>
<td>Induction and Inhibition of Rat Hepatic Drug Metabolism by N-Substituted Imidazole Drugs.</td>
<td>335</td>
</tr>
<tr>
<td>Influence of Cytochrome b5 on the Stoichiometry of the Different Oxidative Reactions Catalyzed by Liver Microsomal Cytochrome P-450.</td>
<td>344</td>
</tr>
<tr>
<td>The Formation of a Glutathione Conjugate Derived from Propranolol.</td>
<td>349</td>
</tr>
<tr>
<td>The Oxidation of Acrolein by Rat Liver Aldehyde Dehydrogenases. Relation to Allyl Alcohol Hepatotoxicity.</td>
<td>356</td>
</tr>
<tr>
<td>The Disposition and Elimination of Two Sequential Doses of 2,4,5,2',4',5'-Hexachlorobiphenyl.</td>
<td>363</td>
</tr>
<tr>
<td>Absorption, Distribution, Metabolism, and Excretion of 1,2-Dihydro-2,2,4-trimethylquinoline in the Male F344 Rat.</td>
<td>367</td>
</tr>
<tr>
<td>Pharmacokinetics of Griseofulvin in Blood and Skin Suction Blister Fluid of Rats.</td>
<td>374</td>
</tr>
<tr>
<td>Tissue Distribution, Disposition, and Metabolism of Cyclosporin in Rats.</td>
<td>377</td>
</tr>
<tr>
<td>Metabolism of Cyclosporin A. I. Study in Freshly Isolated Rabbit Hepatocytes.</td>
<td>384</td>
</tr>
<tr>
<td>Metabolism of Cyclosporin A. II. Implication of the Macrolide Antibiotic Inducible Cytochrome P-450.</td>
<td>391</td>
</tr>
<tr>
<td>Urinary Metabolites in Busulfan in the Rat.</td>
<td>399</td>
</tr>
<tr>
<td>Liver Metabolism of Budesonide in Rat, Mouse, and Man. Comparative Aspects.</td>
<td>403</td>
</tr>
<tr>
<td>Metabolic Acetal Splitting of Budesonide. A Novel Inactivation Pathway for Topical Glucocorticoids.</td>
<td>412</td>
</tr>
</tbody>
</table>

__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 Mee-teren-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. Koke, R. Norikura, S. Futaguchi, T. Yamaguchi, K. Sugeno, K. Iwataki, Y. Iken-ishi, 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. Col- burn, 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

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 .................. 437

An Investigation of the Antigenic Determinants on Chloroperoxidase and Purified Rat Liver Microsomal Cytochrome P-450b. RAMENDRA N. PANDAY, STEVEN C. KUEMMERLE, AND PAUL F. HOLLENBERG .................. 511

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

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

Stereoactive 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 Radioiodinated Human β-Endorphin in Rats. An Application of the Capillary Membrane-limited Model. HITOSHI SATO, YUICHI SUIGYAMA, 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 HORIE, MITSUKAZU KITADA, HIDEHUMI YOSHIOKA, YOSHIO KANAKUBO, AND TSUNEO OMURA 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, YOSHIO KANAKUBO, and TSUNEIO OMIURA 560

Drug Metabolism and Disposition: the biological fate of chemicals

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

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

Uptake, Toxicity, and Distribution of Benzo[a]pyrene and Monooxygenase Induction in the Topminnows Poeciliopsis monacha and Poeciliopsis lucida. KATHRYN A. GODDARD, 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. DEANNE M. DULIK AND CATHERINE FENSELAU .......... 473

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

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

Stereoactivity 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. BAHNSON ........... 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 Cytoxic Proteins and Its Role in Their Nuclear Translocation. KRISHNAPURA SRINIVASAN, WALTER G. LEVINE, AND MADHU M. BHARGAVA .......... 504


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

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. .......................................................... 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
Drug Metabolism and Disposition: the biological fate of chemicals

September/October 1987

Vol. 15, No. 5

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, CYNTYIA L. SETH, ROBERT H. MCCLEANAHAN, AND SIDNEY D. NELSON 589

The Disposition and Metabolism of 2',3'-Dideoxytubidine, an in Vitro Inhibitor of Human T-Lymphophotrophic Virus Type III Infection, in Mice and Monkeys. JAMES A. KELLEY, CHARLES L. LITTERST, JERI S. ROTH, DAVID T. VESTICA, 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 Trans-2-nonenal in B6C3F1 Mice. 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. SARNQUIST, BEE-LIAN HUANG, ANNE T. WU, LASZLO J. TOKES, SAMUEL BRODER, AND DAVID G. JOHNS 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-Hydroxypyrazole 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 Phencyclidine. 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)benzene[U-14C]sulfonamide in the Rat. D. G. 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. SHOAF, WAYNE S. SCHWARK, CHARLES L. GUARD, AND JOHN G. BABISH 676

The Metabolism of 7-Ethylbenz[a]lanthracene 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 C. FULLERTON, AND CARY, AND JOHN M. VAN GINNEKEN 695

Bioactivation of Tetrachloroethylene. Role of Glutathione S-Transferase-catalyzed Conjugation versus Cytochrome P-450-dependent Phospholipid Alkylation. WOLFGANG DEKANT, GISELA MARTENS, SYPRIDON VAMVAKAS, MANFRED METZLER, 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 Fluocytosine 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
SHORT COMMUNICATIONS

Influence of Gonadal Hormones upon Rat Hepatic Acetaminophen Sulfotransferases. ROBERT E. KANE AND LEE J. CHEN 725

Pharmacokinetics of Acetaminophen, Vancomycin, and Antipyrine in the Hanford Miniature Swine. M. B. BAILIE, D. A. FEDEROWICZ, K. DOLCE, C. KAHN, B. A. MICO, AND M. S. LANDI 729

Effect of Cyclosporine on Hepatic Oxidative and Conjugative Metabolism in Rats. RAYMOND E. GALINSKY, DONALD P. ALEXANDER, AND MICHAEL R. FRANKLIN 731
CONTENTS

The Disposition and Pharmacokinetics of Ketoconazole in the Rat. RORY P. REMMEL, KWAME AMOH, AND MAHMOUD M. ABDEL-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. THOMAS FORGUE, PRASAD R. B. ELIZABETH SUWITA, AMIN ABOU-DONIA, AND RICHARD M. ALLERHEILGEN . 749

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

Species-dependent Enantioselective Glucuronidation of Three 2-Arylpipionic Acids: Naproxen, Ibufrofen, and Benoxaprofen. MOHAMMAD EL MOUELHI, HANS W. RUELUS, CATHERINE FENSELAU, AND DEANNE M. DULIK . 767


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

Monooxygenase-mediated Activation of Chlorotriazine (TACE) in Covariant Binding to Rat Hepatic Microsomal Proteins. MARLENE J. JUDEE, WILLIAM H. BULGER, AND DAVID KUPFER . 786

The Pharmacokinetics of Pentane, a By-product of Lipid Peroxidation. SANDRA R. B. ALLERHEILGEN, 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 Cefepime. S. THOMAS FORGUE, PRASAD KARI, AND RASHMI BARBHAIA . 808

Isolation and Characterization of 4'-Hydroxy T-2 Toxin, a New Metabolite of the Trichothecene Myco toxin 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. NYSSTROM 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. MOORE, AND T. J. WILKE . 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

Evidence for Diazotization of [14C]-Sulfamethazine (4-Amino-N-(4,6-dimethyl-2-pyrimidinyl)benzene-[U-14C]-sulfanamide) in Swine. G. D. PAULSON AND V. J. FEIL . 841

Mechanism-based Inactivation of the Major β-Naphthoflavone-inducible Isozyme of Rat Liver Cytochrome P-450 by the Chloramphenicol Analog N-(2-p-Nitrophenethyl)dichloroacetamide. 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 KWAMOHAMAD ABDUL-MONEM . 877

Continued on next page
<table>
<thead>
<tr>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenolic Metabolites of Amitriptyline and Nortriptyline in Rat Bile. Ursula Breyer-Pfaff, A. Prox, H. Wachsmuth, and Peipei Yao</td>
<td>882</td>
</tr>
<tr>
<td>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</td>
<td>897</td>
</tr>
<tr>
<td>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. Woes- tenborghs, and J. Heykants</td>
<td>905</td>
</tr>
<tr>
<td>Metabolism of (+)-trans-Δ4-Tetrahydrocannabinol in the Mouse in Vitro and in Vivo. D. J. Harvey and H. J. Marriage</td>
<td>914</td>
</tr>
</tbody>
</table>

**SHORT COMMUNICATIONS**

<table>
<thead>
<tr>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Identification of the Etodolac Metabolite, 4-Ureido-etodolac, in Mouse, Rat, Dog, and Man. E. S. Ferdinandi, D. Cochran, and R. Gedamke</td>
<td>921</td>
</tr>
<tr>
<td>(3H)Chloramphenicol Metabolism in Human Volunteer: Oxamic Acid as a New Major Metabolite. D. E. Corpet and G. F. Bories</td>
<td>925</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Author Index</td>
<td>928</td>
</tr>
<tr>
<td>Subject Index</td>
<td>930</td>
</tr>
</tbody>
</table>