

# Drug Metabolism and Disposition:

the biological fate of chemicals

September/October 1993

Vol. 21, No. 5

## CONTENTS

Comparison of Human and Rhesus Monkey <i>in Vitro</i> Phase I and Phase II Hepatic Drug Metabolism Activities. JEFFREY C. STEVENS, LISA A. SHIPLEY, JOHN R. CASHMAN, MARK VANDENBRANDEN, AND STEVEN A. WRIGHTON . . . . .	753	Model Systems for Oxidative Drug Metabolism Studies: Catalytic Behavior of Water-soluble Metalloporphyrins Depends on Both the Intrinsic Robustness of the Catalyst and the Nature of Substrates. M. VIDAL, M. BONNAFOUS, S. DEFRANCE, P. LOISEAU, J. BERNADOU, AND B. MEUNIER . . . . .	811
Disposition of Sumatriptan in Laboratory Animals and Humans. C. M. DIXON, D. A. SAYNOR, P. D. ANDREW, J. OXFORD, A. BRADBURY, AND M. H. TARBIT . . . . .	761	Disposition of the <sup>3</sup> H-Labeled Gonadotropin-releasing Hormone Analog Buserelin in Rats. H. BERGER, J. SANDOW, N. HEINRICH, E. ALBRECHT, U. KERTSCHER, AND J. OEHLKE . . . . .	818
Temporal Effects of 1,1-Dichloroethylene on Nonprotein Sulphydryl Content in Murine Lung and Liver. P. GEK FORKERT AND MADELEINE MOUSSA . . . . .	770	Effect of Anticancer Drugs on the Glucuronidation of 3'-Azido-3'-deoxythymidine (AZT) in Human Liver Microsomes. JEAN FRANÇOIS RAJAONARISON, BRUNO LACARELLE, JACQUES CATALIN, ALAIN DURAND, AND JEAN PAUL CANO . . . . .	823
Rat Liver Microsomal Cytochrome P-450 Responsible for Reductive Metabolism of Zonisamide. HIROMITSU NAKASA, MORIYOSHI KOMIYA, SHIGERU OHMORI, TADAAKI RIKIHISA, AND MITSUKAZU KITADA . . . . .	777	<i>N</i> -Chlorination of Sulfamethoxazole and Dapsone by the Myeloperoxidase System. JACK P. UETRECHT, NEIL H. SHEAR, AND NASIR ZAHID . . . . .	830
The Effect of Nutritional Obesity on the Induction of CYP2B Enzymes Following Phenobarbital Treatment. PETER N. ZANNIKOS, ABHIK M. BANDYOPADHYAY, LARRY W. ROBERTSON, AND ROBERT A. BLOUIN . . . . .	782	Pharmacokinetics and Pharmacodynamics of Idrapril in Rats, Dogs, and Humans. MARCO CRISCUOLI, ANNALISA LIPPI, GRAZIA MENGOZZI, GIULIANA SARDELLI, ALESSANDRO SUBISSI, AND ANTONIO GIACCHETTI . . . . .	835
Metabolism of Benzophenone-3 in Rats. CHUKWUEMEKA S. OKEREKE, ABDELRAZAK M. KADRY, MOHAMED S. ABDEL-RAHMAN, RICHARD A. DAVIS, AND MARVIN A. FRIEDMAN . . . . .	788	Targeting of 6-Mercaptopurine to the Kidneys: Metabolism and Kidney-selectivity of <i>S</i> -(6-Puriny)-L-cysteine Analogs in Rats. ADNAN A. ELFARRA AND IN YOUNG HWANG . . . . .	841
<i>N</i> -Glucuronidation Reactions. I. Tetrazole <i>N</i> -Glucuronidation of Selected Angiotensin II Receptor Antagonists in Hepatic Microsomes from Rats, Dogs, Monkeys, and Humans. SU-ER W. HUSKEY, RANDALL R. MILLER, AND SHUET-HING LEE CHIU . . . . .	792	Pharmacokinetics of Cobalt Chloride and Cobalt-protoporphyrin. DANIEL W. ROSENBERG . . . . .	846
Uptake of Alendronate by Bone Tissue in Hypocalcemic and Hypercalcemic Rats. JIUNN H. LIN, I-WU CHEN, AND FLORENCIA A. DELUNA . . . . .	800	Isolation and Identification of a Novel Isomerized Epoxide Metabolite of FK-506 from Erythromycin-induced Rabbit Liver Microsomes. G. LHOËST, N. MATON, AND R. K. VERBEECK . . . . .	850
Differences in the Stereoselective Pharmacokinetics of Pazinaclone (DN-2327), A New Anxiolytic, and Its Active Metabolite after Intravenous and Oral Single Doses to Dogs. ZIAD HUSSEIN, DARCY J. MULFORD, BARBARA A. BOPP, AND G. RICHARD GRANNEMAN . . . . .	805	Pharmacokinetics and Metabolism of 3'-Azido-2',3'-dideoxy-5-methylcytidine in Rhesus Monkeys. F. DOUGLAS BOUDINOT, RAYMOND F. SCHINAZI, KOKILA J. DOSHI, HAROLD M. MCCLURE, AND CHUNG K. CHU . . . . .	855

Continued on next page

DRUG METABOLISM AND DISPOSITION (DMD/ISSN 0090-9556) is an official publication of The American Society for Pharmacology and Experimental Therapeutics and is published bimonthly beginning in January by Williams & Wilkins, 428 E. Preston St., Baltimore, MD 21202-3993. Second class postage paid at Baltimore, MD and at additional mailing offices. POSTMASTER: send address changes to DRUG METABOLISM AND DISPOSITION, 428 E. Preston St., Baltimore, MD 21202-3993. Subscription Rates: U.S.: Personal \$85.00; Institutional \$140.00; Single copy \$24.00. Outside the U.S., except Japan: Personal \$105.00; Institutional \$160.00; Single copy \$28.00. Foreign prices exclude Japan. See Information for Subscribers for detailed instructions. The GST Tax Number for Canadian subscribers is 123394371. Country of origin USA. PRICES ARE SUBJECT TO CHANGE. Indexed by *Index Medicus*, *Current Contents (Life Sciences)*, *Excerpta Medica*, *Reference Update/Research Information Systems*, and *BioSciences Information Service*. Copyright © 1993 by the American Society for Pharmacology and Experimental Therapeutics.

Characterization of Verlukast Metabolites Arising from an Epoxide Intermediate Produced with Hepatic Microsomes from $\beta$ -Naphthoflavone-treated Rodents (P-4501A1). D. A. NICOLL-GRIFFITH, N. CHAURET, J. A. YERGEY, L. A. TRIMBLE, L. FAVREAU, R. ZAMBONI, S. J. GROSSMAN, J. DREY, AND E. HEROLD .....	861	Rates of Excretion of Cotinine, Nicotine Glucuronide, and 3'-Hydroxycotinine Glucuronide in Rat Bile. MARK J. SEATON, GABRIEL A. KYEREMATEN, AND ELLIOT S. VESELL .....	927
Drug Metabolism Studies Using "Intrinsic" and "Extrinsic" Labels: A Demonstration Using $^{15}\text{N}$ vs. Cl in Midazolam. HENGCHANG SONG AND FRED ABRAMSON .....	868	Relationship between Lipophilicity and Hepatic Dispersion and Distribution for a Homologous Series of Barbiturates in the Isolated Perfused <i>in Situ</i> Rat Liver. CHEN-HSI CHOU, ALLAN M. EVANS, GIANFRANCO FORNASINI, AND MALCOLM ROWLAND ..	933
Bioactivation and Irreversible Binding of the Cognition Activator Tacrine Using Human and Rat Liver Microsomal Preparations: Species Difference. THOMAS F. WOOLF, WILLIAM F. POOL, SUSAN M. BJORGE, TSUN CHANG, O. P. GOEL, CLAUDE F. PURCHASE, II, MEL C. SCHROEDER, KENT L. KUNZE, AND WILLIAM F. TRAGER .....	874	Identification of Cytochrome P-450 Isozymes Involved in the Hydroxylation of Dantrolene by Rat Liver Microsomes. Z. JAYYOSI, J. VILLOUTREIX, J. M. ZIEGLER, A. M. BATT, F. DE MAACK, G. SIEST, AND P. E. THOMAS .....	939
Enzymatic Ring-opening Reactions of the Chiral Cardioprotective Agents (+)S-ICRF-187 and its (-)R-Enantiomer ICRF-186 by Dihydropyrimidine Amidohydrolase. BRIAN B. HASINOFF .....	883	Reduction of 3'-Azido-2',3'-dideoxynucleosides to Their 3'-Amino Metabolite is Mediated by Cytochrome P-450 and NADPH-Cytochrome P-450 Reductase in Rat Liver Microsomes. ERIKA M. CRETTON AND JEAN-PIERRE SOMMADOSSI .....	946
Identification of Carbamoylated Thiol Conjugates as Metabolites of the Antineoplastic 1-(2-Chloroethyl)-3-cyclohexyl-1-nitrosourea, in Rats and Humans. ANTHONY G. BOREL AND FRANK S. ABBOTT .....	889	Disposition of Tirilazad (U74006F), A 21-Aminosteroid, in the Plasma, Heart, Brain, and Liver of the Rat. S. CASEY LAIZURE, L. KAREN FRANKLIN, DAVID G. KAISER, CHERI L. WILLIAMS, ROBERT C. STEVENS, PAULA L. SANDERS, AND MARIO MILLER .....	951
Glucuronidation as a Transient Intermediate Metabolic Step in the Elimination of (-)-Carbovir: Identification of (-)-Carbovir-5'-O-glucuronide in Rat Bile. CHERYL L. ZIMMERMAN, KRISHNA R. IYER, A. LAWRENCE FAUDSKAR II, AND RORY P. REMMEL .....	902	Detection and Identification of Human Urinary Metabolites of Biantrazole (CI-941). JOACHIM BLANZ, ULF RENNER, KARL SCHMEER, GERHARD EHNINGER, AND KLAUS-PETER ZELLER .....	955
A Strategy for Characterization of Polyethylene Glycol-derivatized Proteins: A Mass Spectrometric Analysis of the Attachment Sites in Polyethylene Glycol-derivatized Superoxide Dismutase. MARTHA M. VESTLING, CONSTANCE M. MURPHY, DEBORAH A. KELLER, CATHERINE FENSELAU, JONAS DEDINAS, DAVID L. LADD, AND MARK A. OLSEN .....	911	<b>SHORT COMMUNICATIONS</b>	
Metabolism and Elimination of Oxazepam in B6C3F1 and Swiss-Webster Mice. ROBERT J. GRIFFIN AND LEO T. BURKA .....	918	<i>N</i> <sup>G</sup> -Nitro-L-arginine Pharmacokinetics in Rats after a Single Intravascular and Oral Dose: An Appearance of Secondary Concentration Time Peaks. V. K. PIOTROVSKIJ, Z. KÁLLAY, K. KREJCY, J. HORECKÝ, T. TRNOVEC, AND G. RABERGER .....	962
		<i>N</i> -Acetylation Polymorphism in Liver and Pancreas of Inbred Rats. KAREN J. MARTELL AND WENDELL W. WEBER .....	965
		Nitrite Ion Is Not an Active Intermediate in the Vascular Metabolism of Organic Nitrates and Organic Nitrites to Nitric Oxide. ELIZABETH A. KOWALUK, SUK-JAE CHUNG, AND HO-LEUNG FUNG .....	967
		Errata .....	970