Drug Metabolism and Disposition:
the biological fate of chemicals

CONTENTS

ACCELERATED COMMUNICATION

Three-Dimensional Quantitative Structure-Activity Relationship for Inhibitors of Cytochrome P4502C9. Jeffrey P. Jones, Mingxia He, William F. Trager, and Allan E. Rettie .......................... 1

ARTICLES

Trout Liver Slices for Metabolism and Toxicity Studies. Yasmin Singh, Janis B. Cooke, David E. Hinton, and Marion G. Miller ........................................ 7


Erythromycin as a Specific Substrate for Cytochrome P4503A Isozymes and Identification of a High-Affinity Erythromycin N-Demethylase in Adult Female Rats. Xu-Jie Zhang and Paul E. Thomas ........................................... 23

Gender Differences in Toxicokinetics, Liver Metabolism, and Plasma Esterase Activity: Observations from a Chronic (27-Week) Toxicity Study of Enalapril/Diltiazem Combinations in Rats. Layne E. Los, Deborah A. Welsh, Eugene G. Herold, Walter J. Bagdon, and Anthony G. Zacchei ... 28

The Pharmacokinetics and Extra-Hepatic Clearance of Remifentanil, a Short Acting Opioid Agonist, in Male Beagle Dogs during Constant Rate Infusions. J. P. Chism and D. E. Rickert ........................................... 34

N-Acetyl-S-(1,2,2-trichlorovinyl)-L-cysteine and 2,2,2-Trichloroethanol: Two Novel Metabolites of Tetrachloroethene in Humans after Occupational Exposure. Gerhard Birner, Anita Rutkowska, and Wolfgang Dekant ........................................... 41

Pharmacokinetics of Stable Isotopically Labeled l-Histidine in Humans and the Assessment of in Vivo Histidine Ammonia Lyase Activities. Takashi Furuta, Kazuhiro Okamiya, Hiromi Shibasaki, and Yasuji Kasuya ........................................... 49

Synthesis of Putative Metabolites and Investigation of the Metabolic Fate of Gliclazide, [l-(3-Aza-bicyclo(3,3,0)oct-3-yl)-3-(4-methylphenylsulfonyl)urea], in Diabetic Patients. Albert R. Taylor, Robin D. Brownell, Hubert Grandon, Francois Lefoulon, Alain Petit, Wil Luijten, Peter G. Kopelman, and Bernard Walther ........................................... 55


Participation of Cytochromes P4502B and P4503A in Cocaine Toxicity in Rat Hepatocytes. Torka S. Poet, Charlene A. McQueen, and James R. Halpert ........................................... 74

Mouse Liver Microsomal Metabolism of Chloral Hydrate, Trichloroacetic Acid, and Trichloroethanol Leading to Induction of Lipid Peroxidation via a Free Radical Mechanism. Yi-Chang Ni, Tzi-Yee Wong, Roger V. Lloyd, Thomas M. Heinzle, Sharon Shelton, Daniel Casciano, Fred F. Kadlubar, and Peter F. Fu ........................................... 81

Continued on next page
Contents (cont’d.)

Pharmacokinetics, Absolute Bioavailability, and Disposition of [14C]Nefazodone in Humans. RASHMI H. BARBHAIYA, KISHOR A. DANDEKAR, AND DOUGLAS S. GREENE ................................................. 91

Disposition Kinetics of Human Epidermal Growth Factor (hEGF1–53) and Its Truncated Fragment (hEGF1–48) in Rats. BE-SHENG KUO, GERALD D. NORDBLOM, RICHARD C. DUDECK, LORRAINE S. KIRKISH, AND D. SCOTT WRIGHT ......... 96

The 3-Hydroxypyridin-4-ones More Effectively Chelate Aluminum in a Rabbit Model of Aluminum Intoxication Than Does Desferrioxamine. ROBERT A. YOKEL, KATHRYN A. MEURER, THOMAS L. SKINNER, AND ANDREA M. FREDENBURG ....... 105

Propranolol Hydroxylation and N-Desisopropylation by Cytochrome P4502D6: Studies Using the Yeast-Expressed Enzyme and NADPH/O2 and Cumene Hydroperoxide-Supported Reactions. NEVE NEVENE BICHARA, MICHAEL S. CHING, CAROLYN L. BLAKE, HANY GHABRIAL, AND RICHARD A. SMALLWOOD .... 112

Identification of β-Glucuronidase-Resistant Diastereomeric Glucuronides of 3-Hydroxy-3-methyloxindole Formed during 3-Methylindole Metabolism in Goats. DAVID J. SMITH, MARTIN L. APPLETON, JAMES R. CARLSON, AND GAROLD S. YOST ..... 119