

# Drug Metabolism and Disposition: the biological fate of chemicals

October 1996

Vol. 24, No. 10

## CONTENTS

### LETTER TO THE EDITOR

The Importance of Nonspecific Binding in *In Vitro* Matrices, Its Impact on Enzyme Kinetic Studies of Drug Metabolism Reactions, and Implications for *In Vitro-In Vivo* Correlations. R. SCOTT OBACH. . . . . 1047

### ARTICLES

Stereoselective Irreversible Binding of Ketoprofen Glucuronides to Albumin: Characterization of the Site and the Mechanism. NATHALIE PRESLE, FRANÇOISE LAPICQUE, SYLVIE FOURNEL-GIGLEUX, JACQUES MAGDALOU, AND PATRICK NETTER . . . . . 1050

Systemic Clearance and Demethylation of Caffeine in Sheep and Cattle. TERRY J. DANIELSON AND LORRAINE R. GOLSTEYN . . . . . 1058

Comparative Toxicokinetics of Methanol in Pregnant and Nonpregnant Rodents. KEITH W. WARD AND GARY M. POLLACK . . . . . 1062

Excretion and Metabolism of Tippedane, a Novel Glucocorticoid, in the Rat, Mouse, Monkey, and Human. A. E. COOPER, A. J. GRAY, J. COLLINGTON, H. SEDDON, I. BEATTIE, AND C. J. LOGAN . . . . . 1071

Human CYP2C19 is a Major Omeprazole 5-Hydroxylase, as Demonstrated with Recombinant Cytochrome P450 Enzymes. W. G. KARAM, J. A. GOLDSTEIN, J. M. LASKER, AND B. I. GHANAYEM . . . . . 1081

Reversal of Stereoselectivity in the Hepatic Availability of Verapamil in Isolated Perfused Rat Livers: Role of Protein Binding. REZA MEHVAR AND JAMES REYNOLDS . . . . . 1088

Regulation of Rat Hepatic Sulfotransferase Gene Expression by Glucocorticoid Hormones. MELISSA RUNGE-MORRIS, KELLY ROSE, AND THOMAS A. KOCAREK . . . . . 1095

Disposition of a Novel Recombinant Antithrombotic Agent, RG 12986, in Cynomolgus Monkeys. DAVID S. WELLS, RUSSELL HENSEL, COSTAS LOULLIS, PATRICIA BROPHY, MARY ELLEN MULLIN, EDWARD MURRAY, AND GEORGE RICCA . . . . . 1102

Transfer of Different Nonsteroidal Antiinflammatory Drugs via the Lymphatic System in the Rat. RIEKE OELKERS, MIHAI IONAC, KATHARINA ERB, KAY BRUNE, AND GERD GEISSLINGER . . . . . 1107

Species Differences in the Pharmacokinetics and Metabolism of Indinavir, a Potent Human Immunodeficiency Virus Protease Inhibitor. JUNN H. LIN, MASATO CHIBA, SURESH K. BALANI, I-WU CHEN, GLORIA Y-S. KWEL, KARI J. VASTAG, AND JOY A. NISHIME . . . . . 1111

The Nifedipine-Rifampin Interaction: Evidence for Induction of Gut Wall Metabolism. NORBERT HOLTBECKER, MARTIN F. FROMM, HEYO K. KROEMER, EDGAR E. OHNHAUS, AND HUGO HEIDEMANN . . . . . 1121

Isolation and Identification of Metabolites of Leukotriene A<sub>4</sub> Hydrolase Inhibitor SC-57461 in Rats. JIN H. YUAN, JILL BIRKMEIER, DAI CHANG YANG, JEREMY D. HRIBAR, NORMAN LIU, ROY BIBLE, ELISABETH HAJDU, MARIE ROCK, AND GRANT SCHOENHARD . . . . . 1124

Fluoroquinolone Antibiotics Inhibit Cytochrome P450-Mediated Microsomal Drug Metabolism in Rat and Human. ROMAN A. McLELLAN, ROBERT K. DROBITCH, MARIO MONSHOUWER, AND KENNETH W. RENTON . . . . . 1134

Continued on next page

*Contents (cont'd.)*

<b>Metabolism of an Atypical Antipsychotic Agent, 3-[4-[4-(6-Fluorobenzo[<i>b</i>]thien-3-yl)-1-piperazinyl]-butyl]-2,5,5-trimethyl-4-thiazolidinone (HP236). A. E. MUTLIB, J. JURCAK, AND N. HRIB . . . . .</b>	<b>1139</b>
<b>Characterization of Glucuronidated Phase II Metabolites of the Immunosuppressant Cyclosporine in Urine of Transplant Patients Using Time-of-Flight Secondary-Ion Mass Spectrometry. K. MEYER, M. FOKKER, U. CHRISTIANS, M. ERREN, K.-F. SEWING, G. ASSMANN, AND A. BENNINGHOVEN . . . . .</b>	<b>1151</b>
<b>Role of Altered Metabolism in Dideoxynucleoside Pharmacokinetics: Studies of 2'-<math>\beta</math>-Fluoro-2',3'-Dideoxyinosine and 2'-<math>\beta</math>-Fluoro-2',3'-Dideoxyadenosine in Rats. DHARMENDRA SINGHAL, MICHAEL E. MORGAN, AND BRADLEY D. ANDERSON . . . . .</b>	<b>1155</b>
<b>Stereoselective Disposition of the Enantiomers of the Benzoquinolinone LY191704, a Human Type I 5<math>\alpha</math>-Reductase Inhibitor: Differences Between Rats and Dogs. NAGY A. FARID, KURT M. SCHREINER, NIKOLA L. COLEMAN, ROBERT B. L. VAN LIER, AND STEVEN A. WRIGHTON . . . . .</b>	<b>1162</b>
<b>Erratum. . . . .</b>	<b>1166</b>