

DRUG METABOLISM AND DISPOSITION

A Publication of the American Society for Pharmacology and Experimental Therapeutics

July 2008

Vol. 36, No. 7

CONTENTS

SHORT COMMUNICATIONS

The Antiapoptotic Factor Growth Arrest and DNA-Damage-Inducible 45 β Regulates the Nuclear Receptor Constitutive Active/Androstane Receptor-Mediated Transcription. *Yukio Yamamoto and Masahiko Negishi* **1189**

Hepatocellular Binding of Drugs: Correction for Unbound Fraction in Hepatocyte Incubations Using Microsomal Binding or Drug Lipophilicity Data. *Peter J. Kilford, Michael Gertz, J. Brian Houston, and Aleksandra Galetin* **1194**

An in Vitro Mechanistic Study to Elucidate the Desipramine/Bupropion Clinical Drug-Drug Interaction. *Melinda J. Reese, Robert M. Wurm, Keith T. Muir, Grant T. Generaux, Lisa St. John-Williams, and Donavon J. McConn* **1198**

Aldehyde Oxidase-Catalyzed Metabolism of N^1 -Methylnicotinamide in Vivo and in Vitro in Chimeric Mice with Humanized Liver. *Shigeyuki Kitamura, Kayoko Nitta, Yoshitaka Tayama, Chiaki Tanoue, Kazumi Sugihara, Tae Inoue, Toru Horie, and Shigeru Ohta* **1202**

Inhibitory Effects of Terpenoids on Multidrug Resistance-Associated Protein 2- and Breast Cancer Resistance Protein-Mediated Transport. *Naoko Yoshida, Tappei Takada, Yoshikazu Yamamura, Isao Adachi, Hiroshi Suzuki, and Junichi Kawakami* **1206**

ARTICLES

Osmotic Regulation of a Novel Flavin-Containing Monooxygenase in Primary Cultured Cells from Rainbow Trout (*Oncorhynchus mykiss*). *Gabriela Rodríguez-Fuentes, Rosaura Aparicio-Fabre, Qi Li, and Daniel Schlenk* **1212**

Disposition of Lasofoxifene, a Next-Generation Selective Estrogen Receptor Modulator, in Healthy

Male Subjects. *Chandra Prakash, Kim A. Johnson, and Mark J. Gardner* **1218**

The Biotransformation of Prasugrel, a New Thienopyridine Prodrug, by the Human Carboxylesterases 1 and 2. *Eric T. Williams, Karen O. Jones, G. Douglas Ponsler, Shane M. Lowery, Everett J. Perkins, Steven A. Wrighton, Kenneth J. Ruterbories, Miho Kazui, and Nagy A. Farid* **1227**

Pharmacokinetic Parameters of Chlorzoxazone and Its Main Metabolite, 6-Hydroxychlorzoxazone, after Intravenous and Oral Administration of Chlorzoxazone to Liver Cirrhotic Rats with Diabetes Mellitus. *Choong Y. Ahn, Soo K. Bae, Young S. Jung, Inchul Lee, Young C. Kim, Myung G. Lee, and Wan G. Shin* **1233**

Differential Genotype Dependent Inhibition of CYP2C9 in Humans. *Vikas Kumar, Richard C. Brundage, William S. Oetting, Ilo E. Leppik, and Timothy S. Tracy* **1242**

Closing the Gaps: A Full Scan of the Intestinal Expression of P-Glycoprotein, Breast Cancer Resistance Protein, and Multidrug Resistance-Associated Protein 2 in Male and Female Rats. *Caroline MacLean, Ulla Moenning, Andreas Reichel, and Gert Fricker* **1249**

Prediction of Pharmacokinetic Drug-Drug Interactions Using Human Hepatocyte Suspension in Plasma and Cytochrome P450 Phenotypic Data. II. In Vitro-in Vivo Correlation with Ketoconazole. *Chuang Lu, Panos Hatsis, Cicely Berg, Frank W. Lee, and Suresh K. Balani* **1255**

Prediction of Pharmacokinetic Drug-Drug Interactions Using Human Hepatocyte Suspension in Plasma and Cytochrome P450 Phenotypic Data. III. In Vitro-in Vivo Correlation with Fluconazole. *Chuang Lu, Cicely Berg, Shimoga R. Prakash, Frank W. Lee, and Suresh K. Balani* **1261**

Continued on next page

Pharmacokinetic-Pharmacodynamic Modeling of Biomarker Response and Tumor Growth Inhibition to an Orally Available cMet Kinase Inhibitor in Human Tumor Xenograft Mouse Models. <i>Shinji Yamazaki, Judith Skaptason, David Romero, Joseph H. Lee, Helen Y. Zou, James G. Christensen, Jeffrey R. Koup, Bill J. Smith, and Tatiana Koudriakova</i>	1267
Effect of Plasma Protein Binding on in Vitro-in Vivo Correlation of Biliary Excretion of Drugs Evaluated by Sandwich-Cultured Rat Hepatocytes. <i>Hajime Fukuda, Rikiya Ohashi, Minoru Tsuda-Tsukimoto, and Ikumi Tamai</i>	1275
Effects of Spice Constituents on P-Glycoprotein-Mediated Transport and CYP3A4-Mediated Metabolism in Vitro. <i>Wenxia Zhang and Lee-Yong Lim</i>	1283
The Mibefradil Derivative NNC55-0396, a Specific T-Type Calcium Channel Antagonist, Exhibits Less CYP3A4 Inhibition than Mibefradil. <i>Peter H. Bui, Arnulfo Quesada, Adrian Handforth, and Oliver Hankinson</i>	1291
Drug Transporter and Cytochrome P450 mRNA Expression in Human Ocular Barriers: Implications for Ocular Drug Disposition. <i>Tao Zhang, Cathie D. Xiang, David Gale, Samantha Carreiro, Ellen Y. Wu, and Eric Y. Zhang</i>	1300
Inhibitory Effects of Seven Components of Danshen Extract on Catalytic Activity of Cytochrome P450 Enzyme in Human Liver Microsomes. <i>Furong Qiu, Rong Zhang, Jianguo Sun, Jiye A, Haiping Hao, Ying Peng, Hua Ai, and Guangji Wang</i>	1308
Cellular Accumulation of Chollyl-Glycylamido-Fluorescein in Sandwich-Cultured Rat Hepatocytes: Kinetic Characterization, Transport Mechanisms, and Effect of Human Immunodeficiency Virus Protease Inhibitors. <i>Zhi-wei Ye, Patrick Augustijns, and Pieter Annaert</i>	1315
[S] Functional Expression and Comparative Characterization of Nine Murine Cytochromes P450 by Fluorescent Inhibition Screening. <i>Lesley A. McLaughlin, Leslie J. Dickmann, C. Roland Wolf, and Colin J. Henderson</i>	1322
Comparative Analysis of CYP3A Heteroactivation by Steroid Hormones and Flavonoids in Different in Vitro Systems and Potential in Vivo Implications. <i>Jamie Henshall, Aleksandra Galetin, Anthony Harrison, and J. Brian Houston</i>	1332
Biotransformation of [¹⁴ C]Dasatinib: In Vitro Studies in Rat, Monkey, and Human and Disposition after Administration to Rats and Monkeys. <i>Lisa J. Christopher, Donghui Cui, Wenying Li, Anthony Barros, Jr., Vinod K. Arora, Haiying Zhang, Lifei Wang, Donglu Zhang, James A. Manning, Kan He, Anthony M. Fletcher, Marc Ogan, Michael Lago, Samuel J. Bonacorsi, W. Griffith Humphreys, and Ramaswamy A. Iyer</i>	1341
Metabolism and Disposition of Dasatinib after Oral Administration to Humans. <i>Lisa J. Christopher, Donghui Cui, Chiyuan Wu, Roger Luo, James A. Manning, Samuel J. Bonacorsi, Michael Lago, Alban Allentoff, Francis Y. F. Lee, Betty McCann, Susan Galbraith, Donald P. Reitberg, Kan He, Anthony Barros, Jr., Anne Blackwood-Chirchir, W. Griffith Humphreys, and Ramaswamy A. Iyer</i>	1357
[S] Prediction of the Pharmacokinetics of Atorvastatin, Cerivastatin, and Indomethacin Using Kinetic Models Applied to Isolated Rat Hepatocytes. <i>Stuart W. Paine, Alison J. Parker, Philip Gardiner, Peter J. H. Webborn, and Robert J. Riley</i>	1365
Rate-Limiting Steps in Hepatic Drug Clearance: Comparison of Hepatocellular Uptake and Metabolism with Microsomal Metabolism of Saquinavir, Nelfinavir, and Ritonavir. <i>Alison J. Parker and J. Brian Houston</i>	1375
[S] Trend Analysis of a Database of Intravenous Pharmacokinetic Parameters in Humans for 670 Drug Compounds. <i>R. Scott Obach, Franco Lombardo, and Nigel J. Waters</i>	1385
Use of Online Microdialysis Sampling to Determine the in Vivo Rate of Phenol Glucuronidation in Rainbow Trout. <i>John W. Nichols, Alex D. Hoffman, Patrick N. Fitzsimmons, Gregory J. Lien, and Correne T. Jenson</i>	1406
In Silico Methods for Unraveling the Mechanistic Complexities of Intestinal Absorption: Metabolism-Efflux Transport Interactions. <i>Lana X. Garmire and C. Anthony Hunt</i>	1414
[S] Bioactivation of Flutamide Metabolites by Human Liver Microsomes. <i>Ping Kang, Deepak Dalvie, Evan Smith, Sue Zhou, Alan Deese, and James A. Nieman</i>	1425
Down-Regulation of a Hepatic Transporter Multidrug Resistance-Associated Protein 2 Is Involved in Alteration of Pharmacokinetics of Glycyrrhizin and Its Metabolites in a Rat Model of Chronic Liver Injury. <i>Toshiaki Makino, Nobuhiro Ohtake, Akito Watanabe, Naoko Tsuchiya, Sachiko Imamura, Seiichi Iizuka, Makoto Inoue, and Hajime Mizukami</i>	1438
[S] Evaluation of HepaRG Cells as an in Vitro Model for Human Drug Metabolism Studies. <i>Kajsa P. Kanebratt and Tommy B. Andersson</i>	1444

[S] Supplemental material is available online at <http://dmd.aspetjournals.org>.

About the cover: Expression of mRNA for 44 genes in cryopreserved human hepatocytes and in differentiated HepaRG cells cultured with and without dimethyl sulfoxide ($n = 3$, human hepatocyte batches 1, 4, and 5). See article by Kanebratt and Andersson on page 1444 of this issue.