

# DRUG METABOLISM AND DISPOSITION

A Publication of the American Society for Pharmacology and Experimental Therapeutics

March 2009

Vol. 37, No. 3

## CONTENTS

### SHORT COMMUNICATIONS

Pinoline May be Used as a Probe for CYP2D6 Activity. *Xi-Ling Jiang, Hong-Wu Shen, and Ai-Ming Yu* . . . . . **443**

Use of Sandwich-Cultured Human Hepatocytes to Predict Biliary Clearance of Angiotensin II Receptor Blockers and HMG-CoA Reductase Inhibitors. *Koji Abe, Arlene S. Bridges, and Kim L. R. Brouwer* . . . . . **447**

Sex-Related Differences in the Expression of *mfG-STA2*, a Novel *GST* Identified in Cynomolgus Monkey (*Macaca fascicularis*). *Yasuhiro Uno, Tsukasa Ohuchi, Shotaro Uehara, Go Kito, Tetsuya Kamataki, and Ryoichi Nagata* . . . . . **453**

Evaluation of *Escherichia coli* Membrane Preparations of Canine CYP1A1, 2B11, 2C21, 2C41, 2D15, 3A12, and 3A26 with Coexpressed Canine Cytochrome P450 Reductase. *Charles W. Locu-son, Brian T. Ethell, Michael Voice, David Lee, and Kenneth L. Feenstra* . . . . . **457**

### ARTICLES

Ⓢ Hepatic Flavin-Containing Monooxygenase Gene Regulation in Different Mouse Inflammation Models. *Jun Zhang, Madhusudana R. Chaluvadi, Rob Reddy, Meike S. Motika, Terrilyn A. Richardson, John R. Cashman, and Edward T. Morgan* . . . . . **462**

Ⓢ Mechanism of Vitamin D Receptor Inhibition of Cholesterol 7 $\alpha$ -Hydroxylase Gene Transcription in Human Hepatocytes. *Shuxin Han and John Y. L. Chiang* . . . . . **469**

Investigation of the in Vitro Metabolism of the Analgesic Flupirtine. *Karen Methling, Przyemslaw Reszka, Michael Lalk, Oldrich Vrana, Eberhard Scheuch, Werner Siegmund, Bernd Terhaag, and Patrick J. Bednarski* . . . . . **479**

5'-Aminocarbonyl Phosphonates as New Zidovudine Depot Forms: Antiviral Properties, Intracellular Transformations, and Pharmacokinetic Parameters. *Anastasia L. Khandazhinskaya, Dmitry V. Yanvarev, Maxim V. Jasko, Alexander V. Shipitsin, Vsevolod A. Khalizev, Stanislav I. Shram, Yuriy S. Skoblov, Elena A. Shirokova, and Marina K. Kukhanova* . . . . . **494**

An Inhibitory Metabolite Leads to Dose- and Time-Dependent Pharmacokinetics of (*R*)-*N*-{1-[3-(4-Ethoxy-phenyl)-4-oxo-3,4-dihydro-pyrido[2,3-*d*]-pyrimidin-2-yl]-ethyl}-*N*-pyridin-3-yl-methyl-2-(4-trifluoromethoxy-phenyl)-acetamide (AMG 487) in Human Subjects After Multiple Dosing. *George R. Tonn, Simon G. Wong, Sylvia C. Wong, Michael G. Johnson, Ji Ma, Robert Cho, Leslie C. Floren, Kathryn Kersey, Karen Berry, Andrew P. Marcus, Xuemei Wang, Bettina Van Lengerich, Julio C. Medina, Paul G. Pearson, and Bradley K. Wong* . . . . . **502**

Identification of a Cranberry Juice Product that Inhibits Enteric CYP3A-Mediated First-Pass Metabolism in Humans. *Ngoc Ngo, Zhixia Yan, Tyler N. Graf, Daniel R. Carrizosa, Angela D. M. Kashuba, E. Claire Dees, Nicholas H. Oberlies, and Mary F. Paine* . . . . . **514**

Developmental Expression and Endocrine Regulation of CYP1B1 in Rat Testis. *Grace S. Leung, Masahiko Kawai, Jenny K. Tai, Jie Chen, Stelvio M. Bandiera, and Thomas K. H. Chang* . . . . . **523**

*Continued on next page*

*Drug Metabolism and Disposition* (ISSN 0090-9556) is published monthly (one volume per year) by the American Society for Pharmacology and Experimental Therapeutics, 9650 Rockville Pike, Bethesda, MD 20814-3995; e-mail: subscriptions@aspet.org; web site: aspet.org. Periodicals postage paid at Bethesda, MD, and at additional mailing offices. POSTMASTER: Send address changes to *Drug Metabolism and Disposition*, 9650 Rockville Pike, Bethesda, MD 20814-3995. Subscription rates: U.S.: \$400.00; outside the U.S.: \$479. Single copy: \$36. GST Tax Number for Canadian subscribers: BN:13489 2330 RT. Indexed or abstracted by *Biochemistry & Biophysics Citation Index*®, *Biological Abstracts*, *BIOSIS Previews Database*, *BioSciences Information Services*, *Current Awareness in Biological Sciences*, *Current Contents*®/Life Sciences, *EMBASE/Excerpta Medica*, *Index Medicus*, *International Pharmaceutical Abstracts*, *Medical Documentation Service*®, *Reference Update*®, *Research Alerts*®, *Science Citation Index*®, *SciSearch*®, and *SIC Data Bases* Copyright © 2009 by the American Society for Pharmacology and Experimental Therapeutics. All rights reserved. Printed in the U.S.A.


Downloaded from dmd.aspetjournals.org at ASPET Journals on December 21, 2024

DRUG METABOLISM & DISPOSITION

Fexofenadine Brain Exposure and the Influence of Blood-Brain Barrier P-Glycoprotein After Fexofenadine and Terfenadine Administration. <i>Rong Zhao, J. Cory Kalvass, Souzan B. Yanni, Arlene S. Bridges, and Gary M. Pollack</i> . . . . .	<b>529</b>	strates Using Small GTP-Binding Protein Rab8-Null Mice. <i>Yukio Kato, Tomoko Sugiura, Yasuhiro Nakadera, Mikihiro Sugiura, Yoshiyuki Kubo, Takashi Sato, Akihiro Harada, and Akira Tsuji</i> . . . . .	<b>602</b>
Absorption, Metabolism, and Excretion of [ <sup>14</sup> C]-Vildagliptin, a Novel Dipeptidyl Peptidase 4 Inhibitor, in Humans. <i>Handan He, Phi Tran, Hequn Yin, Harold Smith, Yannick Batard, Lai Wang, Heidi Einolf, Helen Gu, James B. Mangold, Volker Fischer, and Dan Howard</i> . . . . .	<b>536</b>	SIMDOT-AbMe: Microphysiologically Based Simulation Tool for Quantitative Prediction of Systemic and Local Bioavailability of Targeted Oral Delivery Formulations. <i>Nahor Haddish-Berhane, Ashkan Farhadi, Chell Nyquist, Kamyar Haghighi, and Ali Keshavarzian</i> . . . . .	<b>608</b>
Disposition of Vildagliptin, a Novel Dipeptidyl Peptidase 4 Inhibitor, in Rats and Dogs. <i>Handan He, Phi Tran, Hequn Yin, Harold Smith, Dennis Flood, Roger Kramp, Ron Filipeck, Volker Fischer, and Dan Howard</i> . . . . .	<b>545</b>	Carrier-Mediated Uptake of 1-(2-Methoxyethyl)-2-methyl-4,9-dioxo-3-(pyrazin-2-ylmethyl)-4,9-dihydro-1 <i>H</i> -naphtho[2,3- <i>d</i> ]imidazolium Bromide (YM155 Monobromide), a Novel Small-Molecule Survivin Suppressant, into Human Solid Tumor and Lymphoma Cells. <i>Tsuyoshi Minematsu, Megumi Iwai, Kenji Sugimoto, Nobuaki Shirai, Takahito Nakahara, Takashi Usui, and Hidetaka Kamimura</i> . . . . .	<b>619</b>
The Inhibition of Human Multidrug and Toxin Extrusion 1 Is Involved in the Drug-Drug Interaction Caused by Cimetidine. <i>Soichiro Matsushima, Kazuya Maeda, Katsuhisa Inoue, Kin-ya Ohta, Hiroaki Yuasa, Tsunenori Kondo, Hideki Nakayama, Shigeru Horita, Hiroyuki Kusuhara, and Yuichi Sugiyama</i> . . . . .	<b>555</b>	Mechanism of CYP2C9 Inhibition by Flavones and Flavonols. <i>Dayong Si, Ying Wang, Yi-Han Zhou, Yingjie Guo, Juan Wang, Hui Zhou, Ze-Sheng Li, and J. Paul Fawcett</i> . . . . .	<b>629</b>
Substrate-Dependent Breast Cancer Resistance Protein (Bcrp1/Abcg2)-Mediated Interactions: Consideration of Multiple Binding Sites in in Vitro Assay Design. <i>Nagdeep Giri, Sagar Agarwal, Naveed Shaik, Guoyu Pan, Ying Chen, and William F. Elmquist</i> . . . . .	<b>560</b>	Species Differences in Blood-Brain Barrier Transport of Three Positron Emission Tomography Radioligands with Emphasis on P-Glycoprotein Transport. <i>Stina Syvänen, Örjan Lindhe, Mikael Palner, Birgitte R. Kornum, Obaidur Rahman, Bengt Långström, Gitte M. Knudsen, and Margareta Hammarlund-Udenaes</i> . . . . .	<b>635</b>
Novel Metabolites of Amodiaquine Formed by CYP1A1 and CYP1B1: Structure Elucidation Using Electrochemistry, Mass Spectrometry, and NMR. <i>Tove Johansson, Ulrik Jurva, Gunnar Grönberg, Lars Weidolf, and Collen Masimirembwa</i> . . . . .	<b>571</b>	Decreased Susceptibility of the Cytochrome P450 2B6 Variant K262R to Inhibition by Several Clinically Important Drugs. <i>Jyothi C. Talakad, Santosh Kumar, and James R. Halpert</i> . . . . .	<b>644</b>
Dexamethasone Induction of Murine <i>CYP2B</i> Genes Requires the Glucocorticoid Receptor. <i>Étienne Audet-Walsh and Alan Anderson</i> . . . . .	<b>580</b>	An Intestinal Epithelium-Specific Cytochrome P450 (P450) Reductase-Knockout Mouse Model: Direct Evidence for a Role of Intestinal P450s in First-Pass Clearance of Oral Nifedipine. <i>Qing-Yu Zhang, Cheng Fang, Jin Zhang, Deborah Dunbar, Laurence Kaminsky, and Xinxin Ding</i> . . . . .	<b>651</b>
Mechanism-Based Inhibition of Human Cytochrome P450 2B6 by Ticlopidine, Clopidogrel, and the Thiolactone Metabolite of Prasugrel. <i>Yumi Nishiyama, Katsunobu Hagihara, Takashi Ito, Masami Tajima, Shin-ichi Miura, Atsushi Kurihara, Nagy A. Farid, and Toshihiko Ikeda</i> . . . . .	<b>589</b>	Classification of Cytochrome P450 1A2 Inhibitors and Noninhibitors by Machine Learning Techniques. <i>Poongavanam Vasanthanathan, Olivier Taboureau, Chris Oostenbrink, Nico P. E. Vermeulen, Lars Olsen, and Flemming Steen Jørgensen</i> . . . . .	<b>658</b>
Metabolism of (+)-1,4-Dihydro-7-(trans-3-methoxy-4-methylamino-1-pyrrolidinyl)-4-oxo-1-(2-thiazolyl)-1,8-naphthyridine-3-carboxylic Acid (Voreloxin; Formerly SNS-595), a Novel Replication-Dependent DNA-Damaging Agent. <i>Marc J. Evanchik, Darin Allen, Josh C. Yoburn, Jeffrey A. Silverman, and Ute Hoch</i> . . . . .	<b>594</b>	Effect of CYP2A13 Active Site Mutation N297A on Metabolism of Coumarin and Tobacco-Specific Nitrosamines. <i>Kari E. Schlicht, Jeannette Zinggeler Berg, and Sharon E. Murphy</i> . . . . .	<b>665</b>
Investigation of the Role of Oligopeptide Transporter PEPT1 and Sodium/Glucose Cotransporter SGLT1 in Intestinal Absorption of Their Sub-			

Dehydrogenation of the Indoline-Containing Drug  
4-Chloro-*N*-(2-methyl-1-indoliny)-3-sulfamoyl-  
benzamide (Indapamide) by CYP3A4: Correla-  
tion with in Silico Predictions. *Hao Sun, Chad  
Moore, Patrick M. Dansette, Santosh Kumar,  
James R. Halpert, and Garold S. Yost . . . . .* **672**

Regulation of Drug Transporter Expression in Human  
Hepatocytes Exposed to the Proinflammatory  
Cytokines Tumor Necrosis Factor- $\alpha$  or Interleu-  
kin-6. *Marc Le Vee, Valérie Lecureur, Bruno  
Stieger, and Olivier Fardel . . . . .* **685**

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

*About the cover:* Molecular models of indapamide in the active site of CYP3A4 predicted by AutoDock. See article by Sun et al. on page 672 of this issue.