

# DRUG METABOLISM AND DISPOSITION

A Publication of the American Society for Pharmacology and Experimental Therapeutics

April 2011

Vol. 39, No. 4

## CONTENTS

### SHORT COMMUNICATION

- The Intestine As an Important Contributor to Prasugrel Active Metabolite Formation In Vivo. *Katsunobu Hagihara, Miho Kazui, Hidenori Ikenaga, Toshihiko Nanba, Kiichi Fusegawa, Takashi Izumi, Toshihiko Ikeda, and Atsushi Kurihara* . . . . . **565**

### ARTICLES

- Hepatic Pharmacokinetics of Cationic Drugs in a High-Fat Emulsion-Induced Rat Model of Non-alcoholic Steatohepatitis. *Peng Li, Thomas A. Robertson, Camilla A. Thorling, Qian Zhang, Linda M. Fletcher, Darrell H. G. Crawford, and Michael S. Roberts* . . . . . **571**

- Metabolism and Excretion of Asenapine in Healthy Male Subjects. *S. F. M. van de Wetering-Krebers, P. L. Jacobs, G. J. Kemperman, E. Spaans, P. A. M. Peeters, L. P. C. Delbressine, and M. L. P. S. van Iersel* . . . . . **580**

- Prediction of CYP3A-Mediated Drug-Drug Interactions Using Human Hepatocytes Suspended in Human Plasma. *Jialin Mao, Michael A. Mohutsky, John P. Harrelson, Steven A. Wrighton, and Stephen D. Hall* . . . . . **591**

- Pharmacokinetic Analysis of Continuous Erythropoietin Receptor Activator Disposition in Adult Sheep Using a Target-Mediated, Physiologic Recirculation Model and a Tracer Interaction Methodology. *Mohammed H. El-Komy, John A. Widness, and Peter Veng-Pedersen* . . . . . **603**

- Glucuronidation of the Red Clover Isoflavone Iridone by Liver Microsomes from Different Species and Human UDP-Glucuronosyltransferases. *Ronald Maul, Diana Siegl, and Sabine E. Kulling* . . . . . **610**

- Metabolism of Gambogic Acid in Rats: A Rare Intestinal Metabolic Pathway Responsible for Its Final Disposition. *Jing Yang, Li Ding, Linlin Hu, Wenjuan Qian, Shaohong Jin, Xiaoping Sun, Zhenzhong Wang, and Wei Xiao* . . . . . **617**

- In Vitro Metabolism of 17-(Dimethylaminoethylamino)-17-demethoxygeldanamycin in Human Liver Microsomes. *Nan Zheng, Peng Zou, Shaomeng Wang, and Duxin Sun* . . . . . **627**

- Biotransformation of a Novel Antimitotic Agent, I-387, by Mouse, Rat, Dog, Monkey, and Human Liver Microsomes and In Vivo Pharmacokinetics in Mice. *Sunjoo Ahn, Jeffrey D. Kearbey, Chien-Ming Li, Charles B. Duke III, Duane D. Miller, and James T. Dalton* . . . . . **636**

- Characterization of Niflumic Acid as a Selective Inhibitor of Human Liver Microsomal UDP-Glucuronosyltransferase 1A9: Application to the Reaction Phenotyping of Acetaminophen Glucuronidation. *John O. Miners, Kushari Bowalgaha, David J. Elliot, Pawel Baranczewski, and Kathleen M. Knights* . . . . . **644**

- Pharmacokinetics, Metabolism, and Disposition of Rivoglitazone, a Novel Peroxisome Proliferator-Activated Receptor  $\gamma$  Agonist, in Rats and Monkeys. *Minoru Uchiyama, Haruo Iwabuchi, Fujiko Tsuruta, Koji Abe, Makoto Takahashi, Hiroko Koda, Minoru Oguchi, Osamu Okazaki, and Takashi Izumi* . . . . . **653**

- Role of Catechol-O-Methyltransferase in the Disposition of Luteolin in Rats. *Zhongjian Chen, Meng Chen, Hao Pan, Siyuan Sun, Liping Li, Su Zeng, and Huidi Jiang* . . . . . **667**

- Comparative Metabolism of Cinobufagin in Liver Microsomes from Mouse, Rat, Dog, Minipig, Mon-

Continued on next page

key, and Human. <i>Xiao-Chi Ma, Jing Ning, Guang-Bo Ge, Si-Cheng Liang, Xiu-Li Wang, Bao-Jing Zhang, Shan-Shan Huang, Jing-Kui Li, and Ling Yang</i> . . . . .	<b>675</b>	Discovery of a Novel Allelic Variant of <i>CYP2C8</i> , <i>CYP2C8*11</i> , in Asian Populations and Its Clinical Effect on the Rosiglitazone Disposition In Vivo. <i>Chang-Woo Yeo, Su-Jun Lee, Sang Seop Lee, Soo Kyung Bae, Eun-Young Kim, Ji-Hong Shon, Byoung Doo Rhee, and Jae-Gook Shin</i> . .	<b>711</b>
Metabolic Pathways of the Camptothecin Analog AR-67. <i>Jamie Horn, Marta Milewska, Susanne M. Arnold, and Markos Leggas</i> . . . . .	<b>683</b>	<i>CYP2G2</i> , Pseudogenized in Human, Is Expressed in Nasal Mucosa of Cynomolgus Monkey and Encodes a Functional Drug-Metabolizing Enzyme. <i>Yasuhiro Uno, Shotaro Uehara, Norie Murayama, and Hiroshi Yamazaki</i> . . . . .	<b>717</b>
In Vitro Metabolism of Oxymetazoline: Evidence for Bioactivation to a Reactive Metabolite. <i>Mukesh K. Mahajan, Vinita Uttamsingh, J. Scott Daniels, Liang-Shang Gan, Barbara W. LeDuc, and David A. Williams</i> . . . . .	<b>693</b>	Comparison of the Inhibitory Profiles of Itraconazole and Cimetidine in Cytochrome P450 3A4 Genetic Variants. <i>Takeshi Akiyoshi, Takashi Saito, Saori Murase, Mitsue Miyazaki, Norie Murayama, Hiroshi Yamazaki, F. Peter Guengerich, Katsunori Nakamura, Koujirou Yamamoto, and Hisakazu Ohtani</i> . . . . .	<b>724</b>
In Vitro Evaluation of Potential Drug-Drug Interactions with Ticagrelor: Cytochrome P450 Reaction Phenotyping, Inhibition, Induction, and Differential Kinetics. <i>Diansong Zhou, Tommy B. Andersson, and Scott W. Grimm</i> . . . . .	<b>703</b>		

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

About the cover: LD map of *CYP2C8* single nucleotide polymorphisms in a Korean population ( $n = 50$ ). See the article by Yeo et al. on page 711 of this issue.