

# DRUG METABOLISM AND DISPOSITION

A Publication of the American Society for Pharmacology and Experimental Therapeutics

June 2006

Vol. 34, No. 6

## CONTENTS

### SHORT COMMUNICATIONS

Formation of *N*-Alkylprotoporphyrin IX from Metabolism of Diallyl Sulfone in Lung and Liver. GORDON P. BLACK, KATHY S. COLLINS, DYLAN P. BLACQUIERE, AND POH-GEK FORKERT . . . . . **895**

Identification of a Novel *In Vitro* Metabonate from Liver Microsomal Incubations. CHUN LI, SEKHAR SURAPANENI, QINGPING ZENG, BRIAN MARQUEZ, DAVID CHOW, AND GONDI KUMAR . . . . . **901**

### ARTICLES

Anti-Phencyclidine Monoclonal Antibody Binding Capacity Is Not the Only Determinant of Effectiveness, Disproving the Concept that Antibody Capacity Is Easily Surmounted. GRZEGORZ PITAS, ELIZABETH M. LAURENZANA, D. KEITH WILLIAMS, S. MICHAEL OWENS, AND W. BROOKS GENTRY . . . **906**

Absorption and Metabolism of Astragali Radix Decoction: *In Silico*, *In Vitro*, and A Case Study *In Vivo*. FENG XU, YUE ZHANG, SHENGYUAN XIAO, XIAOWEI LU, DONGHUI YANG, XIAODA YANG, CHANGLING LI, MINGYING SHANG, PENGFEI TU, AND SHAOQING CAI . . . . . **913**

Application of Biocatalysis to Drug Metabolism: Preparation of Mammalian Metabolites of a Biaryl-Bis-Sulfonamide AMPA ( $\alpha$ -Amino-3-hydroxy-5-methylisoxazole-4-propionic acid) Receptor Potentiator Using *Actinoplanes missouriensis*. MILTON ZMIJEWSKI, TODD A. GILLESPIE, DAVID A. JACKSON, DOUGLAS F. SCHMIDT, PING YI, AND PALANIAPPAN KULANTHAIVEL . . . . . **925**

Demethylation of the Pesticide Methoxychlor in Liver and Intestine from Untreated, Methoxychlor-Treated, and 3-Methylcholanthrene-Treated

Channel Catfish (*Ictalurus punctatus*): Evidence for Roles of CYP1 and CYP3A Family Isozymes. LEAH D. STUCHAL, KEVIN M. KLEINOW, JOHN J. STEGEMAN, AND MARGARET O. JAMES . . . . . **932**

Contrary to Adult, Neonatal Rats Show Pronounced Brain Uptake of Corticosteroids. VIKRAM ARYA, VINCENT G. DEMARCO, MANISH ISSAR, AND GÜNTHER HOCHHAUS . . . . . **939**

Importance of UDP-Glucuronosyltransferase 1A10 (UGT1A10) in the Detoxification of Polycyclic Aromatic Hydrocarbons: Decreased Glucuronidative Activity of the UGT1A10<sup>139LYS</sup> Isoform. RYAN W. DELLINGER, JIA-LONG FANG, GANG CHEN, REBECCA WEINBERG, AND PHILIP LAZARUS . . **943**

Autoinduction of MKC-963 [(*R*)-1-(1-Cyclohexylethylamino)-4-phenylphthalazine] Metabolism in Healthy Volunteers and Its Retrospective Evaluation Using Primary Human Hepatocytes and cDNA-Expressed Enzymes. TOSHIYUKI SHIMIZU, KEI AKIMOTO, TAKUYA YOSHIMURA, TAKURO NIWA, KAORU KOBAYASHI, MICHIO TSUNOO, AND KAN CHIBA . . . . . **950**

A Pharmacokinetic Study of Diphenhydramine Transport Across the Blood-Brain Barrier in Adult Sheep: Potential Involvement of a Carrier-Mediated Mechanism. SAM C. S. AU-YEUNG, DAN W. RURAK, NANCY GRUBER, AND K. WAYNE RIGGS . . **955**

Metabolism of [<sup>14</sup>C]Gemopatrilat after Oral Administration to Rats, Dogs, and Humans. JILL C. M. WAIT, NIMISH VACCHARAJANI, JAMES MITROKA, MOHAMMED JEMAL, SANAUULLAH KHAN, SAMUEL J. BONACORSI, J. KENT RINEHART, AND RAMASWAMY A. IYER . . . . . **961**

*In Vitro* Blood Distribution and Plasma Protein Binding of the Iron Chelator Deferasirox

*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: info@aspet.org; Web site: http://www.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.: \$339.00 for institutions and \$177.00 for non-ASPET members. Outside the U.S.: \$408.00 for institutions and \$246.00 for non-ASPET members. Single copy: \$35.00. 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 Service*, *Current Awareness in Biological Sciences*, *Current Contents*®/*Life Sciences*, *EMBASE/Excerpta Medica*, *Index Medicus*, *International Pharmaceutical Abstracts*, *Medical Documentation Service*®, *Reference Update*®, *Research Alert*®, *Science Citation Index*®, *SciSearch*®, and *SIIC Data Bases*. Copyright © 2006 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 November 21, 2019

DRUG METABOLISM & DISPOSITION

(ICL670) and Its Iron Complex Fe-[ICL670] <sub>2</sub> for Rat, Marmoset, Rabbit, Mouse, Dog, and Human. H. MARKUS WEISS, MARCEL FRESNEAU, GIAN P. CAMENISCH, OLIVIER KRETZ, AND GERHARD GROSS . . . . .	<b>971</b>	Ethinylestradiol Increases Expression and Activity of Rat Liver Mrp3. MARÍA L. RUIZ, SILVINA S. M. VILLANUEVA, MARCELO G. LUQUITA, MARY VORE, ALDO D. MOTTINO, AND VIVIANA A. CATANIA . . . . .	<b>1030</b>
Comparison of Methods for the Prediction of the Metabolic Sites for CYP3A4-Mediated Metabolic Reactions. DIANSONG ZHOU, LOVISA AFZELIUS, SCOTT W. GRIMM, TOMMY B. ANDERSSON, RANDY J. ZAUHAR, AND ISMAEL ZAMORA . . . . .	<b>976</b>	Biotransformation of Fluticasone: In Vitro Characterization. ROBIN E. PEARCE, J. STEVEN LEEDER, AND GREGORY L. KEARNS . . . . .	<b>1035</b>
Flutamide Metabolism in Four Different Species in Vitro and Identification of Flutamide Metabolites in Human Patient Urine by High Performance Liquid Chromatography/Tandem Mass Spectrometry. ANNICA TEVELL, HANS LENNERNÄS, MATS JÖNSSON, MARIA NORLIN, BO LENNERNÄS, ULF BONDESSON, AND MIKAEL HEDELAND . . . . .	<b>984</b>	Saturable Binding of Indisulam to Plasma Proteins and Distribution to Human Erythrocytes. ANTHE S. ZANDVLIET, WILLIAM COPALU, JAN H. M. SCHELLENS, JOS H. BEIJNEN, AND ALWIN D. R. HUITEMA . . . . .	<b>1041</b>
Galactosamine Prevents Ethinylestradiol-Induced Cholestasis. FERNANDO A. CROCENZI, JOSÉ M. PELLEGRIANO, VIVIANA A. CATANIA, MARCELO G. LUQUITA, MARCELO G. ROMA, ALDO D. MOTTINO, AND ENRIQUE J. SÁNCHEZ POZZI . . . . .	<b>993</b>	Comparison of Mouse and Rat Cytochrome P450-Mediated Metabolism in Liver and Intestine. MARCELLA MARTIGNONI, GENY GROOTHUIS, AND RUBEN DE KANTER . . . . .	<b>1047</b>
Comparison of Drug Efflux Transport Kinetics in Various Blood-Brain Barrier Models. CORBIN J. BACHMEIER, WILLIAM J. TRICKLER, AND DONALD W. MILLER . . . . .	<b>998</b>	In Vitro Characterization of Lamotrigine N2-Glucuronidation and the Lamotrigine-Valproic Acid Interaction. ANDREW ROWLAND, DAVID J. ELLIOT, J. ANDREW WILLIAMS, PETER I. MACKENZIE, RONALD G. DICKINSON, AND JOHN O. MINERS . . . . .	<b>1055</b>
Metabolism and Disposition of a Potent and Selective GABA-A <sub>α2/3</sub> Receptor Agonist in Healthy Male Volunteers. STACEY L. POLSKY-FISHER, STANLEY VICKERS, DONGHUI CUI, RAJU SUBRAMANIAN, BYRON H. ARISON, NANCY G. B. AGRAWAL, THANH V. GOEL, LAURA K. VESSEY, M. GAIL MURPHY, KENNETH C. LASSETER, RICHARD C. SIMPSON, JOSE M. VEGA, AND A. DAVID RODRIGUES . . . . .	<b>1004</b>	Cytochrome P450 Gene Induction in Rats Ex Vivo Assessed by Quantitative Real-Time Reverse Transcriptase-Polymerase Chain Reaction (Taq-Man). SANDRA J. BALDWIN, JO L. BRAMHALL, CHARLOTTE A. ASHBY, LIN YUE, PAUL R. MURDOCK, STEVEN R. HOOD, ANDREW D. AYRTON, AND STEPHEN E. CLARKE . . . . .	<b>1063</b>
Involvement of Hepatocyte Nuclear Factor 4α in the Different Expression Level between CYP2C9 and CYP2C19 in the Human Liver. SACHIYO KAWASHIMA, KAORU KOBAYASHI, KAORI TAKAMA, TOMOAKI HIGUCHI, TOMOMI FURIHATA, MASAKIYO HOSOKAWA, AND KAN CHIBA . . . . .	<b>1012</b>	□ N-Methylpurine DNA Glycosylase and 8-Oxoguanine DNA Glycosylase Metabolize the Antiviral Nucleoside 2-Bromo-5,6-dichloro-1-(β-D-ribofuranosyl)benzimidazole. PHILIP L. LORENZI, CHRISTOPHER P. LANDOWSKI, ANDREA BRANCALE, XUEQIN SONG, LEROY B. TOWNSEND, JOHN C. DRACH, AND GORDON L. AMIDON . . . . .	<b>1070</b>
Comparative Metabolism of Geranyl Nitrile and Citronellyl Nitrile in Mouse, Rat, and Human Hepatocytes. RAYMOND A. KEMPER, DIANE L. NABB, SHAWN A. GANNON, TIMOTHY A. SNOW, AND ANNE MARIE API . . . . .	<b>1019</b>		
		<b>ERRATA</b>	
		Correction to “Binding of Drugs to Hepatic Microsomes: Comment and Assessment of Current Prediction Methodology with Recommendation for Improvement” . . . . .	<b>1078</b>
		Correction to “P-Glycoprotein Plays a Major Role in the Efflux of Fexofenadine in the Small Intestine and Blood-Brain Barrier, but Only a Limited Role in Its Biliary Excretion” . . . . .	<b>1079</b>

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

About the cover: Molecular modeling. See the article by Lorenzi et al. on page 1070 of this issue.