

DRUG METABOLISM AND DISPOSITION

A Publication of the American Society for Pharmacology and Experimental Therapeutics

August 2024

Vol. 52, No. 8

Contents

SPECIAL SECTION ON MECHANISMS OF DRUG METABOLISM IN ACETAMINOPHEN-INDUCED HEPATOTOXICITY

Special Section Mechanisms of Drug Metabolism in Acetaminophen-Induced Hepatotoxicity—Editorial <i>Yurong Lai and Xiao-Bo Zhong</i>	704
Acetaminophen-Induced Hepatic Necrosis: A Reminiscence <i>David Jollow</i>	707
Central Mechanisms of Acetaminophen Hepatotoxicity: Mitochondrial Dysfunction by Protein Adducts and Oxidant Stress <i>Hartmut Jaeschke and Anup Ramachandran</i>	712
Good Cells Go Bad: Immune Dysregulation in the Transition from Acute Liver Injury to Liver Failure After Acetaminophen Overdose <i>James P. Luyendyk, Elena Morozova, and Bryan L. Copple</i>	722
The Role of Mechanistic Biomarkers in Understanding Acetaminophen Hepatotoxicity in Humans <i>Mitchell R. McGill</i>	729
Deciphering Acetaminophen-Induced Hepatotoxicity: The Crucial Role of Transcription Factors like Nuclear Factor Erythroid 2–Related Factor 2 as Genetic Determinants of Susceptibility to Drug-Induced Liver Injury <i>Ankit P. Laddha, Hangyu Wu, and José E. Manautou</i>	740
The Discovery of Gut Microbial Metabolites as Modulators of Host Susceptibility to Acetaminophen-Induced Hepatotoxicity <i>Hyunwoo Lee, Xiaotong Yang, Pei-Ru Jin, Kyoung-Jae Won, Chang H. Kim, and Hyunyoung Jeong</i>	754

ARTICLES

☐ Human Pharmacokinetic and CYP3A Drug–Drug Interaction Prediction of GDC-2394 Using Physiologically Based Pharmacokinetic Modeling and Biomarker Assessment <i>Jesse Yu, Fei Tang, Fang Ma, Susan Wong, Jing Wang, Justin Ly, Liuxi Chen, and Jialin Mao</i>	765
☐ Covalent Binding of Reactive Anhydride of Cantharidin to Biological Amines <i>Yaya Fan, Lin Chen, Qiuyi Jing, Xiaoli Li, Hong Pan, Chao Fang, Jianyong Zhang, and Fuguo Shi</i>	775
☐ Development and Verification of a Full Physiologically Based Pharmacokinetic Model for Sublingual Buprenorphine in Healthy Adult Volunteers that Accounts for Nonlinear Bioavailability <i>Matthijs W. van Hoogdalem, Ryota Tanaka, Trevor N. Johnson, Alexander A. Vinks, and Tomoyuki Mizuno</i>	785
☐ Evaluation and Optimization of a Microcavity Plate–Based Human Hepatocyte Spheroid Model for Predicting Clearance of Slowly Metabolized Drug Candidates <i>David A. Kukla, David G. Belair, and David M. Stresser</i>	797
☐ Integrative Analysis of Histone Acetylation Regulated CYP4F12 in Esophageal Cancer Development <i>Yanhong Chen, Li Wang, Yuchen Wang, Yanyan Fang, Wenyang Shen, Yingxue Si, Xiaoli Zheng, and Su Zeng</i>	813

☐ Supplemental material is available at dmd.aspetjournals.org.

About the cover: “Overview of gut microbial metabolites known to modulate APAP-induced liver injury.” See the article by Lee et al. ([dx.doi.org/10.1124/dmd.123.001541](https://doi.org/10.1124/dmd.123.001541)).

☐	Drug Disposition in Neonatal Göttingen Minipigs: Exploring Effects of Perinatal Asphyxia and Therapeutic Hypothermia <i>Marina-Stefania Stroe, Miao-Chan Huang, Pieter Annaert, Karen Leys, Anne Smits, Karel Allegaert, Lieselotte Van Bockstal, Allan Valenzuela, Miriam Ayuso, Chris Van Ginneken, and Steven Van Cruchten</i>	824
☐	The Cytochrome P450 2C8*3 Variant (rs11572080) Is Associated with Improved Asthma Symptom Control in Children and Altered Lipid Mediator Production and Inflammatory Response in Human Bronchial Epithelial Cells <i>Marysol Almestica-Roberts, Nam D. Nguyen, Lili Sun, Samantha N. Serna, Emmanuel Rapp, Katherine L. Burrell-Gerbers, Tosifa A. Memon, Bryan L. Stone, Flory L. Nkoy, John G. Lamb, Cassandra E. Deering-Rice, Joseph E. Rower, and Christopher A. Reilly</i>	836
☐	Mass Balance, Metabolic Pathways, Absolute Bioavailability, and Pharmacokinetics of Giredestrant in Healthy Subjects <i>Smita Kshirsagar, Ya-Chi Chen, Jiajie Yu, Mary R. Gates, Sonoko Kawakatsu, S Cyrus Khojasteh, Shuguang Ma, Luna Musib, Vikram Malhi, Uyi Osaghae, Jing Wang, Sungjoon Cho, Yang (Thomas) Tang, Donglu Zhang, Weiping Zhao, and Tom De Bruyn</i>	847
☐	Alpibectir: Early Qualitative and Quantitative Metabolic Profiling from a First-Time-in-Human Study by Combining ¹⁹ F-NMR (Nuclear Magnetic Resonance), ¹ H-NMR, and High-Resolution Mass Spectrometric Analyses <i>Daniel J. Weston, Steve Thomas, Gary W. Boyle, and Michel Pieren</i>	858
	Modulation of Angiotensin II-Induced Cellular Hypertrophy by Cannflavin-C: Unveiling the Impact on Cytochrome P450 1B1 and Arachidonic Acid Metabolites <i>Ahmad H. Alammari, Fadumo Ahmed Isse, Conor O’Croinin, Neal M. Davies, and Ayman O. S. El-Kadi</i>	875
☐	Mechanistic Account of Distinct Change in Organic Anion Transporting Polypeptide 1B (OATP1B) Substrate Pharmacokinetics during OATP1B-Mediated Drug-Drug Interactions Using Physiologically Based Pharmacokinetic Modeling <i>Pooja V. Hegde and Bridget L. Morse</i>	886
	Cardiac Uptake of the Adrenergic Imaging Agent <i>meta</i> -Iodobenzylguanidine (mIBG) Is Mediated by Organic Cation Transporter 3 (Oct3) <i>Antonio J. López Quiñones, Leticia Salvador Vieira, and Joanne Wang</i>	899
	Quinuclidine <i>N</i> -Oxygenation Mediated by Flavin-Containing Monooxygenases 1 and 3 in Kidney and Liver Microsomes from Humans, Monkeys, Dogs, and Pigs <i>Makiko Shimizu, Miaki Makiguchi, Yasuhiro Uno, and Hiroshi Yamazaki</i>	906
☐	Arsenite-Induced Drug–Drug Interactions in Rats <i>Jingyu Zhang, Weiwei Li, Ying Liu, Yan He, Zihao Cheng, Ximei Li, Yu Chen, Aihua Zhang, Ying Peng, and Jiang Zheng</i>	911
☐	After 50 Years of Hepatic Clearance Models, Where Should We Go from Here? Improvements and Implications for Physiologically Based Pharmacokinetic Modeling <i>K. Sandy Pang, Weijia Ivy Lu, and Gerard J. Mulder</i>	919