

The Journal of
PHARMACOLOGY
And Experimental Therapeutics

A Publication of the American Society for Pharmacology and Experimental Therapeutics

January 2010

Vol. 332, No. 1

Contents

EDITOR'S NOTE	1
HIGHLIGHTED PAPER	3
BEHAVIORAL PHARMACOLOGY	
Reducing Abuse Liability of GABA _A /Benzodiazepine Ligands via Selective Partial Agonist Efficacy at α_1 and $\alpha_{2/3}$ Subtypes <i>Nancy A. Ator, John R. Atack, Richard J. Hargreaves, H. Donald Burns, and Gerard R. Dawson</i>	4
WS-50030 [7-{4-[3-(1 <i>H</i> -inden-3-yl)propyl]piperazin-1-yl}-1,3-benzoxazol-2(3 <i>H</i>)-one]: A Novel Dopamine D ₂ Receptor Partial Agonist/Serotonin Reuptake Inhibitor with Preclinical Antipsychotic-Like and Antidepressant-Like Activity <i>Julie A. Brennan, Radka Graf, Steven M. Grauer, Rachel L. Navarra, Claudine M. Pulicchio, Zoë A. Hughes, Qian Lin, Caitlin Wantuch, Sharon Rosenzweig-Lipson, Farhana Pruthi, Margaret Lai, Deborah Smith, Wouter Goutier, Martina van de Neut, Albert J. Robichaud, David Rotella, Rolf W. Feenstra, Chris Kruse, Pierre Broqua, Chad E. Beyer, Andrew C. McCreary, Mark H. Pausch, and Karen L. Marquis</i>	190
Dopamine D3 Receptors Mediate the Discriminative Stimulus Effects of Quinpirole in Free-Feeding Rats <i>Michelle G. Baladi, Amy H. Newman, and Charles P. France</i>	308
CARDIOVASCULAR	
Sublethal Doses of an Anti-erbB2 Antibody Leads to Death by Apoptosis in Cardiomyocytes Sensitized by Low Prosenescent Doses of Epirubicin: The Protective Role of Dexrazoxane <i>Paolo Spallarossa, Paola Altieri, Paolo Pronzato, Concetta Aloï, Giorgio Ghigliotti, Antonio Barsotti, and Claudio Brunelli</i>	87
□ Angiotensin II-Induced Migration of Vascular Smooth Muscle Cells Is Mediated by p38 Mitogen-Activated Protein Kinase-Activated c-Src through Spleen Tyrosine Kinase and Epidermal Growth Factor Receptor Transactivation <i>Benon E. Mugabe, Fariborz A. Yaghini, Chi Young Song, Cuneyt K. Buharalioglu, Christopher M. Waters, and Kafait U. Malik</i>	116
Endogenous Nitric Oxide Contributes to Bradykinin-Stimulated Glucose Uptake but Attenuates Vascular Tissue-Type Plasminogen Activator Release <i>Mias Pretorius and Nancy J. Brown</i>	291
CELLULAR AND MOLECULAR	
20-Hydroxy-5,8,11,14-eicosatetraenoic Acid Mediates Endothelial Dysfunction via I κ B Kinase-Dependent Endothelial Nitric-Oxide Synthase Uncoupling <i>Jennifer Cheng, Cheng-Chia Wu, Katherine H. Gotlinger, Frank Zhang, John R. Falck, Dubasi Narsimhaswamy, and Michal Laniado Schwartzman</i>	57

The Journal of Pharmacology and Experimental Therapeutics (ISSN 0022-3565) is published monthly by the American Society for Pharmacology and Experimental Therapeutics, 9650 Rockville Pike, Bethesda, MD 20814-3995; email: subscriptions@aspet.org; Web site: aspet.org. Periodicals postage paid at Bethesda, MD, and at additional mailing offices. POSTMASTER: Send address changes to *The Journal of Pharmacology and Experimental Therapeutics*, 9650 Rockville Pike, Bethesda, MD 20814-3995. Subscription rates: U.S.: \$975; outside the U.S.: \$1,140. Single copy: \$85. 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*, *Medical Documentation Service*®, *PsycINFO*, *Reference Update*®, *Research Alerts*®, *Science Citation Index*®, *SciSearch*®, and *SIIC Data Bases*. Copyright © 2010 by the American Society for Pharmacology and Experimental Therapeutics. All rights reserved. Printed in the U.S.A.

A Conserved Motif in the Membrane Proximal C-Terminal Tail of Human Muscarinic M ₁ Acetylcholine Receptors Affects Plasma Membrane Expression <i>Gregory W. Sawyer, Frederick J. Ehler, and Crystal A. Shults</i>	76
Early Intervention of Tyrosine Nitration Prevents Vaso-Obliteration and Neovascularization in Ischemic Retinopathy <i>Mohammed A. Abdelsaid, Bindu A. Pillai, Suraporn Matragoon, Roshini Prakash, Mohamed Al-Shabrawey, and Azza B. El-Remessy</i>	125
☐ Nicotinamide Glycolates Antagonize CXCR2 Activity through an Intracellular Mechanism <i>Dean Y. Maeda, Mark T. Quinn, Igor A. Schepetkin, Liliya N. Kirpotina, and John A. Zebala</i>	145
☐ NF546 [4,4'-(Carbonylbis(imino-3,1-phenylene-carbonylimino-3,1-(4-methyl-phenylene)-carbonylimino))-bis(1,3-xylene- α,α' -diphosphonic Acid) Tetrasodium Salt] Is a Non-Nucleotide P2Y ₁₁ Agonist and Stimulates Release of Interleukin-8 from Human Monocyte-Derived Dendritic Cells <i>Sabine Meis, Alexandra Hamacher, Darunee Hongwiset, Claudia Marzian, Michael Wiese, Niels Eckstein, Hans-Dieter Royer, Didier Communi, Jean-Marie Boeynaems, Ralf Hausmann, Günther Schmalzing, and Matthias U. Kassack</i>	238

CHEMOTHERAPY, ANTIBIOTICS, AND GENE THERAPY

☐ Topotecan Triggers Apoptosis in p53-Deficient Cells by Forcing Degradation of XIAP and Survivin Thereby Activating Caspase-3-Mediated Bid Cleavage <i>Maja T. Tomacic, Markus Christmann, and Bernd Kaina</i>	316
--	-----

ENDOCRINE AND DIABETES

Glyceollin I, a Novel Antiestrogenic Phytoalexin Isolated from Activated Soy <i>M. Carla Zimmermann, Syreeta L. Tilghman, Stephen M. Boué, Virgilio A. Salvo, Steven Elliott, K. Y. Williams, Elena V. Skripnikova, Hasina Ashe, Florastina Payton-Stewart, Lyndsay Vanhoy-Rhodes, Juan Pablo Fonseca, Cynthia Corbitt, Bridgette M. Collins-Burow, Melanie H. Howell, Michelle Lacey, Betty Y. Shih, Carol Carter-Wientjes, Thomas E. Cleveland, John A. McLachlan, Thomas E. Wiese, Barbara S. Beckman, and Matthew E. Burow</i>	35
---	----

INFLAMMATION, IMMUNOPHARMACOLOGY, AND ASTHMA

☐ Inhibition of Phosphoinositide 3-Kinase Ameliorates Dextran Sodium Sulfate-Induced Colitis in Mice <i>Xiao-dong Peng, Xiao-hua Wu, Li-juan Chen, Zhen-ling Wang, Xiao-hong Hu, Li-fang Song, Chun-mei He, You-fu Luo, Zhi-zhi Chen, Ke Jin, Hong-gang Lin, Xiao-lei Li, Yong-sheng Wang, and Yu-quan Wei</i>	46
---	----

METABOLISM, TRANSPORT, AND PHARMACOGENOMICS

Hepatobiliary Disposition of Troglitazone and Metabolites in Rat and Human Sandwich-Cultured Hepatocytes: Use of Monte Carlo Simulations to Assess the Impact of Changes in Biliary Excretion on Troglitazone Sulfate Accumulation <i>Jin Kyung Lee, Tracy L. Marion, Koji Abe, Changwon Lim, Gary M. Pollock, and Kim L. R. Brouwer</i>	26
A Single Amino Acid Controls the Functional Switch of Human Constitutive Androstane Receptor (CAR) 1 to the Xenobiotic-Sensitive Splicing Variant CAR3 <i>Tao Chen, Leslie M. Tompkins, Linhao Li, Haishan Li, Gregory Kim, Yuxin Zheng, and Hongbing Wang</i>	106
Species Difference in the Effect of Grapefruit Juice on Intestinal Absorption of Talinolol between Human and Rat <i>Yoshiyuki Shirasaka, Erika Kuraoka, Hildegard Spahn-Langguth, Takeo Nakanishi, Peter Langguth, and Ikumi Tamai</i>	181
Nicotine Metabolism in African Americans and European Americans: Variation in Glucuronidation by Ethnicity and UGT2B10 Haplotype <i>Jeannette Zinggeler Berg, Jesse Mason, Angela J. Boettcher, Dorothy K. Hatsukami, and Sharon E. Murphy</i>	202
Transport of the Photodynamic Therapy Agent 5-Aminolevulinic Acid by Distinct H ⁺ -Coupled Nutrient Carriers Coexpressed in the Small Intestine <i>Catriona M. H. Anderson, Mark Jevons, Muthusamy Thangaraju, Noel Edwards, Nichola J. Conlon, Steven Woods, Vadivel Ganapathy, and David T. Thwaites</i>	220
☐ Erythropoietic Response to Endogenous Erythropoietin in Premature Very Low Birth Weight Infants <i>Kevin J. Freise, John A. Widness, and Peter Veng-Pedersen</i>	229
☐ Pharmacological Characterization of Human Incretin Receptor Missense Variants <i>Jean-Philippe Fortin, Jonathan C. Schroeder, Yuantee Zhu, Martin Beinborn, and Alan S. Kopin</i>	274
The Ethanol Metabolite Acetaldehyde Increases Paracellular Drug Permeability In Vitro and Oral Bioavailability In Vivo <i>Scott J. Fisher, Peter W. Swaan, and Natalie D. Eddington</i>	326

NEUROPHARMACOLOGY

- Benzodiazepine Binding Site Occupancy by the Novel GABA_A Receptor Subtype-Selective Drug 7-(1,1-Dimethylethyl)-6-(2-ethyl-2H-1,2,4-triazol-3-ylmethoxy)-3-(2-fluorophenyl)-1,2,4-triazolo[4,3-b]pyridazine (TPA023) in Rats, Primates, and Humans 17
John R. Atack, Dean F. Wong, Tim D. Fryer, Christine Ryan, Sandra Sanabria, Yun Zhou, Robert F. Dannals, Wai-si Eng, Raymond E. Gibson, H. Donald Burns, Jose M. Vega, Laura Vessy, Paul Scott-Stevens, John S. Beech, Jean-Claude Baron, Bindi Sohal, Michael L. Schrag, Franklin I. Aigbirhio, Ruth M. McKernan, and Richard J. Hargreaves
- Predominance of Adenosine Excitatory over Inhibitory Effects on Transmission at the Neuromuscular Junction of Infant Rats 153
Paula A. Pousinha, Alexandra M. Correia, Ana M. Sebastião, and Joaquim A. Ribeiro
- Regional Differential Effects of the Novel Histamine H₃ Receptor Antagonist 6-[(3-Cyclobutyl-2,3,4,5-tetrahydro-1H-3-benzazepin-7-yl)oxy]-N-methyl-3-pyridinecarboxamide hydrochloride (GSK189254) on Histamine Release in the Central Nervous System of Freely Moving Rats 164
Patrizia Giannoni, Andrew D. Medhurst, Maria Beatrice Passani, Maria Grazia Giovannini, Chiara Ballini, Laura Della Corte, and Patrizio Blandina
- ☐ An $\alpha 7$ Nicotinic Acetylcholine Receptor-Selective Agonist Reduces Weight Gain and Metabolic Changes in a Mouse Model of Diabetes 173
Mario B. Marrero, Rudolf Lucas, Christina Salet, Terry A. Hauser, Anatoly Mazurov, Patrick M. Lippiello, and Merouane Bencherif
- Inhibition of Presynaptic Release-Facilitatory Kainate Autoreceptors by Extracellular Cyclic GMP 210
Chiara Cervetto, Guido Maura, and Manuela Marcoli
- Spinal D-Amino Acid Oxidase Contributes to Neuropathic Pain in Rats 248
Wen-Juan Zhao, Zhen-Yu Gao, Hong Wei, Hui-Zhen Nie, Qian Zhao, Xiang-Jun Zhou, and Yong-Xiang Wang
- Direct Agonist Activity of Tricyclic Antidepressants at Distinct Opioid Receptor Subtypes 255
Pierluigi Onali, Simona Dedoni, and Maria C. Olanas
- Sex-Specific Effects of Chronic Fluoxetine Treatment on Neuroplasticity and Pharmacokinetics in Mice 266
Georgia E. Hodes, Tiffany E. Hill-Smith, Raymond F. Suckow, Thomas B. Cooper, and Irwin Lucki
- ☐ Nelotanserin, a Novel Selective Human 5-Hydroxytryptamine_{2A} Inverse Agonist for the Treatment of Insomnia 281
Hussien A. Al-Shamma, Christen Anderson, Emil Chuang, Remy Luthringer, Andrew J. Grottick, Erin Hauser, Michael Morgan, William Shanahan, Bradley R. Teegarden, William J. Thomsen, and Dominic Behan
- ☐ Corticotropin-Releasing Factor (CRF) Sensitization of Ethanol Withdrawal-Induced Anxiety-Like Behavior is Brain Site Specific and Mediated by CRF-1 Receptors: Relation to Stress-Induced Sensitization 298
Mae M. Huang, David H. Overstreet, Darin J. Knapp, Robert Angel, Tiffany A. Wills, Montserrat Navarro, Jean Rivier, Wylie Vale, and George R. Breese

TOXICOLOGY

- Critical Cysteine Residues of Kelch-Like ECH-Associated Protein 1 in Arsenic Sensing and Suppression of Nuclear Factor Erythroid 2-Related Factor 2 66
Xiaoqing He and Qiang Ma
- ☐ Cyanide-Induced Apoptosis of Dopaminergic Cells Is Promoted by BNIP3 and Bax Modulation of Endoplasmic Reticulum-Mitochondrial Ca²⁺ Levels 97
Lu Zhang, Li Li, Heather W. Leavesley, Xun Zhang, Joseph L. Borowitz, and Gary E. Isom
- ☐ Antagonism of Aryl Hydrocarbon Receptor Signaling by 6,2',4'-Trimethoxyflavone 135
Iain A. Murray, Colin A. Flaveny, Brett C. DiNatale, Chris R. Chairo, Jennifer C. Schroeder, Ann Kusnadi, and Gary H. Perdew

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

About the cover: 4-Hydroxytamoxifen and glyceollin I in the binding cavity of the ligand binding domain of ER α interacting with histidine 524, arginine 394, and glutamate 353. See the article by Zimmermann et al. on page 35 of this issue.