

# The Journal of PHARMACOLOGY

## And Experimental Therapeutics

A Publication of the American Society for Pharmacology and Experimental Therapeutics

October 2006

Vol. 319, No. 1

### Contents

#### PERSPECTIVES IN PHARMACOLOGY

- An Overview of Drug Combination Analysis with Isobolograms Ronald J. Tallarida 1

#### BEHAVIORAL PHARMACOLOGY

- Metabotropic Glutamate 5 Receptor Antagonism Is Associated with Antidepressant-Like Effects in Mice Xia Li, Anne B. Need, Melvyn Baez, and Jeffrey M. Witkin 254
- Confirmation and Fine Mapping of Ethanol Sensitivity Quantitative Trait Loci, and Candidate Gene Testing in the LXS Recombinant Inbred Mice Beth Bennett, Phyllis Carosone-Link, Nancy R. Zahniser, and Thomas E. Johnson 299

#### CARDIOVASCULAR

- A Role for Nitric Oxide-Mediated Peroxynitrite Formation in a Model of Endotoxin-Induced Shock Salvatore Cuzzocrea, Emanuela Mazzon, Rosanna Di Paola, Emanuela Esposito, Heather Macarthur, George M. Matuschak, and Daniela Salvemini 73
- The Prototypical Inhibitor of Cholesterol Esterification, Sah 58-035 [3-[Decyldimethylsilyl]-N-[2-(4-methylphenyl)-1-phenylethyl]propanamide], Is an Agonist of Estrogen Receptors Philippe de Medina, Nadia Boubekeur, Patrick Balaguer, Gilles Favre, Sandrine Silvente-Poirot, and Marc Poirot 139
- Regional Hemodynamic Effects of Neutral Endopeptidase Inhibition and Angiotensin (AT<sub>1</sub>) Receptor Antagonism Alone or in Combination in Conscious Spontaneously Hypertensive Rats S. M. Gardiner, J. E. March, P. A. Kemp, S. A. Ballard, and T. Bennett 340
- Simvastatin Improves Diabetes-Induced Coronary Endothelial Dysfunction Huda E. Tawfik, Azza B. El-Remessy, Suraporn Matragoon, Guochuan Ma, Ruth B. Caldwell, and R. William Caldwell 386
- Corpus Cavernosum from Men with Vasculogenic Impotence Is Partially Resistant to Adenosine Relaxation due to Endothelial A<sub>2B</sub> Receptor Dysfunction Miguel Faria, Teresa Magalhães-Cardoso, José-Maria Lafuente-de-Carvalho, and Paulo Correia-de-Sá 405
- Chronic Treatment with the  $\beta_2$ -Adrenoceptor Agonist Prodrug BRL-47672 Impairs Rat Skeletal Muscle Function by Inducing a Comprehensive Shift to a Faster Muscle Phenotype David J. Baker, D. Constantin-Teodosiu, Simon W. Jones, James A. Timmons, and Paul L. Greenhaff 439

#### CELLULAR AND MOLECULAR

- Differential Effects of 5-Methyl-1-[[2-[(2-methyl-3-pyridyl)oxyl]-5-pyridyl]carbonyl]-6-trifluoromethylindone (SB 243213) on 5-Hydroxytryptamine<sub>2C</sub> Receptor-Mediated Responses Kelly A. Berg, Sylvia Navailles, Teresa A. Sanchez, Yamille M. Silva, Martyn D. Wood, Umberto Spampinato, and William P. Clarke 260
- Discovery of Pyrrolo[2,3-*b*]pyrazines Derivatives as Submicromolar Affinity Activators of Wild Type, G551D, and F508del Cystic Fibrosis Transmembrane Conductance Regulator Chloride Channels Sabrina Noel, Christelle Faveau, Caroline Norez, Christian Rogier, Yvette Mettey, and Frédéric Becq 349

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: info@aspet.org; web site: www.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.: \$817.00 for institutions and \$356.00 for non-ASPET members. Outside the U.S.: \$964.00 for institutions and \$502.00 for non-ASPET members.

Single copy: \$82.00. 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 Services*, *Current Awareness in Biological Sciences*, *Current Contents/Life Sciences*, *EMBASE/Excerpta Medica*, *Index Medicus*, *Medical Documentation Service*, *PsycINFO*, *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.

<b>Enzyme-Mediated Protein Haptenation of Dapsone and Sulfamethoxazole in Human Keratinocytes: I. Expression and Role of Cytochromes P450</b>	Piyush M. Vyas, Sanjoy Roychowdhury, Farah D. Khan, Thomas E. Prisinzano, Jatinder Lamba, Erin G. Schuetz, Joyce Blaisdell, Joyce A. Goldstein, Kimber L. Munson, Ronald N. Hines, and Craig K. Svensson	488
<b>Enzyme-Mediated Protein Haptenation of Dapsone and Sulfamethoxazole in Human Keratinocytes: II. Expression and Role of Flavin-Containing Monooxygenases and Peroxidases</b>	Piyush M. Vyas, Sanjoy Roychowdhury, Sevasti B. Koukouritaki, Ronald N. Hines, Sharon K. Krueger, David E. Williams, William M. Nauseef, and Craig K. Svensson	497
<b>CHEMOTHERAPY, ANTIBIOTICS, AND GENE THERAPY</b>		
<b>Inhibition of the Enzymatic Activity of Heme Oxygenases by Azole-Based Antifungal Drugs</b>	Robert T. Kinobe, Ryan A. Dercho, Jason Z. Vlahakis, James F. Brien, Walter A. Szarek, and Kanji Nakatsu	277
<b>ENDOCRINE AND DIABETES</b>		
<b>Inhibition of Protein Kinase C<math>\beta</math> Protects against Diabetes-Induced Impairment in Arachidonic Acid Dilatation of Small Coronary Arteries</b>	Wei Zhou, Xiao-Li Wang, Kathryn G. Lamping, and Hon-Chi Lee	199
<b>GASTROINTESTINAL, HEPATIC, PULMONARY, AND RENAL</b>		
<b>Intracellular Delivery of the p38 Mitogen-Activated Protein Kinase Inhibitor SB202190 [4-(4-Fluorophenyl)-2-(4-hydroxyphenyl)-5-(4-pyridyl)1H-imidazole] in Renal Tubular Cells: A Novel Strategy to Treat Renal Fibrosis</b>	Jai Prakash, Maria Sandovici, Vinay Saluja, Marie Lacombe, Roel Q. J. Schaapveld, Martin H. de Borst, Harry van Goor, Robert H. Henning, Johannes H. Proost, Frits Moolenaar, György Kéri, Dirk K. F. Meijer, Klaas Poelstra, and Robbert J. Kok	8
☐ <b>Y<sub>4</sub> Receptors Mediate the Inhibitory Responses of Pancreatic Polypeptide in Human and Mouse Colon Mucosa</b>	Iain R. Tough, Nicholas D. Holliday, and Helen M. Cox	20
<b>Role of Renal Nerves and Salt Intake on Erythropoietin Secretion in Rats following Carbon Monoxide Exposure</b>	Cathérine Gebhard, Fotios Petroktistis, Hua Zhang, Daniel Kammerer, Christoph Köhle, Karin Klingel, Margitta Albinus, Christoph H. Gleiter, Hartmut Osswald, and Almut Grenz	111
<b>Acid-Induced Release of Platelet-Activating Factor by Human Esophageal Mucosa Induces Inflammatory Mediators in Circular Smooth Muscle</b>	Ling Cheng, Weibiao Cao, Jose Behar, Claudio Fiocchi, Piero Biancani, and Karen M. Harnett	117
<b>Therapeutic Potential of (-)-Epigallocatechin 3-O-Gallate on Renal Damage in Diabetic Nephropathy Model Rats</b>	Noriko Yamabe, Takako Yokozawa, Takeshi Oya, and Mujo Kim	228
☐ <b>5-Amino-2-hydroxy-benzoic Acid 4-(5-Thioxo-5H-[1,2]-dithiol-3yl)-phenyl Ester (ATB-429), a Hydrogen Sulfide-Releasing Derivative of Mesalamine, Exerts Antinociceptive Effects in a Model of Postinflammatory Hypersensitivity</b>	Eleonora Distrutti, Luca Sediari, Andrea Mencarelli, Barbara Renga, Stefano Orlandi, Giuseppe Russo, Giuseppe Caliendo, Vincenzo Santagada, Giuseppe Cirino, John L. Wallace, and Stefano Fiorucci	447
<b>Prostaglandin/Cyclooxygenase Pathway in Ghrelin-Induced Gastroprotection against Ischemia-Reperfusion Injury</b>	Tomasz Brzozowski, Peter C. Konturek, Zbigniew Sliwowski, Robert Pajdo, Danuta Drozdowicz, Sławomir Kwiecien, Grzegorz Burnat, Stanislaw J. Konturek, and Wieslaw W. Pawlik	477
<b>INFLAMMATION, IMMUNOPHARMACOLOGY, AND ASTHMA</b>		
<b>Interleukin-10 Protects Lipopolysaccharide-Induced Neurotoxicity in Primary Midbrain Cultures by Inhibiting the Function of NADPH Oxidase</b>	Li Qian, Michelle L. Block, Sung-Jen Wei, Chiou-feng Lin, Jeffrey Reece, Hao Pang, Belinda Wilson, Jau-Shyong Hong, and Patrick M. Flood	44
<b>Peripheral Phosphodiesterase 4 Inhibition Produced by 4-[2-(3,4-Bis-difluoromethoxyphenyl)-2-[4-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-phenyl]-ethyl]-3-methylpyridine-1-oxide (L-826,141) Prevents Experimental Autoimmune Encephalomyelitis</b>	C. S. Moore, N. Earl, R. Frenette, A. Styhler, J. A. Mancini, D. W. Nicholson, A. L. O. Hebb, T. Owens, and G. S. Robertson	63
<b>Glucocerebroside Ameliorates the Metabolic Syndrome in OB/OB Mice</b>	Maya Margalit, Zvi Shalev, Orit Pappo, Miriam Sklair-Levy, Ruslana Alper, Moshe Gomori, Dean Engelhardt, Elazar Rabbani, and Yaron Ilan	105

<b>Poly(ADP-Ribose) Glycohydrolase Activity Mediates Post-Traumatic Inflammatory Reaction after Experimental Spinal Cord Trauma</b>	Salvatore Cuzzocrea, Tiziana Genovese, Emanuela Mazzon, Concetta Crisafulli, Wookee Min, Rosanna Di Paola, Carmelo Muià, Jia-He Li, Emanuela Esposito, Placido Bramanti, Weizheng Xu, Edmond Massuda, Jie Zhang, and Zhao-Qi Wang	127
<b>Cannabinoid Treatment Suppresses the T-Helper Cell-Polarizing Function of Mouse Dendritic Cells Stimulated with <i>Legionella pneumophila</i> Infection</b>	Tangying Lu, Cathy Newton, Izabella Perkins, Herman Friedman, and Thomas W. Klein	269
<b>Basilolides, a Class of Tetracyclic C19 Dilactones from <i>Thapsia garganica</i>, Release Ca<sup>2+</sup> from the Endoplasmic Reticulum and Regulate the Activity of the Transcription Factors Nuclear Factor of Activated T Cells, Nuclear Factor <math>\kappa</math>B, and Activator Protein 1 in T Lymphocytes</b>	Carmen Navarrete, Rocío Sancho, Francisco J. Caballero, Federica Pollastro, Bernd L. Fiebich, Olov Sterner, Giovanni Appendino, and Eduardo Muñoz	422
<b>Phosphodiesterase Type 4 Inhibitors Cause Proinflammatory Effects in Vivo</b>	Kerryn McCluskie, Uwe Klein, Chris Linnevers, Yu-hua Ji, Alfred Yang, Craig Husfeld, and G. Roger Thomas	468
<b>METABOLISM, TRANSPORT, AND PHARMACOGENOMICS</b>		
<b>Expression and Transport Activity of Breast Cancer Resistance Protein (Bcrp/Abcg2) in Dually Perfused Rat Placenta and HRP-1 Cell Line</b>	Frantisek Staud, Zuzana Vackova, Katerina Pospechova, Petr Pavek, Martina Ceckova, Antonin Libra, Lenka Cygalova, Petr Nachtigal, and Zdenek Fendrich	53
<b>A Mechanistic Study on Reduced Toxicity of Irinotecan by Coadministered Thalidomide, a Tumor Necrosis Factor-<math>\alpha</math> Inhibitor</b>	Xiao-Xia Yang, Ze-Ping Hu, An-Long Xu, Wei Duan, Yi-Zhun Zhu, Min Huang, Fwu-Shan Sheu, Qiang Zhang, Jin-Song Bian, Eli Chan, Xiaotian Li, Jian-Cheng Wang, and Shu-Feng Zhou	82
<b>Human Organic Anion Transporter 3 Gene Is Regulated Constitutively and Inducibly via a cAMP-Response Element</b>	Ken Ogasawara, Tomohiro Terada, Jun-ichi Asaka, Toshiya Katsura, and Ken-ichi Inui	317
<b>The Role of Retinoid X Receptor <math>\alpha</math> in Regulating Alcohol Metabolism</b>	Maxwell Afari Gyamfi, Michael George Kocsis, Lin He, Guoli Dai, Alphonse John Mendy, and Yu-Jui Yvonne Wan	360
<b>Differential Involvement of Mrp2 (Abcc2) and Bcrp (Abcg2) in Biliary Excretion of 4-Methylumbelliferyl Glucuronide and Sulfate in the Rat</b>	Maciej J. Zamek-Gliszczynski, Keith A. Hoffmaster, Joan E. Humphreys, Xianbin Tian, Ken-ichi Nezasa, and Kim L. R. Brouwer	459
<b>NEUROPHARMACOLOGY</b>		
<b>Heterogeneous Dopamine Neurochemistry in the Striatum: The Fountain-Drain Matrix</b>	Manuel Rodriguez, Ingrid Morales, Isabel Gomez, Sergio Gonzalez, Tomas Gonzalez-Hernandez, and Jose Luis Gonzalez-Mora	31
<b>Role for Neuronal Nitric-Oxide Synthase in Cannabinoid-Induced Neurogenesis</b>	Sun Hee Kim, Seok Joon Won, Xiao Ou Mao, Catherine Ledent, Kunlin Jin, and David A. Greenberg	150
<b>Iptakalim Modulates ATP-Sensitive K<sup>+</sup> Channels in Dopamine Neurons from Rat Substantia Nigra Pars Compacta</b>	Jie Wu, Jun Hu, Yu-Ping Chen, Teruko Takeo, Sechiko Suga, Jamie DeChon, Qiang Liu, Ke-Chun Yang, Paul A. St. John, Gang Hu, Hai Wang, and Makoto Wakui	155
<b>Involvement of Multitargets in Paoniflorin-Induced Preconditioning</b>	Dong-Mei Chen, Liang Xiao, Xin Cai, Rong Zeng, and Xing-Zu Zhu	165
<b>Gabapentin-Lactam Induces Dendritic Filopodia and Motility in Cultured Hippocampal Neurons</b>	Frank Henle, Jost Leemhuis, Catharina Fischer, Hans H. Bock, Kerstin Lindemeyer, Thomas J. Feuerstein, and Dieter K. Meyer	181
<b>A Polyclonal Antibody to the Prepore Loop of Transient Receptor Potential Vanilloid Type 1 Blocks Channel Activation</b>	Lana Klionsky, Rami Tamir, Bob Holzinger, Xiaojuan Bi, Jane Talvenheimo, Helen Kim, Frank Martin, Jean-Claude Louis, James J. S. Treanor, and Narender R. Gavva	192
<b>An Isoflurane- and Alcohol-Insensitive Mutant GABA<sub>A</sub> Receptor <math>\alpha_1</math> Subunit with Near-Normal Apparent Affinity for GABA: Characterization in Heterologous Systems and Production of Knockin Mice</b>	C. M. Borghese, D. F. Werner, N. Topf, N. V. Baron, L. A. Henderson, S. L. Boehm II, Y. A. Blednov, A. Saad, S. Dai, R. A. Pearce, R. A. Harris, G. E. Homanics, and N. L. Harrison	208

<b>Knockin Mice with Ethanol-Insensitive <math>\alpha</math>1-Containing <math>\gamma</math>-Aminobutyric Acid Type A Receptors Display Selective Alterations in Behavioral Responses to Ethanol</b>	David F. Werner, Yuri A. Blednov, Olusegun J. Ariwodola, Yuval Silberman, Exazevia Logan, Raymond B. Berry, Cecilia M. Borghese, Douglas B. Matthews, Jeffrey L. Weiner, Neil L. Harrison, R. Adron Harris, and Gregg E. Homanics	219
<b>Interaction of Amphetamines and Related Compounds at the Vesicular Monoamine Transporter</b>	John S. Partilla, Allison G. Dempsey, Ameet S. Nagpal, Bruce E. Blough, Michael H. Baumann, and Richard B. Rothman	237
<b>Separation of Binding Affinity and Intrinsic Activity of the Potent <math>\mu</math>-Opioid 14-Methoxymetopon</b>	Loriann Mahurter, Carrie Garceau, Jacqueline Marino, Helmut Schmidhammer, Géza Tóth, and Gavril W. Pasternak	247
<b>Partial Recovery of Striatal Nicotinic Receptors in 1-Methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)-Lesioned Monkeys with Chronic Oral Nicotine</b>	Tanuja Bordia, Neeraja Parameswaran, Hong Fan, J. William Langston, J. Michael McIntosh, and Maryka Quik	285
<b>Pharmacological Characterization of cGMP Regulation by the Biarylpropylsulfonamide Class of Positive, Allosteric Modulators of <math>\alpha</math>-Amino-3-hydroxy-5-methyl-4-isoxazolepropionic Acid Receptors</b>	John W. Ryder, Julie F. Falcone, Jason R. Manro, Kjell A. Svensson, and Kalpana M. Merchant	293
<b>Utilization of Combined Chemical Modifications to Enhance the Blood-Brain Barrier Permeability and Pharmacological Activity of Endomorphin-1</b>	Hong-Mei Liu, Xue-Feng Liu, Jin-Long Yao, Chang-Lin Wang, Ye Yu, and Rui Wang	308
<b>Interaction of Riluzole with the Closed Inactivated State of Kv4.3 Channels</b>	Hye Sook Ahn, Sung Eun Kim, Hyun-Jong Jang, Myung-Jun Kim, Duck-Joo Rhie, Shin-Hee Yoon, Yang-Hyeok Jo, Myung-Suk Kim, Ki-Wug Sung, and Sang June Hahn	323
<b>NAP Enhances Neurodevelopment of Newborn Apolipoprotein E-Deficient Mice Subjected to Hypoxia</b>	Michael Rotstein, Haim Bassan, Naam Kariv, Zipora Speiser, Shaul Harel, and Illana Gozes	332
<b>The Magnitude of <math>\alpha</math>7 Nicotinic Receptor Currents in Rat Hippocampal Neurons Is Dependent upon GABAergic Activity and Depolarization</b>	Hélio R. Santos, Helizane S. Ribeiro, Pedro Setti-Perdigão, Edson X. Albuquerque, and Newton G. Castro	376
<b>Antiallodynic and Antihyperalgesic Effects of Selective Competitive <math>GLU_{K5}</math> (GluR5) Ionotropic Glutamate Receptor Antagonists in the Capsaicin and Carrageenan Models in Rats</b>	Carrie K. Jones, Andrew Alt, Ann Marie Ogden, David Bleakman, Rosa M. A. Simmons, Smriti Iyengar, Esteban Dominguez, Paul L. Ornstein, and Harlan E. Shannon	396
<b>Multiple High Doses of Methamphetamine Increase the Number of Preproenkephalin mRNA-Expressing Neurons in the Striatum of Rat via a Dopamine D1 Receptor-Dependent Mechanism</b>	Kristen A. Horner, Scot C. Westwood, Glen R. Hanson, and Kristen A. Keefe	414
<b>Effects of Ethanol on Tonic GABA Currents in Cerebellar Granule Cells and Mammalian Cells Recombinantly Expressing <math>GABA_A</math> Receptors</b>	Megumi Yamashita, William Marszalec, Jay Z. Yeh, and Toshio Narahashi	431
<b>TOXICOLOGY</b>		
<b>Identification and Characterization of Functional Rat Arylamine <i>N</i>-Acetyltransferase 3: Comparisons with Rat Arylamine <i>N</i>-Acetyltransferases 1 and 2</b>	Jason M. Walraven, Mark A. Doll, and David W. Hein	369
<b>ERRATUM</b>		
<b>Correction to "Mitochondrial Arginase II Modulates Nitric-Oxide Synthesis through Nonfreely Exchangeable L-Arginine Pools in Human Endothelial Cells"</b>	Gökce Topal, Annie Brunet, Laurence Walch, Jean-Luc Boucher, and Monique David-Dufilho	506

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

*About the cover:* B to D, anti-LZM immunohistochemical staining on kidney sections. Masson staining shows renal morphology in untreated animals (E) and SB-ULZ-LZM-treated animals at 24 (F) and 72 (G) h at 200 $\times$  magnification. See the article by Prakash et al. on page 8 of this issue.