

The Journal of PHARMACOLOGY

And Experimental Therapeutics

A Publication of the American Society for Pharmacology and Experimental Therapeutics

January 2006

Vol. 316, No. 1

Contents

PERSPECTIVES IN PHARMACOLOGY

- The Role of Protein Kinase C Isoforms in Modulating Injury and Repair of the Intestinal Barrier A. Farhadi, A. Keshavarzian, Z. Ranjbaran, J. Z. Fields, and A. Banan 1

ABSORPTION, DISTRIBUTION, METABOLISM, AND EXCRETION

- Evaluation of Tributyrin Lipid Emulsion with Affinity to Low-Density Lipoprotein: Pharmacokinetics in Adult Male Wistar Rats and Cellular Activity on Caco-2 and HepG2 Cell Lines Jie Su, Li He, Ningning Zhang, and Paul C. Ho 62

- Sexually Dimorphic Regulation of Hepatic Isoforms of Human Cytochrome P450 by Growth Hormone Ravindra N. Dhir, Wojciech Dworakowski, Chellappagounder Thangavel, and Bernard H. Shapiro 87

- The Dual Actions of Morin (3,5,7,2',4'-Pentahydroxyflavone) as a Hypouricemic Agent: Uricosuric Effect and Xanthine Oxidase Inhibitory Activity Zhifeng Yu, Wing Ping Fong, and Christopher H. K. Cheng 169

- Preparation of a Claudin-Targeting Molecule Using a C-Terminal Fragment of *Clostridium perfringens* Enterotoxin Chiaki Ebihara, Masuo Kondoh, Naoki Hasuike, Motoki Harada, Hiroyuki Mizuguchi, Yasuhiko Horiguchi, Makiko Fujii, and Yoshiteru Watanabe 255

- Inactivation of CYP2A6 and CYP2A13 during Nicotine Metabolism Linda B. von Weymarn, Kathryn M. Brown, and Sharon E. Murphy 295

- The Utility of in Vitro Cytochrome P450 Inhibition Data in the Prediction of Drug-Drug Interactions R. Scott Obach, Robert L. Walsky, Karthik Venkatakrishnan, Emily A. Gaman, J. Brian Houston, and Larry M. Tremaine 336

- The Impact of Plasma Protein Binding on the Renal Transport of Organic Anions Daniel A. J. Bow, Jennifer L. Perry, John D. Simon, and John B. Pritchard 349

- A Biosynthetic Pathway Generating 12-Hydroxy-5,8,14-eicosatrienoic Acid from Arachidonic Acid Is Active in Mouse Skin Microsomes Liping Du, Valery Yermalitsky, David L. Hachey, Setti G. Jagadeesh, John R. Falck, and Diane S. Keeney 371

BEHAVIORAL PHARMACOLOGY

- Depressive-Like Effects of the κ -Opioid Receptor Agonist Salvinorin A on Behavior and Neurochemistry in Rats William A. Carlezon, Jr., Cécile Béguin, Jennifer A. DiNieri, Michael H. Baumann, Michele R. Richards, Mark S. Todtenkopf, Richard B. Rothman, Zhongze Ma, David Y.-W. Lee, and Bruce M. Cohen 440

CARDIOVASCULAR

- YC-1 [3-(5'-Hydroxymethyl-2'-furyl)-1-benzyl Indazole] Inhibits Neointima Formation in Balloon-Injured Rat Carotid through Suppression of Expressions and Activities of Matrix Metalloproteinases 2 and 9 Yi-Nan Liu, Shiow-Lin Pan, Chieh-Yu Peng, Jih-Hwa Guh, Dong-Ming Huang, Ya-Ling Chang, Chun-Hung Lin, Hui-Chen Pai, Sheng-Chu Kuo, Fang-Yu Lee, and Che-Ming Teng 35

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.

Increased Superoxide Anion Production by Interleukin-1β Impairs Nitric Oxide-Mediated Relaxation in Resistance Arteries	Francesc Jiménez-Altayó, Ana M. Briones, Jesús Giraldo, Anna M. Planas, Mercedes Salaices, and Elisabet Vila	42
Pressor Responses to Ephedrine Are Mediated by a Direct Mechanism in the Rat	John T. Liles, Paul A. Dabisch, Keith E. Hude, Leena Pradhan, Kurt J. Varner, Johnny R. Porter, Alissa R. Hicks, Conni Corll, Syed R. Baber, and Philip J. Kadowitz	95
Hyperlipidemia Attenuates the Infarct Size-Limiting Effect of Ischemic Preconditioning: Role of Matrix Metalloproteinase-2 Inhibition	Zoltán Giricz, Manoj M. Lalu, Csaba Csonka, Péter Bencsik, Richard Schulz, and Péter Ferdinandy	154
The Amiodarone Derivative KB130015 [2-Methyl-3-(3,5-diiodo-4-carboxymethoxybenzyl)benzofuran] Induces an Na⁺-Dependent Increase of [Ca²⁺] in Ventricular Myocytes	Virginie Bito, Dieter Dauwe, Fons Verdonck, Kanigula Mubagwa, and Karin R. Sipido	162
Dosing Time-Dependent Effect of Temocapril on the Mortality of Stroke-Prone Spontaneously Hypertensive Rats	Masahiko Nozawa, Koh-ichi Sugimoto, Masami Ohmori, Hitoshi Ando, and Akio Fujimura	176
Bepridil, an Antiarrhythmic Drug, Opens Mitochondrial K_{ATP} Channels, Blocks Sarcolemmal K_{ATP} Channels, and Confers Cardioprotection	Toshiaki Sato, Alexandre D. T. Costa, Tomoaki Saito, Takehiko Ogura, Hideyuki Ishida, Keith D. Garlid, and Haruaki Nakaya	182
Blockade of Electron Transport before Cardiac Ischemia with the Reversible Inhibitor Amobarbital Protects Rat Heart Mitochondria	Qun Chen, Charles L. Hoppel, and Edward J. Lesnefsky	200
Chronic Ethanol Consumption Enhances Phenylephrine-Induced Contraction in the Isolated Rat Aorta	Carlos R. Tirapelli, Johnny Al-Khoury, Ghassan Bkaily, Pedro D'Orléans-Juste, Vera L. Lanchote, Sergio A. Uyemura, and Ana M. de Oliveira	233
A Nonthiazolidinedione Peroxisome Proliferator-Activated Receptor γ Agonist Reverses Endothelial Dysfunction in Diabetic (db/db^{-/-}) Mice	Andrew G. Howarth, William B. Wiehler, Malarvannan Pannirselvam, Yanfen Jiang, Joel P. Berger, David Severson, Todd J. Anderson, and Chris R. Triggle	364
Multiple Cellular Electrophysiological Effects of a Novel Antiarrhythmic Furoquinoline Derivative HA-7 [N-Benzyl-7-methoxy-2,3,4,9-tetrahydrofuro[2,3-b]quinoline-3,4-dione] in Guinea Pig Cardiac Preparations	Gwo-Jyh Chang, Ming-Jai Su, Sheng-Chu Kuo, Tsung-Ping Lin, and Ying-Shiung Lee	380
Induction of β_3-Adrenergic Receptor Functional Expression following Chronic Stimulation with Noradrenaline in Neonatal Rat Cardiomyocytes	Renée Germack and John M. Dickenson	392
ARD-353 [4-((2<i>R</i>,5<i>S</i>)-4-(<i>R</i>)-(4-Diethylcarbamoylphenyl)(3-hydroxyphenyl)methyl)-2,5-dimethylpiperazin-1-ylmethyl)-benzoic Acid], A Novel Nonpeptide δ Receptor Agonist, Reduces Myocardial Infarct Size without Central Effects	Michael. J. Watson, Jonathon D. S. Holt, Scott J. O'Neill, Ke Wei, William Pendergast, Garrett J. Gross, Peter J. Gengo, and Kwen-Jen Chang	423
CELLULAR AND MOLECULAR		
Nitric Oxide-Donating Aspirin Inhibits Colon Cancer Cell Growth via Mitogen-Activated Protein Kinase Activation	Thomas R. Hundley and Basil Rigas	25
HIV Protease Inhibitors: Suppression of Insulin Secretion by Inhibition of Voltage-Dependent K⁺ Currents and Anion Currents	Yvonne Neye, Martina Düfer, Gisela Drews, and Peter Krippel-Drews	106
Molecular Mechanisms for Large Conductance Ca²⁺-Activated K⁺ Channel Activation by a Novel Opener, 12,14-Dichlorodehydroabiatic Acid	Kazuho Sakamoto, Taro Nonomura, Susumu Ohya, Katsuhiko Muraki, Tomohiko Ohwada, and Yuji Imaizumi	144
3-<i>O</i>-Acetyl-11-keto-boswellic Acid Decreases Basal Intracellular Ca²⁺ Levels and Inhibits Agonist-Induced Ca²⁺ Mobilization and Mitogen-Activated Protein Kinase Activation in Human Monocytic Cells	Daniel Poeckel, Lars Tausch, Sven George, Johann Jauch, and Oliver Werz	224
□ Niemann-Pick C1 Protein Facilitates the Efflux of the Anticancer Drug Daunorubicin from Cells According to a Novel Vesicle-Mediated Pathway	Yuping Gong, Muralikrishna Duvvuri, Michael B. Duncan, Jian Liu, and Jeffrey P. Krise	242
Constitutive Activity and Inverse Agonism at the M₂ Muscarinic Acetylcholine Receptor	Carl P. Nelson, Stefan R. Nahorski, and R. A. John Challiss	279
Proline 326 in the C Terminus of Murine CX3CR1 Prevents G-Protein and Phosphatidylinositol 3-Kinase-Dependent Stimulation of Akt and Extracellular Signal-Regulated Kinase in Chinese Hamster Ovary Cells	Christopher N. Davis and Jeffrey K. Harrison	356

Erythropoietin Receptor Signal Transduction Requires Protein Geranylgeranylation	Sumaya N. Hamadmad, Matthew K. Henry, and Raymond J. Hohl	403
The Mitogen-Activated Protein Kinase/Extracellular Signal-Regulated Kinase Kinase Inhibitor PD184352 (CI-1040) Selectively Induces Apoptosis in Malignant Schwannoma Cell Lines	Raymond R. Mattingly, Janice M. Kraniak, Joshua T. Dilworth, Patricia Mathieu, Beverly Bealmeare, James E. Nowak, Joyce A. Benjamins, Michael A. Tainsky, and John J. Reiners, Jr.	456
CHEMOTHERAPY, ANTIBIOTICS, AND GENE THERAPY		
Hpr6 (Heme-1 Domain Protein) Regulates the Susceptibility of Cancer Cells to Chemotherapeutic Drugs	Gerard Crudden, Rachel E. Chitti, and Rolf J. Craven	448
ENDOCRINE AND DIABETES		
Long-Term Treatment with Novel Glycogen Synthase Kinase-3 Inhibitor Improves Glucose Homeostasis in ob/ob Mice: Molecular Characterization in Liver and Muscle	Oksana Kaidanovich-Beilin and Hagit Eldar-Finkelman	17
GASTROINTESTINAL, HEPATIC, PULMONARY, AND RENAL		
Expression and Response to Angiotensin-Converting Enzyme Inhibition of Matrix Metalloproteinases 2 and 9 in Renal Glomerular Damage in Young Transgenic Rats with Renin-Dependent Hypertension	Juliane Bolbrinker, Snezana Markovic, Markus Wehland, Wynand B. W. H. Melenhorst, Harry van Goor, and Reinhold Kreutz	8
Evidence That Hydrogen Sulfide Exerts Antinociceptive Effects in the Gastrointestinal Tract by Activating K_{ATP} Channels	Eleonora Distrutti, Luca Sediari, Andrea Mencarelli, Barbara Renga, Stefano Orlandi, Elisabetta Antonelli, Fiorenza Roviezzo, Antonio Morelli, Giuseppe Cirino, John L. Wallace, and Stefano Fiorucci	325
Energy Homeostasis and Gastric Emptying in Ghrelin Knockout Mice	B. De Smet, I. Depoortere, D. Moechars, Q. Swennen, B. Moreaux, K. Cryns, J. Tack, J. Buyse, B. Coulie, and T. L. Peeters	431
INFLAMMATION AND IMMUNOPHARMACOLOGY		
Activation of the Adenosine A₃ Receptor in RAW 264.7 Cells Inhibits Lipopolysaccharide-Stimulated Tumor Necrosis Factor-α Release by Reducing Calcium-Dependent Activation of Nuclear Factor-κB and Extracellular Signal-Regulated Kinase 1/2	Lynn Martin, Sandeep C. Pingle, Daniel M. Hallam, Leonard P. Rybak, and Vickram Ramkumar	71
Inhibition of Inducible Nitric-Oxide Synthase Expression by (5R)-5-hydroxytryptolide in Interferon-γ- and Bacterial Lipopolysaccharide Stimulated Macrophages	Ru Zhou, Shen-Xi Zheng, Wei Tang, Pei-Lan He, Xiao-Yu Li, Yi-Fu Yang, Yuan-Chao Li, Jian-Guo Geng, and Jian-Ping Zuo	121
Antixudative Effects of Opioids and Expression of κ- and δ-Opioid Receptors during Intestinal Inflammation in Mice: Involvement of Nitric Oxide	Natalia Jiménez, Margarita M. Puig, and Olga Pol	261
Blockade of Nuclear Factor-κB Signaling Pathway and Anti-Inflammatory Activity of Cardamomin, a Chalcone Analog from <i>Alpinia conchigera</i>	Jeong-Hyung Lee, Haeng Sun Jung, Phan Minh Giang Xuejun Jin, Sangku Lee, Phan Tong Son, Dongho Lee, Young-Soo Hong, Kyeong Lee, and Jung Joon Lee	271
NEUROPHARMACOLOGY		
Evaluation of Drug Penetration into the Brain: A Double Study by in Vivo Imaging with Positron Emission Tomography and Using an in Vitro Model of the Human Blood-Brain Barrier	Véronique Jossierand, Hélène Pélerin, Béatrice de Bruin, Benoît Jégo, Bertrand Kuhnast, Françoise Hinnen, Frédéric Ducongé, Raphaël Boisgard, Frédéric Beuvon, Francine Chassoux, Catherine Daumas-Duport, Eric Ezan, Frédéric Dollé, Aloïse Mabondzo, and Bertrand Tavitian	79
Dopamine-Mediated Disinhibition in the CA1 Region of Rat Hippocampus via D₃ Receptor Activation	Hana Hammad and John J. Wagner	113
Characterization of Prejunctional Serotonin Receptors Modulating [³H]Acetylcholine Release in the Human Detrusor	Gianluigi D'Agostino, Anna M. Condino, Paola Gallinari, Gian P. Franceschetti, and Marcello Tonini	129

Targeted Antioxidative and Neuroprotective Properties of the Dopamine Agonist Pramipexole and Its Nondopaminergic Enantiomer SND919CL2x [(+)-2-Amino-4,5,6,7-tetrahydro-6-L-propylamino-benzothiazole Dihydrochloride]	R. Danzeisen, B. Schwalenstoecker, F. Gillardon, E. Buerger, V. Krzykalla, K. Klinder, L. Schild, B. Hengerer, A. C. Ludolph, C. Dorner-Ciossek, and L. Kussmaul	189
Volatile Anesthetic Effects on Glutamate versus GABA Release from Isolated Rat Cortical Nerve Terminals: Basal Release	Robert I. Westphalen and Hugh C. Hemmings, Jr.	208
Volatile Anesthetic Effects on Glutamate versus GABA Release from Isolated Rat Cortical Nerve Terminals: 4-Aminopyridine-Evoked Release	Robert I. Westphalen and Hugh C. Hemmings, Jr.	216
Tobacco Smoke Chemicals Attenuate Brain-to-Blood Potassium Transport Mediated by the Na,K,2Cl-Cotransporter during Hypoxia-Reoxygenation	Jennifer R. Paulson, Karen E. Roder, Ghia McAfee, David D. Allen, Cornelis J. Van der Schyf, and Thomas J. Abbruscato	248
Ketamine Produces Lasting Disruptions in Encoding of Sensory Stimuli	Christina R. Maxwell, Richard S. Ehrlichman, Yuling Liang, Danielle Trief, Stephen J. Kanes, Jonathan Karp, and Steven J. Siegel	315
TPA023 [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], an Agonist Selective for α2- and α3-Containing GABA_A Receptors, Is a Nonsedating Anxiolytic in Rodents and Primates	John R. Atack, Keith A. Wafford, Spencer J. Tye, Susan M. Cook, Bindi Sohal, Andrew Pike, Cyrille Sur, David Melillo, Linda Bristow, Fran Bromidge, Ian Ragan, Julie Kerby, Les Street, Robert Carling, José L. Castro, Paul Whiting, Gerard R. Dawson, and Ruth M. McKernan	410
Systemic and Intrathecal Effects of a Novel Series of Phospholipase A₂ Inhibitors on Hyperalgesia and Spinal Prostaglandin E₂ Release	Tony L. Yaksh, George Kokotos, Camilla I. Svensson, Daren Stephens, Christoforos G. Kokotos, Bethany Fitzsimmons, Dimitra Hadjipavlou-Litina, Xiao-Ying Hua, and Edward A. Dennis	466
TOXICOLOGY		
Neurotoxicity of Ecstasy Metabolites in Rat Cortical Neurons, and Influence of Hyperthermia	João Paulo Capela, Andreas Meisel, Artur Reis Abreu, Paula Sérgio Branco, Luísa Maria Ferreira, Ana Maria Lobo, Fernando Remião, Maria Lurdes Bastos, and Félix Carvalho	53
Deltamethrin, a Pyrethroid Insecticide, Is a Potent Inducer for the Activity-Dependent Gene Expression of Brain-Derived Neurotrophic Factor in Neurons	Lisa Imamura, Makoto Yasuda, Kozue Kuramitsu, Daichi Hara, Akiko Tabuchi, and Masaaki Tsuda	136
4,4'-Methylenedianiline-Induced Hepatotoxicity Is Modified by N-Acetyltransferase 2 (NAT2) Acetylator Polymorphism in the Rat	Xiaoyan Zhang, Jason C. Lambert, Mark A. Doll, Jason M. Walraven, Gavin E. Arteel, and David W. Hein	289
Arsenic Trioxide Induces Apoptosis of Human Monocytes during Macrophagic Differentiation through Nuclear Factor-κB-Related Survival Pathway Down-Regulation	Anthony Lemarie, Claudie Morzadec, Delphine Mérino, Olivier Micheau, Olivier Fardel, and Laurent Vernhet	304
LETTERS TO THE EDITOR		
Comments on "Isobolographic Analysis for Combinations of a Full and Partial Agonist: Curved Isoboles"	J. Ignacio Lorenzo and Paula Sánchez-Marín	476
Response to Comments on "Isobolographic Analysis for Combinations of a Full and Partial Agonist: Curved Isoboles"	Ronald J. Tallarida	479

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

About the cover: Whole-body PET images acquired over 2 min after the intravenous injection of the [¹⁸F]fluoropyridinyl derivatives. See the article by Josserand et al. on page 79 of this issue.