

Department of Pharmaceutical Sciences 2005 Annual Report

Peer-Reviewed Research or Review Papers in 2005.

Thomas Abbruscato, Ph.D.

Rudd, K., Raehl, C.L., **Abbruscato, T.J.**, Bond, C.A., Stenhouse, A.C. Current Approaches to Assessing Medication-Related Anticholinergic Potential. *Pharmacotherapy* 11: 1592-1601, 2005.

-collaboration on IHA grant.

Lockman, P.R., McAfee, G., Geldenhuys, W.J., Van der Schyf, C.J., **Abbruscato, T.J.**, and Allen, D.D. Brain uptake kinetics of nicotine and cotinine after chronic nicotine exposure. *J. Pharmacol. Exp. Ther.* 314(2):636-642, 2005.

-supports RO1 NS 046526

Mdzinarishvili, A., Geldenhuys, W.J., **Abbruscato, T.J.**, Bickel, U., Klein, J., Van der Schyf, C.J. NGP1-01, a lipophilic polycyclic cage amine, is neuroprotective in focal ischemia. *Neuros. Lett.* 314(2):636-642, 2005.

-PATOS collaboration

Lockman, P.R., Van der Schyf, C.J., **Abbruscato, T.J.**, and Allen, D.D. Chronic nicotine exposure alters blood-brain barrier permeability and diminishes brain uptake of methyllycaconitine. *J. Neurochem.* 94(1): 37-44, 2005.

-supports RO1 NS 046526

Paulson, J.R., Roder, K.E., McAfee, G., Allen, D.D., Van der Schyf, C.J., **Abbruscato, T.J.** Tobacco smoke chemicals attenuate brain-to-blood potassium transport mediated by Na,K,2Cl-cotransporter during hypoxia-reoxygenation. *J. Pharmacol. Exp. Ther.* 316(1): 248-254, 2006.

-supports RO1 NS 046526

Yang, T., Roder, K.E., Bhat, G.J., Thekkumkara, T.J. and **Abbruscato, T.J.** Protein kinase C family members in the regulation of blood-brain barrier Na,K,2Cl-cotransporter during in vitro stroke conditions and nicotine exposure. *Pharm. Res.* (In Press) 2006.

-supports RO1 NS 046526

Lockman, P.R., Gaasch, J., McAfee, G. **Abbruscato, T.J.**, Van der Schyf, C.J., and Allen, D.D. Nicotine exposure does not alter plasma to brain choline transfer. *Neurochem. Res.* (In Press) 2006.

-supports RO1 NS 046526

Fakhrul Ahsan, Ph.D.

A. Hussain, Q.H. Majumder, **F. Ahsan*** (2005) Inhaled insulin is better absorbed when administered as a dry powder compared to solution in the presence or absence of alkylglycosides. *Pharmaceutical Research*, Electronic version is available at journal website since Dec 7, 2005.

A. Hussain, **F. Ahsan*** (2005) Pulmonary Delivery of monomeric and hexameric insulin. *European Journal of Pharmaceutical Sciences.* 25, 289-298.

A. Hussain, **F. Ahsan*** (2005) The vagina as a route for systemic drug delivery. *Journal of Controlled Release* 103: 301-313.

T. Yang, JJ Arnold, **F. Ahsan*** (2005) Tetradecylmaltoside (TDM) enhances *in vitro* and *in vivo* intestinal absorption of enoxaparin, a low molecular weight heparin. *Journal of Drug Targeting* 13: 29-38.

F. Ahsan* and J. Klein (2005) Microarray analysis and response of the lungs to inhaled insulin. *Diabetes Technology and Therapeutic* 7:525-527.

Ulrich Bickel, M.D.

Bickel, U. How to measure brain uptake. *NeuroRX* 2:15-26, 2005 (new journal, no impact factor yet available)

Fischer, D., Bhattacharya, R., Osburg, B., and **Bickel, U.** Inhibition of monocyte adhesion on brain-derived endothelial cells by NF-kappaB decoy/polyethylenimine complexes *J. Gene Med.* J. 7:1063-1076, 2005. (Impact Factor 3.22)

Mdzinarishvili, A., Geldenhuys, W.J., Abbruscato, T.J., **Bickel, U.**, Klein, J., Van der Schyf, C.J. NGP1-01, a lipophilic polycyclic cage amine, is neuroprotective in focal ischemia. *Neurosci. Lett.* 383:49-53, 2005 (Impact Factor 2.02)

Jayarama Gunaje, Ph.D.

Yang, T., Roder, K.E., **Bhat, G.J.** Thekkumkara, T.J. and Abbruscato, T.J. (2006). Protein kinase C family members as a target for regulation of blood brain barrier Na,K,2Cl-cotransporter during in vitro stroke conditions and nicotine exposure. *Pharm. Res.* (in press). A copy of the above paper which is in press is attached. A copy of the E-mail from the associate editor indicating its acceptance for publication is also attached.

Jochen Klein, Ph.D.

C. Kiewert, J. Hartmann, C.J. van der Schyf, T. Thekkumkara, J. Stoll and **J. Klein**: NGP1-01 is a brain-permeable dual blocker of neuronal voltage- and ligand-operated calcium channels. Accepted for publication in *Neurochem. Res.*

B. Schatter, S. Jin, K. Löffelholz and **J. Klein** (2005) Ethanol-induced apoptosis in astrocytes: cross-talk between phosphatidic acid and ceramide. *BMC Pharmacology* 5: 3 (11 pages).

A. Mdzinarishvili, W.J. Geldenhuys, T.J. Abbruscato, U. Bickel, **J. Klein** and C.J. van der Schyf: NGP1-01, a lipophilic polycyclic cage amine, is neuroprotective in focal ischemia. *Neurosci. Lett.* 383: 49-53.

J. Klein (2005) Functions and pathophysiological roles of phospholipase D in the brain. *J. Neurochem.* 94, 1473-1487 (Review).

Paul Lockman, Ph.D.

Lockman PR, Gaasch JA, Van der Schyf CJ, Allen DD. (2006) Chronic nicotine exposure does not alter plasma to brain choline transfer. *Neurochem Res.* (Accepted).

Koziara JM, **Lockman PR**, Allen DD, Mumper RJ. (2006) The Blood-brain barrier and drug delivery. *J Nanosci Nanotech*, Invited Review (Accepted)

Muldoon LL, Tratnyek P, Jacobs PM, Doolittle ND, Christoforidis GA, Frank J, Lindau M, **Lockman PR**, Manninger S, Qiang Y, Spence A, Stupp S, Zhang M, Neuwelt E. (2006) Imaging and nanomedicine for diagnosis and therapy in the CNS: Report of the eleventh annual blood-brain barrier disruption consortium meeting. *American Journal of Neuroradiology*, In press.

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Geldenhuys WJ, **Lockman PR**, Philip AE, Miller BL, McCurdy CR, Allen DD. (2005) Inhibition of choline uptake by *N*-cyclohexylcholine, a high affinity ligand for the choline transporter at the Blood-Brain Barrier. *J Drug Targ* 13(4) 259-66.

Lockman PR, Van der Schyf CJ, Abbruscato TJ, Allen DD. (2005) Chronic nicotine exposure alters blood-brain barrier permeability and diminishes brain uptake of methyllycaconitine *J Neurochem.* 94 (1): 37-44.

Geldenhuis WJ, **Lockman PR**, Nguyen T, Van der Schyf CJ, Crooks PA, Dwoskin LP, Allen DD. (2005) 3D-QSAR study bis-azaaromatic quaternary ammonium analogs at the blood-brain barrier choline transporter *Bioorg Med Chem* 13 (13): 4253-61.

Cui Z, **Lockman PR**, Atwood CS, Allen DD, Mumper RJ. (2005) novel d-penicillamine carrying nanoparticles for metal chelation therapy in alzheimer's and other CNS diseases. *Eur J Pharm Biopharm.* 59 (2): 263-72.

Reza Mehvar, Pharm.D., Ph.D.

Vuppugalla R and **Mehvar R**, Enzyme-Selective Effects of Nitric Oxide on Affinity and Maximum Velocity of Various Rat Cytochromes P450. *Drug Metab. Dispos*, 33:829-836 (2005).

Mehvar R, Role of Protein Binding in Pharmacokinetics. *Am. J. Pharm. Educ.*, 69 (5) (article 100):1-8 (2005).

Chimalakonda AP, Montgomery DL, Weidanz J, Shaik I, Nguyen JH, Lemasters JJ, Kobayashi E, and **Mehvar R**. Attenuation of Acute Rejection in a Rat Liver Transplantation Model by a Liver-Targeted Dextran Prodrug of Methylprednisolone. *Transplantation*, In press.

Mehvar R and Vuppugalla R, Hepatic Disposition of the Cytochrome P450 2E1 Marker Chlorzoxazone and Its Hydroxylated Metabolite in Isolated Perfused Rat Livers. *J. Pharm. Sci.*, accepted for publication.

Majid Moridani, Pharm.D., Ph.D.

Moridani, Moore, Bartsch, Yang, Heibati-Sadati. Structural toxicity relationship of 4-alkoxyphenols' cytotoxicity towards murine B16-F0 melanoma cell culture. *J. Pharm. Pharm. Sci.*, 2005; 8(2):348-360.

Moridani, The significance of Pharmacogenomics in Pharmacy Education and Practice, *J Am Pharm Edu*, 2005; **69(2)**: 249-250.

U.S. Rao, Ph.D.

Rao, P.S., Govindarajan, R., Mallya, K.B., West, W. and Rao, U.S. (2005) Characterization of a new antibody raised against the NH2 terminus of P-glycoprotein. *Clin Cancer Res.* 11, 5833-5839.

Quentin Smith, Ph.D.

Doolittle ND, Abrey LE, Bleyer WA, Brem S, Davis TP, Dore-Duffy P, Drewes LR, Hall WA, Hoffman JM, Korfel A, Martuza R, Muldoon LL, Peereboom D, Peterson DR, Rabkin SD, **Smith Q**, Stevens GH, Neuwelt EA. New Frontiers in Translational Research in Neuro-oncology and the Blood-Brain Barrier: Report of the Tenth Annual Blood-Brain Barrier Disruption Consortium Meeting. *Clin Cancer Res.* 11:421-8, 2005.

Smith QR. Carrier-mediated transport to enhance drug delivery to brain. *International Congress Series* 1277: 63-74, 2005.

Kalkunte S. Srivenugopal, Ph.D.

Niture SK, Velu CS, Bailey NI, and **Srivenugopal KS**, S-Thiolation mimicry: Quantitative and kinetic analysis of redox status of protein cysteines by glutathione-affinity chromatography. *Arch Biochem Biophys.* 444, 174-184, 2005 – copy of the article provided.

Niture SK, Doneanu CE, Velu CS, Bailey NI, and **Srivenugopal KS**. Proteomic analysis of human O6-methylguanine-DNA methyltransferase by affinity chromatography and tandem mass spectrometry. *Biochem Biophys Res Commun.* 337, 1176-1184, 2005 – copy of the article provided.

Motlekar NA, **Srivenugopal KS**, **Wachtel MS**, and **Youan BB**. Oral delivery of low-molecular-weight heparin using sodium caprate as absorption enhancer reaches therapeutic levels. *J. Drug Targeting*, 13, 573-583, 2005 - [copy of the article provided](#).

James Stoll, PhD

Kiewert C, Hartmann J, **Stoll J**, Thekkumkara TJ, Van der Schyf C, Klein J. 'NGP1-01 is a brain-permeable dual blocker of neuronal voltage- and ligand-operated calcium channels', *Neurochemical Research* (in press)

Neels Van der Schyf, B.Pharm., D.Sc.

Steyn, S.J., Pieterse, D.J., Mienie, L.J., and **Van der Schyf, C.J.** Measurement of mitochondrial respiration in permeabilized murine neuroblastoma (N-2 α) cells, a simple and rapid in situ assay to investigate mitochondrial toxins. *Journal of Biochemical and Biophysical Methods*, 2005, 62, 25-40.

Geldenhuys, W.J., Malan, S.F., Bloomquist, J.R., Marchand, A.P., and **Van der Schyf, C.J.** Pharmacology and structure-activity relationships of bioactive polycyclic cage compounds: A focus on pentacycloundecane derivatives. *Medicinal Research Reviews*, 2005, 25, 21-48 (featured on journal cover).

Dheyongera, J.P., Geldenhuys, W.J., Dekker, T.G., and **Van der Schyf, C.J.** Synthesis, biological evaluation and molecular modeling of novel thioacridone derivatives related to the anti-cancer alkaloid acronycine. *Bioorganic & Medicinal Chemistry*, 2005, 13, 689-698.

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Massicotte, C., Knight, K., **Van der Schyf, C.J.**, Jortner, B.S. and Ehrich, M. Effects of organophosphorus compounds on ATP production in cultured cells. *Neurotoxicity Research*, 2005, 7, 203-217.

Lockman, P.R., **Van der Schyf, C.J.**, Abbruscato, T.J., and Allen, D.D. Chronic nicotine exposure alters blood-brain barrier permeability and diminishes brain uptake of methyllycaconitine. *Journal of Neurochemistry*, 2005, 94, 37-44.

Geldenhuys, W.J., Lockman, P.R., Nguyen, T., **Van der Schyf, C.J.**, Crooks, P.A., Dwoskin, L.P., and Allen, D.D. 3D-QSAR study of bis-azaaromatic quaternary ammonium analogs at the blood-brain barrier choline transporter. *Bioorganic & Medicinal Chemistry*, 2005, 13, 4253-4261.

Mdzinarishvili, A., Geldenhuys, W.J., Abbruscato, T.J., Bickel, U., Klein, J., and **Van der Schyf, C.J.** NGP1-01, a dual-mechanism calcium channel blocker, is neuroprotective in focal ischemia. *Neuroscience Letters*, 2005, 383, 49-53.

Lockman, P.R., McAfee, G., Geldenhuys, W.J., **Van der Schyf, C.J.**, Abbruscato, T.J., and Allen, D.D. Brain uptake kinetics of nicotine and cotinine after chronic nicotine exposure. *Journal of Pharmacology & Experimental Therapeutics*, 2005, 314, 636-642.

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Ming-Hai Wang, M.D., Ph.D.

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Jon Weidanz, M.P.H., Ph.D.

Weidanz, JA, Jacobson, L.M., Muehrer, R.J., Djamali, A., Hullett, D.A., Chiriva-Internati, M., Thekkumkara, T., Wittman, V., and Becker, B.N. *AT₁R blockade reduces IFN- γ production in lymphocytes in vitro and in vivo.* (2005) *Kidney International*, Vol. 67, pp. 2134-2142.

Margaret T. Weis, Ph.D.

Weis, M.T., Brady, M., Moore, M., Crumley, J., Stallone, J.N. Inhibiting long chain fatty acyl CoA synthetase does not increase agonist-induced release of arachidonate metabolites from human endothelial cells. *J. Vascular Res.* 42:275-283, 2005.

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Bi-Botti Celestin Youan, Ph.D.

Motlekar NA, Srivenugopal KS, Wachtel MS, **Youan BBC** (2005). Oral delivery of low-molecular weight heparin using sodium caprate as absorption enhancer reaches therapeutic levels. *J Drug Target* 13(10): 573-83.