Daniel T. Smith

Department of Industrial and Physical Pharmacy
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WORK EXPERIENCE

Director, Pharmaceutical Manufacturing Facility July 2009 – Present
Visiting Assistant Professor July 2008 – Present
Research Assistant Professor January 2007 – June 2008
Post-Doctoral Research Assistant November 1999 – December 2006
Purdue University
Department of Industrial and Physical Pharmacy
West Lafayette, Indiana 47907

Medicinal Chemistry Research

Drug Design and Discovery

- Directed a drug discovery program aimed at discovering novel pharmaceutical interventions for spinal cord injury
  - Rationally identified, synthesized and purified potentially active derivatives of the potassium channel blocker 4-aminopyridine for testing
  - Manufactured and coated tablets in support of *in vivo* testing
  - Responsible for direction of late stage pre-clinical development of the lead compound arising from this effort
- Identified potential alternatives to the acrolein scavenger hydralazine as possible treatments for acute spinal cord injury
- Explored the feasibility of a combined treatment for acute spinal cord injury by coupling acrolein scavenging drugs with poly(ethylene glycol)
- Synthesized fluorescently labeled compounds as biological markers, including: inosine, poly(ethylene glycol) and hydralazine

Translational Research and Drug Development

- Formulated, manufactured and coated tablets (4-aminopyridine and derivatives) for clinical testing in dogs
- Conducted content uniformity and dissolution testing of the tablets
- Provided analytical support of veterinary testing of 4-aminopyridine by determining the plasma level of 4-aminopyridine in plasma by HPLC
- Detection and identification of impurities in 4-aminopyridine by HPLC

Pharmaceutical Science Research

- Created novel formulations of HIV/AIDS drugs that significantly boost their solubility in aqueous environments
- Studied the polymer induced formation and stabilization of the amorphous form of active pharmaceutical ingredients
- Developed a means of achieving content uniformity in ultra-low dose pharmaceuticals
- Explored the possibility of determining the polymorphic outcome of crystallization through monitoring pre-nucleation events with NMR and UV spectroscopy

Consultant
Neurometrix, Inc.
Waltham, MA 02451

WORK EXPERIENCE (Cont.)

Consultant
Cyberkinetics Neurotechnology Systems, Inc.
Foxborough, Massachusetts 02035
February 2006 – March 2008

Technical Founder
Consultant
Andara Life Sciences, Inc.
Indianapolis, Indiana 46278
February 2005 – February 2006

Research Chemist I
Great Lakes Chemical Corporation
West Lafayette, Indiana 47906
February 2000 – June 2000

Areas of Responsibility:

- Synthesized various low molecular weight oligomers for testing as non-blooming flame retardants
- Developed chemistry and explored process issues for the commercial synthesis of phosphate esters including: solvent requirements, by-product identification, minimization and removal, work-up procedures and elimination of metal salts in the product

Post-Doctoral Research Assistant
The University of Virginia
Department of Chemistry
Charlottesville, Virginia 22901
Research Advisor: James A. Marshall
April 1997 - June 1999

Areas of Research:

- Completed the non-racemic total synthesis of an *Annonaceous* acetogennin homologue, *bis*-homo-bullanin, for further biological testing

EDUCATION

Ph.D., Organic Chemistry
The Pennsylvania State University
Department of Chemistry
University Park, Pennsylvania 16802
Research Advisor: Steven M. Weinreb
August 1991 - March 1997

Areas of Research:

- Explored the scope and limitations of a novel intramolecular ene reaction between allenylsilanes and various functional groups
- Examined the total synthesis of three *Lycopodium* alkaloids using a palladium-mediated tandem carbon-carbon bond forming strategy

B.S., Chemistry
Miami University
Oxford, Ohio 45056
Research Advisor: Benjamin W. Gung
August 1987 - May 1991

Area of Research:

- Studied the selectivity of the addition of allylstannanes to aldehydes

PUBLICATIONS

1. Sun, W.; Smith, D.T.; Byrn, S.R.; Borgens, R.B.; Shi, R. *N*-(4-Pyridyl) Methyl Carbamate Inhibits Fast Potassium Currents in Guinea Pig Dorsal Root Ganglion Cells. *J. Neurol. Sci.* **2009**, *277*(1-2), 114.

2. Guerrieri, P.P.; Smith, D.T.; Taylor, L.S. Phase Behavior of Ranitidine HCl in the Presence of Degradants and Atmospheric Moisture-Impact on Chemical Stability. *Langmuir.* **2008**, *24*(8), 3850.

3. Shi, R., Borgens, R.B., Smith, D.T. Dosage of 4-Aminopyridine Derivatives for Treatment of Central Nervous System Injuries. PCT Appl. WO 200706155-A2. **2007**.

4. McBride, J.M., Smith, D.T., Byrn, S.R., Borgens, R.B. and Shi, R. 4-Aminopyridine Derivatives Enhance Impulse Conduction in Guinea Pig Spinal Cord Following Traumatic Injury. *Neuroscience*. **2007**, *148*(1), 44.

5. Liu-Snyder, P., Peasly Logan, M., Shi, R., Smith, D.T., Borgens, R.B. Neuroprotection from Secondary Injury by Polyethylene glycol Requires Its Internalization. *J. Exp. Biol.* **2007**, *210*, 1455.

6. McBride, J.M., Smith, D.T., Byrn, S.R., Borgens, R.B. and Shi, R. Dose Responses of Three 4-Aminopyridine Derivatives Following Spinal Cord Trauma. *Eur. J. Pharm. Sci.* **2006**, *27*, 237.

7. Smith, D.T., Shi, R., Borgens, R.B., McBride, J., Jackson, K., Byrn, S. Development of Novel 4-Aminopyridine Derivatives as Potential Treatments for Neurological Disease and Injury. *Eur. J. Med. Chem.* **2005**, *40*(9), 908.

8. Borgens, R.B., Shi, R., Byrn, S.R., Smith, D.T. Pyridines for Treating Injured Mammalian Nerve Tissue. US Patent Appl. No. 2004-0171587-A1. **2004**.

9. Weinreb, S.M., Smith, D.T., Jin, J. Thermal and Lewis Acid Catalyzed Intramolecular Ene Reactions of Allenylsilanes. *Synthesis* **1998**, 509.

10. Smith, D.T. Ph.D. Dissertation, The Pennsylvania State University, **1997**. Part One: Scope and Application of Novel Intramolecular Ene Reactions Utilizing Allenylsilanes as the Ene Component. Part Two: Approaches to the Synthesis of the Magellanane Group of Lycopodium Alkaloids.

11. Martoglio, P.A., Schiering, D.W., Smith, M.J., Smith, D.T. Direct Monitoring of Combinatorial Chemistry Reactions by Infrared Microspectroscopy. *Microscopy Today*, April **1996**.

12. Jin, J., Smith, D.T., Weinreb, S.M. Novel Intramolecular Ene Reactions of Allenyl Silanes. *J. Org. Chem.* **1995**, *60*, 5366.

13. Nylund, C.S., Smith, D.T., Klopp, J.M., Weinreb, S.M. A Palladium - Mediated Tandem Carbon - Carbon Bond Forming Method Featuring Nucleophilic Substitution of Intermediate π-Allylpalladium Complexes Produced via the Heck Reaction. *Tetrahedron* **1995**, *51*, 9301.

14. Gung, B.W., Ohm, K.W., Smith, D.T. Regio- and Diastereofacial Selective Hydroboration of Chiral Allylic Stannanes, Silanes, and Germanes. *Synth. Commun.* **1994**, *24*, 167.

15. Gung, B.W., Smith, D.T., Wolf, M.A. Evidence for Synclinal Transition State in the Reactions of Aromatic Aldehydes with α-(Alkoxy)allylstannanes. *Tetrahedron* **1992**, *48*, 5455.

16. Gung, B.W., Peat, A.J., Snook, B.M., Smith, D.T. An Anomalous Case of Diastereofacial Selectivity in the Addition of Chiral Allylstannanes to Benzaldehyde: Is the "Inside Alkoxy" Effect Involved? *Tetrahedron Lett.* **1991**, *32*, 453

17. Gung, B.W., Smith, D.T.,Wolf, M.A. Remarkable Increase in the Diastereofacial Selectivity of the Addition of β-Methyl α-(Alkoxy)allylstannane to Aldehydes: Substituent Effects on Diastereofacial Selectivity. *Tetrahedron Lett.* **1991**, *32*, 13.

PRESENTATIONS

"Global Health in Focus". A side event at the opening of the 62nd Session of the United Nations General Assembly hosted by the Permanent Observer Mission of the Vatican. New York, NY "Transfer of Pharmacy Graduate Programs and a Drug Manufacturing Facility to Tanzania". September 25, 2007

DePauw University. Greencastle, IN "Discovery and Development of Potential Treatments for Spinal Cord Injury". November 8, 2007

WHO Partners Meeting for Better Medicines for Children. Geneva, Switzerland. "Pharmaceutical Education and Research at Purdue University: Improving Medicines for All", May 2009.

TEACHING EXPERIENCE

Teaching Assistant
General Chemistry Lab (Chemistry 014), Fall 1991
Organic Chemistry Lab (Chemistry 036), Spring 1992
Department of Chemistry, Pennsylvania State University

Supporting Staff
Manufacturing Processes (IPPH 562), 2008 - 2009
Department of Industrial and Physical Pharmacy, Purdue University
- Lectured and supervised the lab for the pharmaceutical manufacturing course.

Guest Lecturer
Basic Pharmaceutics II (IPPH 363)

CURRENT RESEARCH SUPPORT

Reformulation Approach to Improving the Oral Absorption of the HIV/AIDS Drugs Lopinavir, Atazanavir and Ritonavir. Phase II: Bioavailability in Rats.
PI: Daniel T. Smith
Agency: William J. Clinton HIV/AIDS Initiative
1/1/10 – 12/31/10

COMPLETED RESEARCH SUPPORT

Novel 4-Aminopyridine Derivatives as Potential Treatments for Multiple Sclerosis
PI: Daniel T. Smith
Agency: Purdue University Office of Technology Commercialization
Type: Trask Technology Innovation Award
7/01/07 – 6/30/08

Reformulation Approach to Improving the Oral Absorption of HIV/AIDS Drugs
PI: Daniel T. Smith
Agency: William J. Clinton Foundation HIV/AIDS Initiantive
$24,479 total direct costs
12/29/08 – 12/28/09

Optimization of the Crystallization of Tenofovir Disoproxil Fumarate
PI: Daniel T. Smith
Agency: William J. Clinton Foundation HIV/AIDS Initiantive
$50,000 total direct costs
12/29/08 – 12/28/09

Reformulation Approach to Improving the Oral Absorption of Atazanavir
PI: Daniel T. Smith
Agency: William J. Clinton Foundation HIV/AIDS Initiantive
$30,000 total direct costs
1/6/08 – 1/5/10

COMPLETED RESEARCH SUPPORT (Cont.)

Once-a-Day Generic Drug Reformulations
PI: Stephen R. Byrn
Role: Co-PI
Alfred Mann Institute for Biomedical Engineering at Purdue University
$98,000 total direct costs
12/01/08 – 5/31/09

Restoring Conduction in Chronically Injured Spinal Cord: Synthesis and in Vitro Testing of Novel Pharmacological Targets.
PI: Daniel T. Smith (50% effort)
Agency: NIH/NINDS
Type: R21 ($231,252 total direct costs)
09/01/05 – 05/31/07