

## PERSONAL PROFILE

*Career Goal:* To enhance the quality of healthcare for society through meaningful contributions in the areas of education, patient care, and research.

*Birthplace:* Gainesville, Fl

*Apo E Genotype:* ε3/ε3

*Drug Metabolism Phenotypes:* CYP2C9 EM, CYP2D6 EM

*Spouse:* Lynne Twiest (maiden)

*Children:* Dawne M. Gentile and C. Heather Gentile

*Military Service:* U.S. Navy, 1970 – 1974

*Hobbies:* Hiking, running, science fiction, and investing

*Home Address:* 105 Ludlow Court, Cary, NC

*Home Phone* (919) 481-3560

### EDUCATION

**Pharm.D., University of North Carolina**, Chapel Hill, NC, 27599 Degree: 05/2000  
Division of Pharmacotherapy, School of Pharmacy  
Study concentration in Clinical Oncology at UNC Hospitals and Duke Univ. Med. Center.

**Postdoctoral Fellowship, Wellcome Research Laboratories** 1982 -1984  
Dept. Pharmacokinetics and Drug Metabolism, Biochemical Pharmacology Section.  
Research focus on the biochemical basis for sex and strain differences in certain drug toxicities and chemically induced neoplasms in mice.

**Ph.D., University of Florida**, Gainesville, FL, 32611 Degree: 05/1983  
Department of Pharmacology and Experimental Therapeutics, College of Medicine.  
Thesis title, "A Genetic Approach to the Regulation of Cytochrome P450-Mediated Testosterone Hydroxylations". (Dr. Allen Neims, M.D.,Ph.D.).

**B.S., University of West Florida**, Pensacola, FL, 32514 Degree: 05/1978  
Chemistry with minor in Marine Biology

### Licensure

North Carolina Registered Pharmacist #15635

### Honors

Rho Chi Pharmaceutical Honor Society, 1998  
Cum Laude, University of West Florida, 1978

### MEMBERSHIPS IN ACADEMIC AND PROFESSIONAL ASSOCIATIONS

American Society of Pharmacology and Experimental Therapeutics	1986 – 1994
American Association of Colleges of Pharmacy	2000 – present
American College of Clinical Pharmacy	2001 – present
North Carolina Association of Pharmacists	2005

### Academic Organizations

UNC Center for Gastrointestinal Biology and Disease	2002 – present
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### Journal Referee

Life Sciences	2005
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**PROFESSIONAL SUMMARY**

The foundation for all clinical and basic research activities reside in the regulation of cytochrome P450s and hepatobiliary transporters and their use as determinants of drug response, and in their role in the pathobiology of liver disease. Current translational research objectives are centered on the development of new *in vitro* models to investigate the effects of chronic hepatitis C infection on cytochrome P450s and hepatobiliary transporters involved in the disposition of critical intracellular hormones for the evaluation of new treatment modalities for prevention, or delayed progression of liver disease, and for improving treatment outcomes in patients with chronic hepatitis C infection.

Technical, scientific, managerial, clinical and teaching skills include:

- successful implementation and preclinical development of drug discovery programs by expert application of basic and applied research knowledge and astute problem solving ability.
- demonstrated knowledge and expertise in drug and steroid metabolism, liver physiology and toxicology, and bioanalytical methods development.
- ability to oversee the planning and preclinical development of concurrent drug discovery programs through application of matrix management methods.
- capacity to function at the drug discovery/drug development interface due to a broad background in drug metabolism/pharmacokinetics and experience in drug discovery research.
- expert knowledge of enzyme kinetics and cytochrome P450 regulation obtained during the development of competitive inhibitors for single and multi-step biochemical pathways, and mechanism-based irreversible inhibitors of cytochrome P450 catalyzed reactions.
- expertise in developing *in vitro*, cell culture, or binding assays, and analytical methods such as HPLC with radiochemical detection to study steroid, lipid, and bile acid biochemistry.
- experience in developing SAR and patent defense strategies from background in chemistry.
- excellent oral and written communication skills, and experience developing international and academic scientific collaborations.
- experience with clinical problem-based learning as facilitator for pharmacotherapy courses for the School of Pharmacy and interdisciplinary cases for UNC Health Affairs.
- clinical pharmacist with experience with the UNC Hospitals Hematology/Oncology inpatient and GI/Hepatology outpatient services.

**Patient Care Service**

2003 – present

*Hepatology/GI Outpatient Clinic at UNC Hospitals*

Conduct weekly individual or group teaching sessions for patients with chronic hepatitis C infection who are initiating pegylated-interferon/ribavirin therapy; conduct follow-up during patient HCV Clinic visits for adverse effects related to interferon/ribavirin therapy and report findings to Nurse Practitioner, monitor patients for compliance, conduct medication reviews, review new orders and make pharmacotherapy recommendations for the control of pain, and nausea. Monitor for ribavirin-induced anemia.

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2002-2003,

*Hematology/Oncology (MED E) In-patient Service at UNC Hospitals*

Rounded with MED E teams, reviewed MAR's, screened chemo orders, monitored methotrexate and aminoglycoside levels and high dose methotrexate, ifosfamide, and cisplatin infusions.

Made pharmacotherapy recommendations and interventions for the control of nausea and vomiting, and pain. Attended quarterly *Oncology Patient Services Group* meeting with Clinical oncology house staff and Pharmacy administrators to establish pharmaceutical care services, to review results of DUEs, and to monitor needs for new clinical pharmacy activities.

### WORK EXPERIENCE

#### School of Pharmacy, University of North Carolina at Chapel Hill

Assistant Professor

2002 – Present

*Division of Pharmacotherapy*

Tenure-track faculty in the Division of Pharmacotherapy are required to demonstrate excellence in teaching, clinical service, and research for consideration of tenure and promotion. In research, excellence is demonstrated by integration of translational research programs into clinical practice and clinical research initiatives.

*Teaching:* Course coordinator for “Introduction to Applied Pharmacogenomics (*PHTH 101*)”

*Course Philosophy:* Pharmacy education is now focused on the development of skills and competencies required of clinical pharmacy practitioners who can interface with interdisciplinary teams to ensure optimal drug therapy outcomes. The practice of evidence-based medicine and the use of clinical practice guidelines will soon evolve to include the application of pharmacogenomic information in order to target specific drug therapies for individual patients. Pharmacy education should respond to this challenge by developing curriculums that prepare clinicians for the integration of objective genetic measures with the practice of pharmacy and medicine.

*Lectures:* Hematology/Oncology Module (*PHCY 151*)

Problems in Pharmacotherapy (*PHCY 169*)

Drug Metabolism (*PHAR 156*)

Infectious Disease (*PHCY 152*)

*Service:* Outpatient GI/Hepatology Clinic at UNC Hospitals one afternoon per week.

*Research:* Research is focused on identification of genetic determinants of dynamic and kinetic modifiers of drug response, and on the development of *in vitro* models to investigate mechanisms of pathogenesis and assess new drug therapies for various liver diseases.

Clinical Assistant Professor

2000 – 2002

*Division of Pharmacotherapy*

Nontenure-track position in the Division of Pharmacotherapy

Major responsibility was to develop excellence in teaching and clinical service.

Clinical Pharmacology Consultant

1998 – 2000

*Division of Pharmacotherapy*

Consulting scientist for Division of Pharmacotherapy faculty

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Major responsibility was to develop translational research programs within the Division and through the *In Vivo–In Vitro* Correlates Program - an interdivisional research group established to maximize industry and extra-mural funding opportunities for research.

### Research Associate

1996 – 1998

#### *Division of Drug Disposition and Delivery*

Major responsibility was to assist in the development of optimal isolation and culture conditions for human hepatocytes.

## **Burroughs Wellcome Co., Research Triangle Park, NC (1982 – 1996)**

### Senior Research Scientist VI

1993 -1996

#### *Division of Pharmacokinetics and Drug Metabolism (PDM)*

Head of a Drug & Lipid Metabolism Section that was responsible for origination and preclinical evaluation of research programs in the Division of PDM related to development of novel hypolipidemic and anti-atherosclerotic agents. Responsibilities and accomplishments include:

- Member of a seven-person PDM Senior Management Team responsible for coordinating the activities of PDM scientists and technicians, and for the allocation of departmental resources to support preclinical development of BW Co. drug discovery programs.
- Champion of two cardiovascular research programs to develop anti-atherosclerotic ACAT inhibitors (20M) and PPAR $\alpha,\gamma$  agonists as antihyperlipidemic/antihyperglycemic agents (20P). Coordinated inter-divisional activities for obtaining efficacy, safety, pharmacokinetic, and metabolism data in various species for project status and IND filings.
- Conducted pre-program research efforts to determine the role of cholesterol 27-hydroxylase (CYP27) in hepatic LDL-receptor regulation and in the etiology of atherosclerotic disease in macrophage and vascular endothelium.

### Senior Research Scientist III-V

1984 - 1993

Supervised and coordinated all basic and applied research work within the PDM drug/lipid metabolism group to identify new mechanisms for drug discovery, to support target validation in animal models, and to develop lead compounds for current research programs.

- Implemented and directed two research programs to discover bioavailable inhibitors of arterial ACAT activity as anti-atherosclerotic agents, and novel ureido fibrate-type compounds as broad spectrum hypotriglyceridemic and hypocholesterolemic agents.
- Conducted bioavailability, metabolism, and mechanism of action studies, and provided clinical chemistry data for preclinical evaluation of hypolipidemic agents in various species.
- Developed mechanism-based irreversible inactivators of fatty acid  $\omega$ -hydroxylation to determine role in hepatic lipid and drug metabolism. Investigated the influence of CYP4A1 on the regulation of fatty acid and triglyceride secretion by novel agents.
- Studied the selective effects of cytochrome P450 inducers and inhibitors on the metabolism of lead compounds to gain insight to isozyme specificity and potential drug interactions.

## **U.S. ENVIRONMENTAL PROTECTION AGENCY, Sabine Island, FL (1976 – 1978)**

### Co-op Student/Marine Biology (University of West Florida)

Conducted biochemical studies on the effects of parathion and paraoxon on acetylcholinesterase activity of the intact dorsal nerve cord of shrimp by potentiometric titration.

**CONTRACTS AND GRANTS RECEIVED**

*Pharmacogenetics in the Elderly: Investigation of Major CYP3A Polymorphisms on the Regulation of CYP3A Activity in Elderly African American Women*

Principle Investigator: UNC Center on Minority Aging – National Institute on Aging

Funded: 9/01 – 5/03

Direct Costs: \$31,897.00

The purpose of this investigation was to determine the independent contributions of CYP3A5 and CYP3A4 genotype and the effect of age on induction of hepatic CYP3A activity in African American women using the erythromycin breath test for *in vivo* clinical investigations, and midazolam and erythromycin for *in vitro* metabolism studies.

*The Effects of Chronic Hepatitis C (HCV) on Drug Disposition Processes*

UNC School of Pharmacy Seed Grant

Funding Period: 01/04 – 01/05

Award: \$ 9,560.00

This seed grant was obtained to provide pilot data to support the re-submission of an R21 grant entitled “The Role of Vitamin A in a Dynamic Human Hepatocyte Model of Chronic HCV Infection” originally submitted to the National Institute of Diabetes and Digestive and Kidney Disease on Oct 1<sup>st</sup>, 2003 in response to RFA-PA-01-129.

*Pharmacology of Cyclophosphamide and Other Alkylators*

Principle Investigator: NIH – R01 (Duke subcontract)

Funding Period: 2/04 – 1/05

Direct Costs: \$61,620.00

The purpose of this research was to determine the isotope effects for various deuterium labeled cyclophosphamide and ifosphamide analogues on the enzyme kinetics of cyclophosphamide and ifosphamide hydroxylation and N-dechloroethylation using cDNA-expressed cytochrome P-450 isozymes for comparison to effects observed with human liver microsomes.

*In Vitro – In Vivo Correlation of Strain Differences in Susceptibility to Cholestatic Liver Injury in Mice*

UNC University Research Council Seed Grant

Award: \$ 3,980.00

Funding Period: 02/05 – 01/07

This seed grant will fund studies that aim to identify a siRNA species capable of potent knockdown of bile salt export protein (bsep) mRNA (gene *Abcb11*) in mouse hepatocytes. The inhibition of bsep-mediated bile salt efflux is a potential mechanism by which some drugs may induce cholestatic liver injury. However, the absence of progressive hepatotoxicity in bsep-knockout mice suggests that unknown factors such as genetic background, disease, or drug metabolism likely influence susceptibility for liver injury. Understanding the genetic regulation of susceptible to cholestatic liver injury will allow identification of the molecular mechanisms underlying many human genetic diseases and drug toxicities that result from dysregulated biliary homeostasis such as in primary biliary cirrhosis, primary sclerosing cholangitis, and drug-induced cholestatic liver injury. The difficulty in establishing direct cause-effect relationships with hepatotoxic drugs preclude their use as positive controls in such investigations. Data obtained with the siRNA species identified in these pilot studies will be used to develop an adenoviral vector for *in vivo* studies that will be conducted in different strains of mice as the basis for a R01 application (PA-03-100 – NIGMS Exploratory Studies for High Impact/High Risk Research).

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### *A Phase I/II Randomized, Placebo Controlled Trial of Silymarin for Hepatitis C*

Co-Investigator: NCCAM/NIDDK – U01, RFA-AT-05-006: Phase I/II Trials of Silymarin for Chronic Liver Diseases

#### **Review Pending:**

The goal of this proposal was to design a collaborative multicenter trial to evaluate the safety and efficacy of silymarin for the treatment of subjects with chronic hepatitis C who did not respond to conventional therapy. Our proposal to participate as a Clinical Center for this cooperative study emphasized the unique attributes and expertise in drug development of the Liver Program and the faculty at the School of Pharmacy at the University of North Carolina at Chapel Hill who will be responsible for pharmacokinetic studies and the evaluation of silymarin's efficacy of surrogate measures of oxidative stress, inflammation, apoptosis, and fibrogenesis.

### *Pharmacokinetics of Milk Thistle in Liver Disease*

Principal Investigator: ACCP Investigator Development TAP GI Award

#### **Review Pending:**

The goal of this study is to determine the pharmacokinetic properties of a high silymarin dose in patients with liver disease who may have reduced capacity for conjugation and biliary excretion, which are the primary mechanisms of silymarin elimination. Information from this study will allow an estimation of the potential for untoward accumulation of the active isomers of silymarin in patients with liver disease and is essential for minimizing potential risks in future clinical trials. The specific aims of this study are two-fold: #1) To characterize the pharmacokinetics of the unconjugated, sulfated, and glucuronidated pools of the four major silymarin isomers (silibinin, isosilibinin, silicristin, and silidianin) as measured by  $AUC_{0-24h}$ ,  $C_{max}$ ,  $t_{max}$ ,  $CL/F$ ,  $V_d$ , and  $t_{1/2}$ , following administration of a 600 mg dose of silymarin to 5 healthy volunteers; and #2) To compare these pharmacokinetic parameters to those obtained from patients with HCV who have minimal (N=5) or cirrhotic (N=5) disease, and from 5 patients with NASH.

## **PATENTS**

Franzmann, K. W., **Hawke, R. L.**, and Welch, R. M., "Anti-Atherosclerotic Aryl Compounds". *WO9206075 (920625)*, Burroughs Wellcome Co., 1992.

Chapman, J. M., **Hawke, R. L.**, Franzmann, K. W., and O'Connor, K. J., "Anti-Atherosclerotic Aryl Compounds". *WO9201468 (920625 U. South Carolina)*, Burroughs Wellcome Co., 1992.

## **PUBLISHED ARTICLES**

### **RESEARCH PAPERS**

**Hawke, R.L.** and Neims, A. H., "Maturation of various testosterone hydroxylase activities in hepatic microsomes from AKR/J mice". *Progress in Clinical Biological Research* 135:25-35 (1983).

**Hawke, R.L.**, Raynor, L., Singh, G. and Neims, A. H., "Differences between kidney and liver in the regulation of microsomal testosterone hydroxylase activities in inbred mice", in *Extra-hepatic Drug Metabolism and Chemical Carcinogenesis* (J. Rydström, J. Montelius, and M. Bengtsson, eds.). Elsevier Science Publishers, Amsterdam, 23-24 (1983).

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Neims, A. H., **Hawke, R.L.**, Raynor, L. and Singh, G., "Regulation of microsomal testosterone 15 $\alpha$ -hydroxylase activity in inbred mouse liver and kidney". *Biochem. Soc. Transactions* 12(1):45-48 (1984).

**Hawke, R.L.** and Welch, R. M., "Major differences in the specificity and regulation of mouse renal cytochrome P-450-dependent monooxygenases: A comparison of xenobiotic and endogenous substrates". *Mol. Pharmacol.* 28(3):283-289 (1985).

Clark, M. J., **Hawke, R.L.** and Welch, R. M., "Separation of hydroxylated metabolites of fatty acid (C<sub>10</sub>-C<sub>18</sub>) on a micro porasil silica column using an isocratic HPLC system". *J. Liquid Chromatography*, 9(8):1711-1725 (1986).

Winegar, D. A., Salisbury, J. A., Sundseth, S. S., **Hawke, R.L.**, "Effects of cyclosporin on cholesterol 27-hydroxylation and LDL receptor activity in HepG2 cells". *J. Lipid Res.* 37(1):179-91, 1996.

**Hawke, R.L.**, Chapman, J. M., Winegar, D.A., Salisbury, J. A., Welch, R. M., Brown, A. R., Franzmann, K. W. and Sigel, C. W., "Potent hypocholesterolemic activity of novel ureido phenoxyisobutyrate correlates with their intrinsic fibrate potency and not with their ACAT inhibitory activity". *J. Lipid Res.* 38(6):1189-203, 1997.

Faucette, S.R., **Hawke, R.L.**, LeCluyse, E.L., Shord, S.S., Yan, B., Laethem, R.M., and Lindley, C.M., "Validation of bupropion hydroxylation as a selective marker of human cytochrome P450 2B6 catalytic activity". *Drug Metab Dispos.* 28(10):1222-1230, 2000.

McCune, J.S., **Hawke, R.L.**, LeCluyse, E.L., Gillenwater, H.H., Hamilton, G., Ritchie, J., and Lindley, C., "In-vivo and in-vitro induction of human cytochrome P4503A4 by dexamethasone". *Clin. Pharmacol. Ther.* 68(4): 356-66, 2000.

Faucette, S.R., **Hawke, R.L.**, Shord, S.S., LeCluyse, E.L., and Lindley, C., "Evaluation of the contribution of cytochrome P450 3A4 to human liver microsomal bupropion hydroxylation". *Drug Metab Dispos.* 29(8):1123-1129, 2001.

Lindley, C., Hamilton, G., McCune J., Faucette, S., Shord, S., **Hawke, R.L.**, Wang, H., Gilbert, D., Jolley, S., Yan, B., and LeCluyse, E., "The effect of cyclophosphamide with and without dexamethasone on cytochrome P450 3A4 and 2B6 in human hepatocytes". *Drug Metab Dispos.* 30 (7):814-821, 2002.

Shord, S.S., Faucette, S.R., Gillenwater, H.H., Pescatore, S.L., **Hawke, R.L.**, Socinski, M.A., and Lindley, C., "Gemcitabine pharmacokinetics and interaction with paclitaxel in patients with advanced non-small-cell lung cancer". *Cancer Chemother Pharmacol.*, 51:328, 2003.

Sunman, J.A., **Hawke, R.L.**, LeCluyse, E.L., and Kashuba, A.D.M. "Kupffer cell-mediated IL-2 suppression of CYP3A activity in human hepatocytes". *Drug Metab Dispos.*, 32(3):359-363, 2004.

Lee, C.R., **Hawke, R.L.**, and Pieper, J. A., "Twenty-four hour tolbutamide plasma concentration as a phenotypic measure of CYP2C9 activity", *Eur. J.Clin. Pharmacol.* 2005; Volume 61(4):315-316, 2005.

### OTHER REFEREED PUBLICATIONS

Cleary, J.D., Walker, L.A., and **Hawke, R.L.**, "Anti-mycotic Discovery in the Age of Genomics", *Am. J. Pharmacogenomics, in press*, 2005.

### ABSTRACTS

Chapman, S. K., **Hawke, R.L.**, Glant, S. K., Mann, S. S., Hwong, K. S. and Doyle, J. W., "Ornithine decarboxylase inhibition and cell proliferation". *Pharmacologist* 21:233 (1979).

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**Hawke, R.L.**, Raynor, L. and Neims, A., "Testosterone hydroxylation in mice and regulation of hepatic cytochromes P-450 by sex and strain". *Pharmacologist* **23**:113 (1981).

Neims, A., **Hawke, R.L.**, and Raynor, L., "Distinct sexual regulation of hepatic 15 $\alpha$ - and 16 $\alpha$ -testosterone hydroxylases in two strains of mice". *Pharmacologist* **23**:188 (1981).

Ferrero, J., **Hawke, R.L.**, Raynor, L. and Neims, A., "Strain comparison in sexual dimorphism of hepatic testosterone hydroxylases and other enzyme activities in inbred mice". *Fed. Proc.* **41**:1219 (1982).

Giger, U., **Hawke, R.L.**, and Neims, A., "Hormonal regulation of sexually dimorphic, cytochrome P-450-dependent testosterone hydroxylations in mouse liver". *Fed. Proc.* **41**:1563 (1982).

**Hawke, R.L.** and Neims, A., "Maturation of regioselective hydroxylations of testosterone by liver microsomes from AKR/J mice". *Fed. Proc.* **41**:1644 (1982).

**Hawke, R.L.**, Raynor, L. and Neims, A., "The interactions between genetic and endocrine factors in the regulation of testosterone 15 $\alpha$ -hydroxylase in mouse hepatic microsomes". *Pharmacol.* **24**:206 (1982).

Neims, A. H., Raynor, L. E. and **Hawke, R.L.**, "Genetic and endocrine factors that influence cytochrome P-450-dependent testosterone 16 $\alpha$ -hydroxylation by mouse hepatic microsomes". *Pharmacologist* **24**:206 (1982).

**Hawke, R.L.**, Brown, A. R. and Welch, R. M., "Major differences in substrate specificity and cytochrome P-450 content between male (M) and female (F) mouse kidney microsomes". *Pharmacologist* **25**:266 (1983).

**Hawke, R.L.**, Marr, H. and Welch, R. M., "Sex, strain and tissue specificity in the  $\omega$  and  $\omega$ -1 hydroxylation of lauric acid by microsomes from inbred mice". *Fed. Proc.* **43**:339 (1984).

Welch, R. M., Brown, A. R., **Hawke, R.L.** and Marr, H. W., "Effect of various hypolipidemic drugs and other aromatic acids on  $\omega$  and  $\omega$ -1 hydroxylations of lauric acid by rat liver microsomes". *Fed. Proc.* **43**:563 (1984).

Brown, A., **Hawke, R.L.** and Welch, R. M., "Kinetics and regulation of dimethylnitrosamine de-methylase activity in mouse renal microsomes: strain and sex comparisons". *Fed. Proc.* **43**:592 (1984).

**Hawke, R.L.**, Brown, A. and Welch, R. M., "Comparison of sex and strain differences in the hydroxylation of testosterone and progesterone by mouse renal microsomes", in *6th International Symposium on Microsomes and Drug Oxidations*, **44** (1984).

**Hawke, R.L.**, Clarke, M. J., Marr, H. B., Welch, R. M., "Dissociation of the  $\omega$  and  $\omega$ -1 hydroxylations of lauric acid by clofibrate induction in primary cultures of rat hepatocytes". *Fed. Proc.* **44**:1259 (1985).

**Hawke, R.L.**, Marr, H. B., Clarke, M. J., Welch, R. M., "Comparison of the inductive properties of ciprofibrate and clofibric acid on peroxisomal  $\beta$ -oxidation ( $\beta$ -OX) and microsomal laurate". *Pharmacologist* **27**:147 (1985).

Clarke, M. J., **Hawke, R.L.**, Welch, R. M., "Separation of hydroxylated metabolites of fatty acids (C<sub>10</sub>-C<sub>18</sub>) on a  $\mu$ Porasil silica column using an isocratic HPLC system". *6th Annual RTP Liquid Chromatography Symposium* (1985).

Clarke, M. J., **Hawke, R.L.**, Zulkoski, J. S., Marr, H. B., Welch, R. M., "Sex differences in triglyceride response to induction of microsomal laurate  $\omega$ -hydroxylation and peroxisomal  $\beta$ -oxidation in rats treated with clofibrate". *Fed. Proc.* **46**:694 (1987).

Zulkoski, J. S., Marr, H. B., Clarke, M. J., **Hawke, R.L.**, Welch, R. M., "Endocrine regulation of clofibrate induction of hepatic lauric acid  $\omega$ -hydroxylation in rats". *Fed. Proc.* **46**:694 (1987).

Marr, H. B., Welch, R. M., **Hawke, R.L.**, Zulkoski, J. S., Clarke, M. J., "Sex difference in the induction of peroxisomal  $\beta$ -oxidation by clofibrate in the rat liver". *Fed. Proc.* **46**:694 (1987).

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Thompson, M. B., **Hawke, R.L.**, Blair, P. C., Zulkoski, J. S., "Quantitation of free and conjugated bile acids in primary cultures of rat hepatocytes using a liquid chromatographic/enzymatic assay". *Aspen Cholesterol and Lipoprotein Conference* (1988).

Clarke, M. J., Hunter, S., **Hawke, R.L.**, Zulkoski, J. S., Welch, R. M., "Influence of sex hormones on the hypolipidemic activity of nicardipine (NIC) in fructose-fed rats (FFRS)". *Pharmacologist* **30**:A17 (1988).

**Hawke, R.L.**, Hodgson, G. L., Zulkoski, J. S., Marr, H. B., Clarke, M. J., Welch, R. M., "Induction of peroxisomal  $\beta$ -oxidation (p $\beta$ OX) by sodium 10-undecynyl sulfate (SUS) in primary cultures of rat hepatocytes". *Pharmacologist* **30**:A194 (1988).

Sundseth, S. S., Foshee, M. K., Zulkoski, J. A., **Hawke, R.L.**, "Regulation of cholesterol 7 $\alpha$ -hydroxylase (CYP7) expression by bezafibrate and cholic acid: Differential effects in normal and hypophysectomized rats". *J. Cell. Biochem.* **18B**:395 (1994).

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Brown, P.J., Stuart, L.W., Hurley, K.P., Chapman, J.M., **Hawke, R.L.**, Kleiwer, S.A., Lehmann, J.M., Winegar, D.A., et al., "The discovery of fibrate PPAR ligands". *Int'l Symposia on Nuclear Orphan Receptors, UK* (1997).

Lindley, C., Faucette, S., LeCluyse, E.L., Shifflett, S., Yan, B., and **Hawke, R.L.**, "Validation of bupropion (B) hydroxylation as a CYP2B6 catalytic marker". *Clin. Pharmacol. & Therapeut.* **67**(2):99 (2000).

Faucette, S., **Hawke, R.L.**, Shifflett, S., LeCluyse, E.L., and Lindley, C., "Assessment of CYP3A4 (3A4) contribution to bupropion (B) hydroxylation in human liver microsomes (HLMs)". *Clin. Pharmacol. & Therapeut.* **67**(2):99 (2000).

Faucette, S., Shifflett, S., LeCluyse, E.L., **Hawke, R.L.**, and Lindley, C., "Diethyldithiocarbamate (DDC) inhibition of CYP2B6 catalytic activity". *Clin. Pharmacol. & Therapeut.* **67**(2):99 (2000).

Carson, S.W., Hill-Zabala, C.E., Roberts, S.H., and **Hawke, R.L.**, "Inhibitory effect of methanolic solution of St. John's Wort (*Hypericum Perforatum*) on cytochrome P450 3A4 activity in human liver microsomes". *Clin. Pharmacol. & Therapeut.* **67**(2):99 (2000).

Kashuba, A.D.M., **Hawke, R.L.**, Tonkin, J., and LeCluyse, E.L., "Direct exposure to interleukins (IL)-2, -10, and -12 does not significantly suppress CYP3A activity in human hepatocytes". *Clin. Pharmacol. & Therapeut.* **67**(2):100 (2000).

**Hawke, R.L.**, Chapman JM, Winegar DA, et al., "N-Alkylureidophenoxyisobutyrate PPAR agonists: Acyl-CoA: Cholesterol acyltransferase inhibitory activity, laurate 12-hydroxylase induction and hypocholesterolemic activity in rodents". *The 27<sup>th</sup> National Medicinal Chemistry Symposium*, (2000).

Shord S, Faucette S, **Hawke, R.L.**, Pescatore S, McCune J, Gillenwater H, Socinski M, Lindley C., "Interindividual variability in gemcitabine pharmacokinetics: Fixed dose rate fails to reliably achieve desired plasma concentrations in patients with non-small cell lung cancer". *Proc. Am. Soc. Clin. Oncol.* **20**(1):92a, (2001).

Faucette S, Shord S, Pescatore S, **Hawke, R.L.**, McCune J, Gillenwater H, Socinski M, Lindley C., "Paclitaxel affects gemcitabine pharmacokinetics in patients with non-small cell lung cancer". *Proc. Am. Soc. Clin. Oncol.* **20**(1):93a, (2001).

Faucette S, Lindley C, **Hawke R.L.**, Shord S, Clarke M, LeCluyse E., "Effects of cytochrome P450 3A4 inducers on CYP 2B6 catalytic activity". *Clin. Pharmacol. & Therapeut.* **69**(2):10, (2001)

Shord S, **Hawke R. L.**, LeCluyse E, Lindley C., "Effects of ifosfamide with and without dexamethasone on cytochrome P450 3A4 activity in human hepatocyte culture". *Clin. Pharmacol. & Therapeut.* **69**(2):70, (2001).

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Kashuba, A.D.M., **Hawke, R.L.**, Tonkin, J., Treadwell, F.R., and LeCluyse, E.L., "Suppression of CYP3A4 activity by interleukin (IL) 2 using a human hepatocyte (H): kupffer cell (K) coculture (CO) system". *Clin. Pharmacol. & Therapeut.* **69**(2):100, (2001).

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