

Graduate Study in Pharmaceutical Chemistry

The University of
KANSAS



Pharmaceutical chemistry at KU is defined by the philosophy that success in understanding drug action, in controlling drug delivery across biological membranes and to a drug receptor site, and in the development of stable formulations and the design of sophisticated analytical methods requires a thorough understanding of physical, biophysical, organic, and (bio)analytical chemistry. These principles are equally important for the development of traditional small molecule drugs and for emerging biotechnology products such as peptides, proteins, and nucleic acids. Pharmaceutical chemistry includes the areas of pharmaceuticals, physical pharmacy, pre-formulation, formulation, and pharmaceutical analysis. All of these areas are represented in the department's research and teaching activities.

Programs of Study

The Department of Pharmaceutical Chemistry offers M.S. and Ph.D. degree programs in pharmaceutical chemistry under the jurisdiction of the Graduate School of the University of Kansas. Students entering the programs are expected to have bachelor's or master's degrees in pharmacy, chemistry, chemical engineering, biology, or related areas. M.S. degree requirements may be met either by satisfactorily completing the course work required for the Ph.D. degree and passing a comprehensive examination or by satisfactorily completing 30 credit hours of course work and research, presenting a thesis or research report based on original research, and passing an oral examination.

For the Ph.D. degree, a student must

1. Spend a minimum of three full academic years in resident study.
2. Demonstrate proficiency in a research skill, which may consist of reading ability in a foreign language, computer programming, use of radioisotopes, research animal care and handling, statistics, and other skills subject to approval by the departmental FLORS (foreign language or research skills) committee.
3. Pass a comprehensive written examination and an oral examination and demonstrate research competency, which qualifies the student for Ph.D. candidacy.
4. Complete work on an original research problem, submit the results in a dissertation, and defend the work in an oral examination.



Students are expected to choose course work in consultation with their major professors in mathematics, statistics, computer science, analytical chemistry, physical chemistry, organic chemistry, and biochemistry as well as advanced courses in the department, including Pharmaceutical Equilibria, Pharmaceutical Mass Transport, Mechanisms of Drug Deterioration and Stabilization, Advanced Topics in Biopharmaceutics and Pharmacokinetics, Issues of Scientific Integrity, and Pharmaceutical Analysis.

The Department

The department has 15 full-time faculty members, about 50 graduate students, 20 to 30 postdoctoral associates and visiting scientists, 10 technicians, and 15 undergraduate research students. It enjoys close collaborative arrangements with other departments in the School of Pharmacy. Faculty members have common research interests with members of the chemistry, chemical engineering, and molecular biosciences departments in Lawrence and oncology and medicine departments at KU Medical Center in Kansas City and Wichita. The department is heavily involved in several interdisciplinary projects involving drug delivery, biotransformation, and phar-

macokinetics that are funded by public agencies. Some graduate students are also trainees under the auspices of the Pharmaceutical Aspects of Biotechnology Training Grant, funded by the National Institute of General Medical Sciences.

In cooperation with other departments of the School of Pharmacy, the Department of Pharmaceutical Chemistry also offers a program of graduate instruction leading to the Ph.D. jointly with the Victorian College of Pharmacy in Melbourne, Australia, under the Intersearch Program.

The bioanalytical areas of research are associated with the Center for Bioanalytical Research where several faculty members from pharmaceutical chemistry and chemistry coordinate projects to develop highly sensitive analytical methods for quantitation of molecules at trace levels in complex biological and environmental systems. Faculty members and graduate students also collaborate on research efforts to develop innovative methodology for drug delivery through the Center for Drug Delivery Research.

Application and Admission

Students with bachelor of science or bachelor of arts degrees in chemistry, pharmacy, the biological sci-

ences, chemical engineering, or related disciplines are eligible to apply for graduate study in pharmaceutical chemistry. Prospective students should submit an application form and request transcripts of grades from their undergraduate institutions. In addition, three letters of recommendation and Graduate Record Examination (GRE) scores are required. Students whose native language is not English should also submit Test of English as a Foreign Language (TOEFL) scores.

An application fee (payable to KU) is required:

Domestic fee is \$55 for paper application or \$45 online
International fee is \$60 for paper application or \$55 online

For further information, contact

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www.graduate.ku.edu



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Facilities

The Department of Pharmaceutical Chemistry is housed in Simons Research Laboratories. An extensive array of equipment and instrumentation is maintained for faculty and student research, including incubators and laminar flow hoods for cell and tissue culture, high-performance liquid chromatography and capillary electrophoresis systems, calorimetric equipment, and a circular dichroism spectrophotometer for the analysis of protein conformation. Microcomputers are available for student use in the department. The department also maintains a library of books and current periodicals.

Additional support is available through a number of specialized laboratories, all staffed by trained personnel.

The **Nuclear Magnetic Resonance Laboratory** provides hands-on access to modern Fourier transform NMR spectrometers.

The **Mass Spectrometry Laboratory** maintains a state-of-the-art double-focusing magnetic deflection high-resolution spectrometer.

The **Molecular Graphics and Modeling Laboratories** are equipped to perform simulations of molecular mechanics and molecular dynamics.

The **Electron Microscopy Laboratory** houses both scanning and transmission electron microscopes.

The **X-Ray Crystallographic Laboratory** has three computer-interfaced diffractometers for the structure determination of both macromolecules and small molecules.

The **Instrument Design Laboratory** collaborates with research groups to develop special-purpose laboratory computers.

The **Biochemical Research Laboratory** carries out delicate and complex biochemical and enzymological techniques, such as amino acid analysis, protein sequencing and oligonucleotide and peptide synthesis.

The **University of Kansas Animal Care Facility** is on the lower two floors of Malott Hall. Ordering, housing, and caring for animals are centralized and coordinated by the veterinarian and the animal care staff.

The **Anschutz Library**, adjacent to Malott Hall, contains more than 200,000 volumes covering chemistry, biology, geology, pharmacy, and physics. The library and the department are equipped for computer searching of commercial data bases such as Chemical Abstracts.

Research Programs

The department is internationally recognized for the strength of its research program. While individual faculty members are engaged in a variety of research activities, four major research areas can be identified for the department as a whole. These are pharmaceutical/bio-analysis, cellular and molecular pharmaceuticals, macromolecular pharmaceuticals, and physical pharmacy. Many faculty members are involved in interdisciplinary research. The department enjoys close collaborative arrangements with members of other departments, including medicinal chemistry, pharmacology, pharmacy practice, chemistry, chemical engineering, and molecular biosciences. Many of these collaborations are supported by federally funded training grants. Graduate student participation in these interdisciplinary programs is encouraged.

Faculty and Research Areas

Kenneth L. Audus, Professor. In vitro characterization of drug transport, regulation of transport processes and metabolism in brain microvessel endothelial cells, nasal and pulmonary epithelium, and the placenta. Steady-state, lifetime, and differential phase fluorometry to probe membrane structure, peptide membrane interaction and ligand-receptor interactions.

Cory Berkland, Assistant Professor. Controlled-release drug delivery systems, design of particles for targeted inhala-



R. Steve Dick/KU University Relations

tion therapy, development of one-shot vaccine formulations, molecular engineering of polymers to produce smart nanoparticles, development of ultrasound contrast agents capable of enhanced visualization and treatment of diseased tissues.

Ronald T. Borhardt, Solon E. Summerfield Distinguished Professor. Epithelial and endothelial cell culture systems for studying drug transport and metabolism. The development of rational strategies to enhance peptide cell membrane permeability. The development of strategies for stabilizing proteins and peptides to prevent their chemical degradation.

Jeffrey Krise, Assistant Professor. Mechanistic analysis of intracellular drug distribution in mammalian cells. Evaluations include correlating the physicochemical properties of drugs with their organelle accumulation capacity. Proteomic approaches and gene silencing techniques are used to identify and characterize proteins that play a role in these processes. Current research focuses on understanding and combating a unique drug resistance phenotype involving drug sequestration observed in certain multi-drug resistant cancer cell lines.

Jennifer Laurence, Assistant Professor. Analysis of protein structure and dynamics using multidimensional NMR and computational methods to elucidate correlations between catalytic and biological function and the proteins' structure and dynamics. Examination of protein-protein, protein-membrane, and protein-ligand interactions using biophysical, biochemical, analytical, and spectroscopic tools.

Susan M. Lunte, Professor. Development of new detection modes for capillary electrophoresis and liquid chromatography. Investigation of drug metabolism and delivery by microdialysis sampling. Trace analysis of anticancer drugs and neurotransmitters in biological fluids and tissues. Development of new analytical approaches for the determination of oxidative modification on proteins.

C. Russell Middaugh, Takeru and Aya Higuchi Distinguished Professor. Proteins with unusual transport properties (growth factors and viral proteins) are being investigated by various biophysical methods. A second broad area of interest concerns gene therapy and genetic vaccination. Investigations involve studies of the mechanism by which polynucleotides enter cells and ultimately gain entry into the nucleus. This information is being used to design vehicles which complex DNA and improve the efficiency of transport across these barriers.

Eric Munson, Associate Professor. Characterization of solid pharmaceutical using solid-state NMR spectroscopy, powder X-ray diffraction, and other techniques. Investigation of the structure and reactivity of pharmaceutical agents in polymer matrices. Transformations between crystalline and amorphous forms of pharmaceutical solids. Peptide and protein stability in formulations.

J. Howard Rytting, Professor. Solution thermodynamics, applications to drug design and delivery. Physical chemistry on biologically active agents, effects of temperature and pressure on biologicals and pharmaceuticals. Dissolution. Stability. Rectal and intestinal drug absorption. Transdermal and intraoral drug delivery.

Christian Schöneich, Professor. Reaction mechanisms of free radicals and reactive oxygen species with biomolecules such as lipids, peptides, and proteins. Investigation of the importance of free radical processes in biochemistry and pathology and possible pharmaceutical interventions.

Richard L. Schowen, Emeritus Professor. Fundamental investigations of enzyme catalysis: studies of agents that will potentially affect the rates of inhibitor release from enzyme-inhibitor complexes. Mechanisms of utilization of ligand-receptor binding energy in achieving receptor function. Development of theoretical methods to establish quantitative relationships between drug structure and pH-sensitive degradation rates to enable general predictions of stability at any pH as a function of structure.

Teruna J. Siahaan, Professor. Peptide and protein conformational studies that relate to their stability and delivery. NMR, CD, FTIR, and computational chemistry are used to understand the biophysical properties of peptides and proteins. Mechanisms of cell-cell and cell-matrix adhesion through protein-protein interactions are under investigation.

Valentino J. Stella, University Distinguished Professor. The application of physical/organic chemistry to the study of factors affecting drug delivery, with an emphasis on chemical kinetics. Preformulation workup of cytotoxic and anti-AIDS drugs. Improved drug delivery through the use of prodrugs. The mechanism of lymphatic drug delivery. The role of chemical and enzymatic reactions on drug dissolution and the pharmaceutical uses of cyclodextrins.

John F. Stobaugh, Professor; Director, Center for Bioanalytical Research. Liquid chromatographic based trace analysis of drugs, peptides and proteins in biological samples. Development of

fluorogenic and electrogenic derivatization reagents. The development of capillary electrophoresis as a micro-analytical technique for biological samples, the resolution of optical isomers, and protein separations. Evaluation of capillary electrochromatography, including new supports, as a new separation technique in pharmaceutical and biomedical analysis.

Elizabeth M. Topp, Professor and Acting Chair. Transport of drugs in physical and biological media. Formation of controlled release devices from biodegradable and biocompatible polymers. Diffusion and convection of chemotherapeutic agents in solid tumors.

George S. Wilson, Higuchi Distinguished Professor. Development of new rapid and sensitive flow injection and sensor-based analytical methods. Implantable biosensors, especially for glucose in vivo monitoring. Use of immunology to characterize proteins and peptides. Peptide and protein stability related to the redox chemistry of methionine.

Financial Support

Most students receive financial support immediately upon admission to the Department of Pharmaceutical Chemistry, usually in the form of research assistantships. No special application for financial support is required. The competitive stipend ensures that students are able to concentrate fully on their studies and research.

Students with particularly outstanding undergraduate records may be eligible for a number of special awards. The Self Fellowship provides stipend and tuition to outstanding students for four years of graduate study. Other university-level awards include the University Honors Fellowship, which is awarded on a competitive basis to incoming graduate students throughout the university. The university also provides dissertation fellowships to outstanding students during their last year of doctoral study. Each year the department awards the Takeru Higuchi and the Siegfried Lindenbaum Fellowships to incoming graduate students with high promise in the department. These fellowships provide a stipend and cover the cost of tuition.

In addition, graduate students in the department have competed successfully for a number of external fellowships, including National Science Foundation (NSF), National Institutes of Health (NIH), American Foundation for Pharmaceutical Education (AFPE), Pharmaceutical Research and Manufacturers' Association (PhRMA), Parenteral Drug Association (PDA), and United States Pharmacopeia (USP) fellowships. Additional application materials must be supplied for many of these awards; interested students should contact the graduate studies adviser in the department for more information.

The University

The University of Kansas is a major educational and research institution with 29,000 students and 2,100 faculty members. KU includes the main campus in Lawrence; the Medical Center in Kansas City, Kansas; the KU Edwards Campus in Overland Park; a clinical campus of the School of Medicine in Wichita; and educational and research facilities throughout the state. KU has 14 major academic divisions: the College of Liberal Arts and Sciences, the Graduate School, and the Schools of Allied Health, Architecture and Urban Design, Business, Education, Engineering, Fine Arts, Journalism and Mass Communications, Law, Medicine, Nursing, Pharmacy, and Social Welfare. Visit KU online, www.ku.edu.

KU set a record of \$258 million for total research expenditures in 2003. The National Science Foundation classifies KU as a major university receiving substantial research support.

The University of Kansas prohibits discrimination on the basis of race, color, religion, sex, national origin, age, ancestry, disability, veteran status, sexual orientation, marital status, and parental status.

Cover photos: Doug Koch, Elissa Monroe, and Aaron Paden. Design: Mo Issa. Produced by the KU Office of University Relations and KU Printing Services, 2004.