

Indispensable News

MinneCeutics

University of Minnesota

Fall 2000

Department of Pharmaceutics

REGULAR FACULTY:

David J.W. Grant
Yueh-Erh Rahman (Emeritus)
Ronald J. Sawchuk
Ronald A. Siegel
Raj G. Suryanarayanan
Timothy S. Wiedmann
Cheryl L. Zimmerman

ASSOCIATE AND ADJUNCT FACULTY:

Walid M. Awni, Abbott Laboratories
Rene A. Braeckman, Ceptyr, Inc.
Keith K.H. Chan, GloboMax
Belinda W.Y. Cheung, University of Minnesota
Lawrence E. Felice, Medtox Laboratories
William H. Frey, II, Alzheimer's Institute at
Regions Hospital

Michael D. Karol, Abbott Laboratories
Eric Munson, University of Minnesota
Aldo Rescigno, University of Parma, Italy
Ray Skwierczynski, 3M Pharmaceuticals
Lian Yu, Eli Lilly & Co.

MESSAGE FROM THE DEPARTMENT HEAD

With fall rolling around and the AAPS national meeting about to occur, I get the opportunity to report to you on what is happening in the Department of Pharmaceutics at the University of Minnesota. Of course, things happen all the time, but this newsletter provides an opportunity to place the most important events in perspective.

Professor Cheryl Zimmerman spent last year on sabbatical at Vanderbilt University. Her purpose was to gain skills in molecular biology which she will apply to her research on molecular and cellular transporters. These transporters are integral components of the machinery underlying absorption, clearance, and distribution of drugs, and may also play a role in drug effects. We welcome Cheryl, with her acquired know-how, back to our Department!

Professor Ronald Sawchuk turned 60 this year. To celebrate this milestone, a symposium was held at the University of Minnesota. At this event, the Ronald J. Sawchuk Graduate Fellowship in Pharmacokinetics was announced, and nearly \$60,000 in gifts and pledges has been raised, with a goal of \$125,000 by 2002. (More about this inside.)

Professor David J. Grant was elected Fellow of the American Association for the Advancement of Science this year, in recognition of his work on crystal engineering of drugs. This award reinforces the leadership role played by our Department in the field of solid state pharmaceutics.

A major event for Pharmaceutics, the College of Pharmacy, and the University of Minnesota was the settlement of the Ziagen® patent infringement suit. A portion of the royalties from sales of this drug will be used to support startup of new faculty. Perhaps more importantly,

it has been announced that the University will use Ziagen® funds to match graduate fellowships when funds raised for such fellowships exceed \$25,000. Thus, your contribution to the Rippie and Sawchuk Fellowships will be twice the value of the check you write!

Our Department, along with other units in the College, is making a thrust into the field of pharmacogenomics. We are initiating searches for two faculty in this area, one at the associate professor level and one at the assistant professor level. Our hope is to define the genomic correlates of pharmacokinetic and pharmacodynamic processes, which can ultimately be used to predict responses to, and potential toxicities of, drugs in individuals. With the draft sequencing of the human genome and the identification of numerous polymorphisms, this goal is now in our sights, but much work remains. We believe that pharmacogenomics will allow the pharmaceutical industry to expand the repertoire of drugs it can develop. Our searches are timely insofar as the Academic Health Center at Minnesota has established the \$2 million Biomedical Genomics Center, complete with scanners and bioinformatics infrastructure that will be available to our faculty.

Thus, we have much to be excited about. I look forward to seeing you at the upcoming Minnesota Alumni Breakfast in Indianapolis!

Best regards,



Ronald A. Siegel, Sc.D.
Professor and Department Head

The opposite of a correct statement is a false statement. But the opposite of a profound truth may well be another profound truth.

—Niels Bohr

MESSAGE FROM THE DIRECTOR OF GRADUATE STUDIES

Dear Alumni, Students, and Friends,

This year has led to some significant changes for our graduate program. First, we have welcomed five new students selected from over 100 applicants, the largest group ever by 20%. With the rich pool of applicants (no doubt they read about our alumni in our web pages), we admitted students from India, China, Egypt and Korea. We also brought aboard a part-time student from 3M. We hope to continue this new direction to cultivate a rich diversity in our student population without compromising the rigorous standards that our illustrious alumni have met.

Second, we have seen an increase in the financial support available for our graduate students. While 3M and the Peters endowments have provided support for a number of years, Pharmacia and most recently Novartis have added support. Pharmacia has introduced the Enz Award, which recognizes a senior student of superior accomplishments. The Novartis Award also is given to a more senior student. Finally, celebration of Professor Sawchuk's 60th birthday allowed the creation of an endowment for the support of graduate students with an interest in pharmacokinetics and pharmacodynamics.

Third, with the greater financial support from our visionary industrial colleagues, we have begun a new program for new students. Each student is allowed to select two different laboratory rotations, each with a six-week experience. Our purpose is to familiarize graduate students with the nature of research early on to help them decide upon a permanent advisor. To make this happen, we do not require extensive teaching assistant duties in the fall semester, aside from shadowing a second-year student, attending seminars, workshops, and English speaking classes, if necessary.

I hope it is evident that we are deeply appreciative for these generous gifts and are using them to further improve our graduate program. The willingness to support our program is the greatest testament of the accomplishments of our alumni. With the greater financial support, we, the faculty, can be held to higher standards in preparing future leaders in the pharmaceutical sciences.



Timothy S. Wiedmann, Ph.D.
Associate Professor

We invite you to join us in catching up on news of fellow Minnesota graduates:

MINNESOTA ALUMNI BREAKFAST

MONDAY, OCTOBER 30, 2000

7:00 - 8:00 a.m.

Westin Hotel Indianapolis



AAPS Annual Meeting and Exposition

October 29 - November 2, 2000

Indiana Convention Center

RONALD J. SAWCHUK FELLOWSHIP IN PHARMACOKINETICS



Advisor and student:
Thomas N. Tozer and Ronald J. Sawchuk



Left to right: Thomas Tozer, William Elmquist,
Ronald Sawchuk and Kenneth Miller

An event to remember was held on May 28, 2000 in honor of Prof. Ronald Sawchuk's milestone birthday and to kick off the Ronald J. Sawchuk Graduate Fellowship in Pharmacokinetics.

The "Ronald J. Sawchuk 60th Birthday Symposium" and tribute were held at the McNamara Alumni Center in the University's new Gateway Building. Joining Prof. Sawchuk were his wife, Lyn, children, David, Holly and Heather, and mother, Mrs. Mary Sawchuk, of Toronto, Ontario, Canada, as well as over 100 friends, colleagues and students, some of whom traveled from as far away as Japan.

Guests were welcomed by College of Pharmacy Dean Marilyn Speedie, and certificates of appreciation were presented to the invited speakers by Prof. Ronald Siegel, Department Head for Pharmaceutics. The announcement of the creation of the Fellowship was kept as a final surprise until the end of the evening, but was not the only surprise. The arrival of Prof. Sawchuk's doctoral advisor and friend, Prof. Thomas N. Tozer, was a closely guarded secret. Prof. Tozer, formerly a faculty at the University of California at San Francisco, was invited to give the first symposium presentation, and brought with him a painting created by both he and Prof. Sawchuk during their years in San Francisco. Presentations and recollections of research and experiences were given by Dr. Kenneth W. Miller of the American Association of Colleges of Pharmacy and former faculty member of the College of Pharmacy, and Prof. William F. Elmquist of the University of Nebraska Medical Center and former graduate advisee of Prof. Sawchuk.

Many thanks go to Dr. Belinda Cheung, who coordinated and publicized the merry event and the fellowship, and to Dean Speedie and Prof. Siegel for providing financial support.

To learn more about contributing to these important graduate fellowships, please contact
Laurel Mallon, Development Director, College of Pharmacy, University of Minnesota,
308 Harvard Street S.E., Minneapolis, MN 55455 (Ph. 612-624-2490)

The Ronald J. Sawchuk Fellowship in Pharmacokinetics
The Edward G. Rippie Fellowship in Pharmaceutics

DRUG DELIVERY CENTER

The Drug Delivery Center's annual Open House, held this year on October 5, featured Dr. Alexander Kabanov, Associate Professor of Drug Delivery at the University of Nebraska Medical Center's Department of Pharmaceutical Sciences, who presented a seminar entitled "Selective Energy Depletion and Sensitization of Multiple Drug-Resistant Cancer Cells by Pluronic Block Copolymers: A Foundation for Novel Chemotherapy". In addition, a short lecture was presented by Dr. Indiran Pather of Cima Laboratories entitled "The Theoretical Basis for the OraVescent™ Drug Delivery Systems". Poster presentations highlighted research by members of the Drug Delivery Center, the University's Cancer Center and Department of Medicinal Chemistry, 3M Pharmaceuticals, Birchpoint Medical, and the FDA's Center for Drug Evaluation and Research.

Since its founding two years ago, members of the Drug Delivery Center have submitted a number of research proposals to further the Center's research activities and educational mission. The Center's collaborative disciplines are represented by faculty from the Departments of Pharmaceutics, Laboratory Medicine and Pathology, Chemistry, Bioengineering, Electrical Engineering, and Computer Engineering at the University of Minnesota.

The Center facilitates industrial research, and companies in turn support research and graduate students financially. Collaborative projects with biotechnology and pharmaceutical companies are ongoing. An Industrial Advisory Board consisting of representatives from local industry has been convened to advise the Center in its research and educational mission and to enable the Center to assist companies interested in drug delivery and biotechnology in Minnesota.

The Drug Delivery Center enables the coordination of efforts in the delivery of peptides, antiviral agents, and nitric oxide donors for the treatment of cancer, infections, inflammation and restenosis, and will lead to new therapies for the treatment of patients suffering from these diseases. Most importantly, the Center helps to bring together the various graduate programs involved and will help to improve

graduate education in the design and optimization of therapeutic delivery systems.

The Drug Delivery Center was featured in a recent issue of the College of Pharmacy's *Pharmacy Record*:

"Quite often, new therapies are hampered by an inability to deliver the active agent to the site of the disease in a controlled manner without impairing normal tissues. Thus, the delivery system is an equal partner with the active agent in successful therapy."

"While the biologists develop methods to analyze drug activity *in vitro* (bioassay and pharmacology) and *in vivo* (pharmacokinetics and pharmacodynamics), the physical scientists choose the appropriate matrix and excipients into which the therapeutic molecule will be incorporated as well as designing dosage forms for the therapeutic agent."

"There are few, if any, programs in the United States that take an interdisciplinary approach to educate graduate students in drug delivery although there is undoubtedly a great demand for these scientists, especially in the pharmaceutical industry."

This initiative is aimed toward developing and expanding collaborations with industry, and will lead to further research grants and contracts with industrial and government sources.



David J.W. Grant, D.Phil., D.Sc.
Professor and Director



Our thanks to Catherine Oslund, editor of the *Pharmacy Record*, for sharing portions of her article.

ALUMNI NEWS

Srini Venkatesh, Ph.D. [1993] Bristol-Myers Squibb Research Institute, was recently promoted to Group Leader of Pharmaceuticals Research and Development at Wallingford, Connecticut.

Yandong Wen, Ph.D. [1996], Bristol-Myers Squibb, is a Research Investigator in the Dept. of Metabolism and Pharmacokinetics in Lawrenceville, New Jersey. "My job responsibilities include design of preclinical and clinical pharmacokinetic studies, perform pharmacokinetic/pharmacodynamic analyses, write study reports, represent the department at project working groups, etc. On my family side, my wife, Jingping Mo, works for Pfizer in New York City as an epidemiologist (assistant director)."

FACULTY NEWS AND ACTIVITIES

PROFESSOR DAVID J.W. GRANT was elected as a Fellow of the American Associate for the Advancement of Science for his fundamental contributions in the crystal engineering of drugs and the properties of drug materials in the solid state. The award was presented in Washington, DC, at the February annual meeting.

At the 10th Annual Meeting of the Association of Crystallization Technology, Prof. Grant was invited to present "Incorporation of Impurity Molecules in Pharmaceutical Crystals: Solid Solutions or Inclusions?" as part of "Session III: Impurities and Their Incorporation into Crystalline Products" in April in New Brunswick, NJ.

Prof. Grant was invited to present "Theory and Origin of Polymorphism" at the Conference on Polymorphism and Crystallization of Pharmaceuticals in Philadelphia, PA in June.

Prof. Grant presented "Polymorphism Among Organic Compounds" at the Royal Institute of Technology in Stockholm, Sweden in June.

PROFESSOR RONALD J. SAWCHUK participated in the offering and organization of a new basic and advanced microdialysis course entitled "Basic and Advanced Aspects of *In Vivo* Microdialysis" at the 2nd International Symposium on Microdialysis in Drug Research and Development in Stockholm, Sweden in June. He included a symposium on distribution of antibiotics to the middle ear by microdialysis entitled "Recovery: Basic Idea and Practical Methods".

Prof. Sawchuk was elected Vice Chair of the PPDM Section of AAPS for 2000-2001. He also chaired the AAPS Microdialysis Focus Group for the second year; the group now has a membership of 110.

Prof. Sawchuk was invited in May to present "*In Vivo* Microdialysis as a Tool to Study Drug Delivery" at the 19th Annual Robert S. Rozman Memorial Symposium in Langhorne, PA.

San Francisco was the site of the Millennial World Congress of Pharmaceutical Sciences at which Prof. Sawchuk was invited to present "*In Vivo* Microdialysis as a Tool to Study Site-Specific Drug Delivery".

PROFESSOR RONALD A. SIEGEL organized "Controlled Release—Into the 21st Century," a short course sponsored by the Controlled Release Society in conjunction with the Millennial World Congress of the FIP in San Francisco in April. He was also a member of the organizing committee for University of Minnesota's Nanotechnology Summit held in March.

Prof. Siegel was a member of an NIH *ad hoc* study section reviewing proposals for Biomedical Engineering Research Partnerships.

Drew University in Madison, NJ invited Prof. Siegel to present an introductory lecture on drug delivery to the Residential Medicinal Chemistry Program.

Prof. Siegel contributed to the following platforms:
♦R.A. Siegel and G.P. Misra. Pulsing Gels for Episodic Drug Delivery: Autonomous Chemomechanical Feedback Oscillations in a Gel/Enzyme System. American Chemical Society National Meeting, San Francisco, CA, March.
♦D.F. Bairamov, A.E. Chalykh, M.M. Feldstein, A.A.

Iordanskii, R.A. Siegel, and N.A. Platé. Kinetic Parameters of Poly(n-Vinyl Pyrrolidone) Spontaneous Mixing with Short Chain Polyethylene Glycol. American Chemical Society National Meeting, San Francisco, CA, March. ♦R.A. Siegel, G.P. Misra and A. Dhanarajan. Multiple Autonomous Swelling/Deswelling Oscillations in an Enzyme/Hydrogel System Exposed to Constant Levels of Glucose. Proceedings from the 27th Intl. Symposium on Controlled Release of Bioactive Materials, Paris, France.

PROFESSOR RAJ G. SURYANARAYANAN was selected by Pharm.D. I students as 2000 Teacher of the Year and Spring Semester 2000.

Prof. Sury gave two presentations at the 1st International Workshop on Physical Characterization of Pharmaceutical Solids in September: "Thermoanalytical Techniques for Characterization of Drugs and Dosage Forms" and "Qualitative and Quantitative Applications of Non-Ambient XRD".

Pfizer Central Research (Groton, CT), Eli Lilly and Co. (Indianapolis, IN), and SSCI, Inc. (West Lafayette, IN) invited Prof. Sury to present "Use of *In Situ* X-ray Powder Diffractometry to Characterize Phase Transitions During Freeze-drying".

Prof. Sury was invited by Bristol-Myers Squibb to present "X-ray Power Diffractometry: Advanced Issues Including Quantitative Analysis" and "Introduction to X-ray Powder Diffractometry: Technique and Utility" in Wallingford, CT.

PROFESSOR TIMOTHY S. WIEDMANN was elected Chair of the Academic Health Center's Faculty Consultative Committee for 2000-01. He is also chair of the College of Pharmacy's Faculty Consultative Committee. This year marks his third year as Director of Graduate Studies for Pharmaceutics.

Prof. Wiedmann is a member of the advisory group for the Structural Biology NMR Laboratory at the University of Minnesota, and is a member of the Cancer Center.

"Interaction of Biological Liquid Crystals with Mucin" was presented to the University's Molecular Simulation Group by Prof. Wiedmann.

Prof. Wiedmann is Chair of the PDD Section Membership Committee of AAPS.

PROFESSOR CHERYL L. ZIMMERMAN returned in August after a year's sabbatical at Vanderbilt University's Department of Biochemistry in Nashville, TN. In addition to hearing a lot of bluegrass music, she worked in the laboratory of Dr. David E. Ong using differential display to search for genes that are co-regulated by retinoic acid and estrogen.

Prof. Zimmerman was the Chair of the PPDM Section of AAPS for the year 2000. She will step down at the AAPS Annual Meeting to become Past Chair for 2001.

Prof. Zimmerman was invited to present "Role of Enzyme Localization in the Intestinal Metabolism of Drugs" at the 33rd Annual Higuchi Research Seminar in Lake Ozark, MO in March.

Agouron, Inc. invited Prof. Zimmerman to present "Role

of Enzyme Localization in the Intestinal Metabolism of Drugs" in April in San Diego, CA.

Prof. Zimmerman was invited to present "Pharmacokinetic Evaluation and Inhibition of First-Pass Metabolism"

at 3M Pharmaceuticals in Maplewood, MN in April.

Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, invited Prof. Zimmerman to present "Role of Enzyme Localization in the Intestinal Metabolism of Drugs".

GRADUATE STUDENT NEWS

NEW STUDENTS

The Department welcomed new students in Fall 2000:

Mr. Luke Bi, 3M Pharmaceuticals, University of Cincinnati, Southern Illinois University at Carbondale, and East China University of Chemical Technology

Mr. Koustuv Chatterjee, University of Toledo (Ohio), and Jadavpur University, Calcutta, India

Mr. Yushi Feng, Ocean University of Qingdao, Shandong, China

Ms. Jee-Eun Lee, University of California at Irvine, and Seoul National University

Mr. Nael Mostafa, Faculty of Pharmacy, University of Tanta, Egypt

DEGREES AWARDED

Ranjeeta Bhatia, M.S.

Thesis: Effect of Acoustic Parameters: Frequency and Power on Ultrasonic Nebulization for Respiratory Drug Delivery (Advisor: Prof. Timothy Wiedmann)

Sophia Yinghua Li, Ph.D.

Thesis: Preparation and Characterization of Amorphous Pharmaceuticals (Advisor: Prof. Raj Suryanarayanan)

Suneel Rastogi, Ph.D.

Thesis: Phase Transitions and Decomposition Reactions in Pharmaceutical Solids (Advisor: Prof. Raj Suryanarayanan)

Ivy Heng Song, Ph.D.

Thesis: Influence of Chemical Structure on the Pharmacokinetics of AZT Phosphoramidate Prodrugs (Advisor: Prof. Cheryl Zimmerman)

SUMMER INDUSTRY INTERNS & TRAINEES

Ms. Sharmistha Datta spent the summer as an intern at Bristol-Myers Squibb Pharmaceutical Research Institute under the supervision of Drs. Srinivasan Venkatesh and Shin-Hong Kang at Wallingford, Connecticut on a project entitled "Studies to Determine Whether Immobilized Artificial Membrane Chromatography Can be Used as High Throughput Screening for Drug Absorption *In Vitro*". (Advisor: Prof. David Grant)

Mr. Zhihong Li worked with his advisor, Prof. Cheryl Zimmerman, at Vanderbilt University during summer 2000.

Mr. Agam Sheth worked as a summer intern with Drs. Ajit Thakur and Krishnaswamy Raghavan at Bristol-Myers Squibb in New Brunswick, New Jersey on a project entitled "Dissolution Behavior of Weakly Acidic Drugs and Their Salts". (Advisor: Prof. David Grant)

AWARDS

Mr. Zedong Dong received a USP Fellowship in Drug Standards Research for 2000-2001. (Advisor: Prof. David Grant)

Mr. Chong-Hui Gu received a travel award to attend the 12th International Symposium on Chirality held in Chamonix-Mont Blanc, France, September 24-28, 2000. (Advisor: Prof. David Grant)

Mr. Yue Huang received the Eli Lilly Award in Pharmacokinetics, Pharmacodynamics and Clinical Sciences for his abstract entitled "Studies of Amoxicillin Distribution Kinetics in Chinchilla Middle Ear Using Microdialysis". The award will be presented at the AAPS Meeting in Indianapolis. (Advisor: Prof. Ronald Sawchuk)

Ms. Prajakti Kothare received a competitive PPDM travel award to the 2000 AAPS Annual Meeting in Indianapolis. (Advisor: Prof. Cheryl Zimmerman)

Ms. Abira Pyne received the Proctor and Gamble Award for her dissertation research which will be presented at the upcoming AAPS Meeting in Indianapolis (Advisor: Prof. Raj Suryanarayanan). Ms. Pyne is the first University of Minnesota recipient of the Enz Award, and presented a research seminar at Pharmacia-Upjohn in October as part of the awards process. (Advisor: Prof. Raj Suryanarayanan)

Mr. Calvin Sun received an AFPE Pre-Doctoral Fellowship for his work entitled "Influence of Crystal and Particulate Properties on the Tableting Performance of Pharmaceutical Powders" (Advisor: Prof. David Grant). Mr. Sun, sponsored by the National Science Foundation, was elected to participate in an intensive short course on particle technology held in July at the University of Clausthal, Germany. (Advisor: Prof. David Grant)

Mr. Rahul Surana's USP Fellowship was renewed for his drug standards research project entitled "Powder Characterization by Inverse Gas Chromatography". (Advisor: Prof. Raj Suryanarayanan)

PEOPLE

Mr. Danir Bairamov, a doctoral student in physical chemistry at the Russian Academy of Sciences in Moscow, was a visiting graduate student this year in Prof. Ronald Siegel's laboratory, developing a novel optical microinterference method to measure interdiffusion of polymeric materials useful in drug delivery.

Ms. Federica Danzi, a doctoral student in pharmacology from the University of Parma, Italy, worked this summer in the laboratory of Prof. Ronald Sawchuk on microdialysis of antibiotics, and assisted with the development of LC-MS methods for the analysis of drugs in dialysates. During this time she also contributed her expertise in biopharmaceutics and drug delivery to research projects involved the kinetics of drug absorption and distribution. Upon completion of her Ph.D., Federica plans to continue her research activities in quantitative microdialysis, and to further pursue its application in pharmacologic and toxicologic studies.

Ms. Cynthia Deye, former laboratory assistant for Prof. Timothy Wiedmann, has begun her M.D./Ph.D. studies at the University of Illinois at Champaign-Urbana, where she is co-chair of the Internal Medicine Club at UIUC. She hopes to do an internship this summer with the World Health Organization's division of Community Health Services. Her family trained and raced dogs that participated in this year's Alaskan Iditarod sled dog race.

Ms. Jean Helders joined the Department in January as a senior secretary. Jean has undergone the University's specialized training for on-line purchasing and payments.

Ms. Heather Herrington has joined Prof. Timothy Wiedmann's group as a laboratory assistant. Heather has a B.S. in Chemical Engineering from the University of Minnesota, and eventually plans to enter the veterinary sciences.

Ms. Anne Johnson, secretary for the *Journal of Pharmaceutical Sciences*, won the Jesse Ventura Broadway Song Contest, hosted by the St. Paul (Minnesota) Pioneer Press. Lyrics to her song, "The White House" (sung to the tune of "Tomorrow" from *Annie*), appeared in the Pioneer Press, and the prize is a trip to New York City to see Jesse's new musical.

Dr. Gauri Misra, a postdoctoral researcher in Prof. Ronald Siegel's laboratory, accepted a faculty position in the Department of Chemistry, Panjab University, in Chadragarh, Punjab State, India.

Dr. Sudha Vippagunta, a postdoctoral associate for Prof. David Grant, has accepted a position in pharmaceutical development at Novartis Pharmaceuticals Corporation in East Hanover, New Jersey.

Dr. Liang Wei will be joining Prof. Timothy Wiedmann's laboratory as a postdoctoral associate. He comes from the National Pharmaceutical Engineering Research Center at Shanghai Institute of Pharmaceutical Industry.

TELEPHONES	FACULTY	E-MAIL ADDRESSES
(612) 624-3956	David J. W. Grant	grant001@tc.umn.edu
(612) 624-0646	Ronald J. Sawchuk	sawch001@tc.umn.edu
(612) 624-6164	Ronald A. Siegel	siege017@tc.umn.edu
(612) 624-9626	Raj G. Suryanarayanan	surya001@tc.umn.edu
(612) 624-5457	Timothy S. Wiedmann	wiedm001@tc.umn.edu
(612) 624-4611	Cheryl L. Zimmerman	zimme005@tc.umn.edu
(612) 624-5151	DEPARTMENT OF PHARMACEUTICS	
(612) 624-0646	Bioanalytic and Pharmacokinetic Services	
(612) 624-4433	Drug Delivery Research Center	
(612) 625-0926	<i>Journal of Pharmaceutical Sciences</i>	
(612) 624-1900	College of Pharmacy	

If you would like to list your e-mail and website addresses in the alumni section of the Pharmaceutics website at the University of Minnesota, please send your information to Candy McDermott at mcder002@tc.umn.edu

<http://www.pharmacy.umn.edu/resgrad/pceutics/pharmaceuticshome.html>

RECENT PUBLICATIONS

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DEPARTMENT OF PHARMACEUTICS
College of Pharmacy
University of Minnesota
308 Harvard Street S.E.
Minneapolis, MN 55455
USA

