From Digitalis to Ziagen

The University of Minnesota’s Department of Medicinal Chemistry

BY

YUSUF J. ABUL-HAJJ
RICHARD BRODERICK

University of Minnesota • Minneapolis
# Table of Contents

Preface .................................................................................................................. v
Acknowledgements ............................................................................................. vii
Chapter 1 • The Age of Wulling ................................................................. 1
Chapter 2 • Research Comes of Age ......................................................... 29
Chapter 3 • From the Natural to the Synthetic ........................................ 51
Chapter 4 • Into the Future ...................................................................... 85
Appendices ........................................................................................................ 133
  A. University of Minnesota Presidents ..................................................... 135
  B. College of Pharmacy Deans .............................................................. 139
  C. Medicinal Chemistry Department Heads ........................................... 141
  D. Outstanding Achievement Awards ..................................................... 143
  E. Books Authored by Medicinal Chemistry Faculty ........................... 149
  F. Graduates of the Department of Medicinal Chemistry ................... 151
  G. Works Cited ...................................................................................... 157
The genesis of this book goes back many years.

During the long period of time when I was head of the Department of Medicinal Chemistry, the department underwent dramatic changes in many different realms, from changing personnel to evolving research trends to sometimes wrenching shifts in administration and institutional structure.

In turn, my interest in the changes that have taken place just since 1968 led me to think that there was a need for a comprehensive history of Medicinal Chemistry beginning with the founding of the University of Minnesota’s College of Pharmacy in 1892 until today. In turn that same period of time—1892 to 2012—also represents the most revolutionary era in the history of the entire discipline of medicinal chemistry, witnessing the transformation of the field from an artisanal, trial-and-error approach to isolating and testing therapeutic elements in natural elements to today’s high-tech, computer-assisted discovery and design of new, targeted drugs.

Of course to tell this story in depth—the history of the University of Minnesota’s Department of Medicinal Chemistry—requires telling the stories of the individuals who created and shaped, and, over the decades, worked in the department.

Perhaps even more than in other disciplines, this primacy of individual contribution holds true in the Department of Medicinal Chemistry for the simple reason that it has been an institution in which individual faculty members have had a major impact in its birth and ongoing development. Those contributions began when Frederick Wulling, one of the giants of the field, agreed to move to Minnesota from his very comfortable career on the East Coast and found the state’s first college of pharmacy in improvised quarters on the campus of the University of Minnesota. For several years, Wulling was not only the school’s first dean but also its first—and only—faculty member in pharmacognosy and pharmaceutical chemistry. His groundbreaking work not just in building the college and department but also in the research into products like digitalis was from the first built upon by other faculty members. These faculty played a key role both in shaping and reshaping the department and in making and remaking the field of medicinal chemistry, playing leading roles in changing the focus and methodology and, ultimately, even the objectives, of medicinal chemistry research.

The achievements of individual faculty members such as Earl Fischer, Ole Gisvold, Taito Soine, Philip Portoghese, John Staba, and Robert Vince lay the groundwork for today’s widely expanded roster of younger faculty whose research involves cutting-edge collaborations with other departments and centers at the University of Minnesota. In undertaking the history of an organization with such a long and varied history—one that encompasses not only revolutionary changes in the goals, methodology, and technology of research but also changes to departmental and college structures necessitated by the explosive growth of the University, especially after World War II, and the school’s emergence as one of the preeminent research institutions in the world—certain challenges had to be overcome.

Not the least of these was in deciding how best to organize that long history in a way that readers would find engaging. Rather than adopting a straightforward year-by-year chronological approach, we organized the department’s rich history into four sections, each corresponding to turning points in the development of medicinal chemistry at the Uni-
versity of Minnesota. Within each of those sections we attempt to tell the story themati-
cally, examining developments in research, personnel, administration, and departmental
structure during the period covered by each section. In every case, we have kept the focus
on the individual faculty members whose contributions in teaching, research, service, and
administration have been critical to the department’s success over the past 120 years.

One final consideration went into the making of this book. While we expect that its
primary audience will be members, both past and present, of the department, as well as
their families, friends, and students, we also hope readers will be others who have no direct
relationship to the department. The Department of Medicinal Chemistry was born in the
middle of the transition of medical remedies from a folk tradition to a modern, research-
driven science. Since its founding in 1892, the department has mirrored the breathtaking
changes that have taken place in the analysis, discovery, and—increasingly—the design of
effective drugs for the treatment of some of humanity’s most deadly and crippling disorders.
And it has more than mirrored those changes, in many cases, playing a critical role effecting
those changes.

We chose to title this book From Digitalis to Ziagen not simply because it’s a catchy name
but also because it captures the one overriding theme that has prevailed throughout the
existence of the Department of Medicinal Chemistry and will continue to prevail into the
future: the never-ending quest to help cure illness and thus make the world a happier and
healthier place in which to live.

Yusuf J. Abul-Hajj
April 2012
Minneapolis
The authors would like to thank the many contributors for compiling the information for this book. Every effort was made to verify the facts such as names, dates, and events, but the flavor of the individual chapters is that of the authors. Some areas of work and periods of time probably are not covered as much as would have been optimal due to lack of records or people to provide an account from collective memory. In particular we also like to thank Erik Moore and other staff members from the University of Minnesota Archives for guiding and accessing the material for chapters 1 and 2. Thanks also to the Minnesota Pharmaceutical Association for using their archived materials.

Thanks go to several faculty members including Mahmoud Abdel-Monem, Elizabeth Amin, Gunda Georg, Patrick Hanna, Rodney Johnson, Philip Portoghese, Rory Remmel, W. Thomas Shier, Marilyn Speedie, Natalia Tretyakova, Robert Vince, and Carston Wagner for historical accounts of their areas and other anecdotes. In particular we thank Drs. Portoghese, Hanna, and Georg for reading and critiquing sections of the manuscript.

We gratefully acknowledge several former faculty and alumni including Lee Schramm, Raymond Counsell, K. H. Lee, Lemont Kier, and William Soine for personal information on several aspects of departmental history during the 1950s and 1960s. Thanks to Dennis Worthen for providing input about the developments and changes to pharmacy education during the 1930s and 1940s and to Heather Wilson, Charles Wilson’s daughter, for providing us with information from her father’s records about pharmaceutical chemistry during the 1940s.

Gratitude is due to Genny Rosing from the Graduate School for the time she spent in double-checking the accuracy of the names, degrees, and dates for all graduate students. Thanks, too, to Drr. Elizabeth Amin for providing the molecular model of Ziagen for the cover.

A special note of appreciation goes to the many staff members over the 70-plus years who have contributed in unique and substantial ways to the work that made this departmental history.

Funding for this project was supported in part by the Wulling Endowment Fund and the Department of Medicinal Chemistry at the University of Minnesota.

Yusuf J. Abul-Hajj
Richard Broderick
April 2012
Minneapolis, Minn.
From the very beginning, medicinal chemistry has been an integral part of pharmacy education and research at the University of Minnesota. Although a formal department of medicinal chemistry did not exist at the University until the mid-1930s, today’s department can track its origins back much earlier—to 1892 and the creation of the College of Pharmacy.

The year 1892 was also when the state Legislature, acting at last on the recommendations of the University of Minnesota Board of Regents and the nine-year-old Minnesota State Pharmaceutical Association (MSPhA), voted to appropriate money to establish a school of pharmacy at the University of Minnesota (Netz, 1971).

Following that vote, the University Regents began to look for someone to lead
the new school. Given his youth, the person they discovered might have seemed like an unlikely candidate to serve as dean and founder of the College of Pharmacy.

Frederick J. Wulling bore an impressive résumé, despite his young age. He was something of a prodigy in the New York City worlds of pharmacy, medicine, and teaching at some of the city’s most important institutions of higher learning.

While still a teenager, Wulling had taken an apprenticeship with a Brooklyn pharmacist. After reading about medicine and studying botany with the family physician and a local pharmacist, he enrolled in the College of Pharmacy of New York—which would eventually become part of Columbia University—and immediately requested, and was granted, a transfer to that year’s graduating class. Wulling then entered Columbia University’s College of Physicians and Surgeons, where one of his professors, Dr. Peter Bedford, convinced him to pursue a degree in pharmacy prior to studying medicine. At the same time, Bedford appointed him as his classroom assistant—a lecture demonstrator—a title soon elevated to assistant lecturer. The promotion followed an incident when Bedford, arriving back in New York from a lobbying trip to Albany later than he’d expected, walked into his classroom in time to hear the end of Wulling’s impromptu lecture delivered in Bedford’s absence. Impressed by his protégé’s performance, Bedford declared that Wulling was “the only student in the world who is an unofficial faculty member, but who possesses the qualification of a full faculty member” (Wulling, 1944).

Although Wulling debated between a career in medicine and pharmacy, pharmacy education ultimately attracted him in the end. During his apprenticeship and education, he explained his choice in an undated talk, “Why I Entered Pharmacy.” He said, “I became aware of two facts: First, that medical men were, except in comparatively few cases, quite insufficiently qualified in materia medica and therapeutics and hence in prescription writing...[and those who were mostly educated in Europe]. ... The second fact I discovered was an inadequacy on the part of pharmacists of a sufficient qualification in their own field, especially in the science divisions. There were no practitional standards and requirements in those days in medicine or pharmacy comparable with those of today.”

In 1886, Wulling further burnished his credentials when he was hired to head a prescription dispensing laboratory in a private New York hospital, where he was put in charge of expanding the facility to include laboratories for pharmaceutical manufacturing, clinical microscopy and chemistry, and research. Soon he took on the job of consulting pharmacist for the whole hospital as well. In his spare time, he traveled to Europe in 1887 and 1889 and played first violin in an amateur orchestra. In 1891, he joined the faculty of the Brooklyn College of Pharmacy as chair of a discipline called “pharmacodynamics.” By this time, he had also developed a sideline performing clinical microscopy and writing and editing articles for journals such as Pharmaceutical Record. All together Wulling’s teaching, writing, and laboratory
work was earning him a more than comfortable income of $6,000 per year.

Having already remarked upon Wulling’s “exasperating efficiency mitigated by a winning friendliness,” Bedford would be among those who enthusiastically recommended Wulling to the University of Minnesota when the school began looking for a dean and principal faculty member at its proposed School of Pharmacy (Wulling, 1944).

In turn, what lured the accomplished and cultivated Wulling to the relative backwoods of Minnesota was this once-in-a-lifetime opportunity: the prospect of organizing the state’s first university-based school of pharmacy.

The opportunity was a challenge that the short, balding, but supremely self-confident Wulling could not pass up. It would turn out to be a challenge that, over the next 10 years, not only severely tested his formidable organizing skills and powers of persuasion—not to mention his equally formidable willpower—but also brought him on several occasions to consider resigning his new post as dean of the University of Minnesota’s School of Pharmacy and return to the more congenial (and certainly more lucrative) climes of the East Coast.

An Idea Germinates

The idea of organizing a school of pharmacy began to germinate about a decade before Wulling’s arrival in Minnesota. Until 1881, no pharmacy regulations existed in Minnesota. Nonetheless, since dispensing prescriptions and other medications was seen as a lucrative profession, the field drew a host of practitioners, including some qualified and many not.

That year, the Minnesota Legislature began to move toward licensing the field, passing an act forbidding the sale of “drugs, medicines, or poisons, except by registered pharmacists” (Anderson & Pennigton, 2005, 5).

Two years later, in 1883, a number of prominent St. Paul druggists, including William A. Frost, W. S. Getty, George Marti, and Fred Kult—no pharmacist from Minneapolis was present, a signal of the relative status of the two cities at that time—met at McMasters and Getty’s Drugstore, located on Third Street in St. Paul. The participants formed a committee to draw up a charter for the Minnesota State Pharmaceutical Association (MSPhA), in which articles of incorporation included a call for the creation of a statewide college of pharmacy. Those articles were adopted at a subsequent meeting a week later and the pharmacy association was officially launched (ibid., 5).

In 1885, the Minnesota Legislature finally acted to fully regulate the licensing and oversight of pharmacy, passing laws mandating that in order to be registered as a pharmacist an applicant needed to be 21, have a degree in either pharmacy or medicine, pass an examination given by the state board of pharmacy, and have four
years’ experience working in a drug store. The bill also specified how poisons such as belladonna, digitalis, potassium cyanide, and others were to be labeled, and, in recognition of pharmacy’s status as a profession, exempted those covered by the act from jury duty. In 1886, the new MSPhA began actively lobbying for the creation of a college of pharmacy at the University of Minnesota.

The time was right for such an effort. “The Education of a Pharmacist,” a pamphlet from the mid-1880s, noted that, “We live in an eminently practical age. … The value of any education is in direct relationship to its utility in the struggle for

existence. … We now want true colleges of pharmacy and true pharmaceutical teaching.” The pamphlet goes on to call for coursework that offered knowledge of how “to store, mix, and prepare drugs, follow the law and identify compounds in drugs, and use laboratory tools” (Eccles, 1885).

By then, a number of states, including Michigan and Wisconsin, had heeded the call for the professionalization of pharmacy and the need to locate such training within institutions of higher learning. The universities of Michigan and Wisconsin were two of the earliest schools to create pharmacy colleges. State pharmaceutical associations had also spread across the country.

For five years, Minnesota’s pharmacy association pushed the Legislature to ap-
appropriate $100,000 for establishment of a pharmacy college at the University. Finally, its efforts paid off, although not as generously as association members had hoped. In 1891, the Legislature appropriated a mere $5,000 for the creation of the new school, and even that money was mostly earmarked for laboratory equipment. No money was set aside to build a laboratory or for instruction in any course except in the basics of pharmacy, all of which were to be provided by whomever was hired to run the college. The remainder of courses were to be furnished by existing departments at the University and paid for out of those departmental budgets. Without the Legislature intending it, the parsimonious appropriation was a formula for years of conflict within the University’s Department of Medicine—where pharmacy was to be housed—over scarce resources.

In addition to lack of funding, there were other reasons why the establishment of a college of pharmacy in Minnesota faced a rocky start (Wulling Collection, undated, 12).

The emergence of pharmacy as a separate discipline was still underway by the time Wulling arrived in Minnesota. Until the mid-19th Century, many American apothecaries were also physicians. In fact, soon after its founding in 1852, the American Pharmaceutical Association conducted a survey of apothecary shops in several states and discovered that only a small fraction of them were owned by individuals actually trained to “prepare and compound drugs.” And an even smaller percentage was college graduates with any kind of degree whatsoever.

Meanwhile, during the late-19th Century the debate over the place of professional schools within university settings was far from settled. Originally conceived as centers of the liberal arts that included theology, American universities were undergoing wrenching changes. In response to industrialization, urbanization, and other forces, universities were transformed into centers of both basic and applied scientific research as well as home to professional schools; medicine was one of the first to make this inroad (Higby, 2005).

This was the backdrop against which Daniel Noyes, a University of Minnesota
regent who was the head of a wholesale drug import company, sent Wulling a letter on March 17, 1892. Noyes informed the young scholar and scientist that a committee created by the Board of Regents to organize a pharmacy department had unanimously chosen him to be the first dean of the College of Pharmacy. The letter coincided with a visit to Wulling’s home in Brooklyn by David Kiehle, another regent who also served as Minnesota’s State Superintendent of Schools, to confirm the offer.

Wulling made it clear that he was interested, but would have to think it over. In the meantime, he received letters from Dr. Perry Millard, dean of the College of Medicine and Surgery, telling Wulling that, if he accepted the offer, he’d be starting the following fall with some 30 students. Dean Millard also offered details for a proposed new building that would contain a laboratory big enough to accommodate as many as 35 students and office space for the new pharmacy dean.

Thus reassured, Wulling made the trek to Minnesota to meet with President Cyrus Northrop, Dean Millard, and others to discuss his possible appointment. Arriving at the University early in May 1892, he found the physical surroundings spare to the point of spartan. At the time the campus consisted of only a handful of buildings and virtually no landscaping to mitigate the dreary impression made by the grounds.

It was not just the campus that struck Wulling as a little on the bleak side; it was also the buildings themselves and the facilities they contained.

President Cyrus Northrop’s offices were in Old Main. The outer office as well
as Northrop’s own chamber were, Wulling recalled, “bare and unattractive,” with an inner sanctum furnished with a small plain table and two chairs.

Fortunately for the history of medicinal chemistry at the University, the two men connected instantly. Wulling recalled that, after shaking Northrup’s hand and being invited to sit, his first words to the young Wulling were, “You must be an angel.” A little nonplussed, Wulling demurred, answering that if he were an angel, he must still be in training since he hadn’t yet sprouted any wings. Wulling then asked a question that revealed much about his state of mind at that moment: Why did Northrop, who’d been a faculty member at Yale, leave the East Coast to take up his current position in Minnesota? To which Northrop gave just the right response to clinch the deal. “For the same reason you are thinking of coming: Because here are bigger opportunities for doing effective and much needed work for and in education” (Wulling, autobiography; Wulling Collection, 3).

After outlining some of the difficulties and disappointments he himself faced in his eight years on the job, such as a public indifference as reflected in a Legislature that (as with pharmacy) was reluctant to allocate sufficient resources to the University, Northrop sent Wulling to meet the man who would prove to be a challenge in the next few years: Dean Perry Millard. It was not an auspicious send off. Northrop confided to Wulling that the two “pressure groups” that gave him “the most headaches” at the University were the physicians and surgeons—a complaint that Wulling would soon share. This additional meeting ended with an ambiguous answer to Wulling’s question of whether the dean of the College of Pharmacy would be answering to Millard or to the president. “He advised me to make every reasonable effort to work with Dean Millard, but in “case of trouble” to come to him—that his door would always be open,” Wulling later wrote (Wulling, 1948, 36).

Shortly thereafter, he met with Millard where he found himself in yet another ambiguous discussion, this time about lines of authority; though Wulling at first found Millard “friendly and apparently not at all the dictatorial person he was said to be.” Millard claimed to be largely responsible for the formation of all the departments and colleges in the Department of Medicine and expected their heads to take direction from him. He and Wulling had their first contretemps at the meeting when, after Wulling stated that it was his understanding that the College of Pharmacy would be located in Medical Hall (later named Millard Hall in 1906, pictured...
on p. 24), Millard replied, “Don’t you believe it. There’s no room for you in that building. You’ll have to find quarters in some other college building” (ibid., 38).

Wulling then asked if pharmacy might be housed in the inadequate space of a temporary building known as the Bowling Alley because of its layout and that was also home to physiology, histology, and medical chemistry (predecessor of biochemistry) but again Millard said no (Kohler, 1982). He then told Wulling that as dean of the new school he would have to plead personally with the heads of several departments to see if pharmacy students would be allowed to attend classes in materia medica, bacteriology, medical chemistry, and other subjects required for graduation. Millard also made it clear that the degree course in pharmacy would be only two years and yet result in a D.Pharm., because doctorate was the only degree granted by the medical school. Wulling objected, but made no headway. It would be several years before he managed to expand the degree program to the four years he wanted in the first place.

Wulling spent the next few days making the rounds of department heads and faculty members in medicine and science, meeting, with few exceptions, with resistance and sometimes barely concealed hostility to the suggestion that pharmacy students be able to attend classes in other disciplines as originally envisioned. Only one faculty member, Conway McMillan, head of the department of botany, had even heard of Wulling because the latter was known for his lectures and articles on the evolution of botany. McMillan greeted Wulling as a colleague and immediately agreed to accept pharmacy students into his department’s classes (Wulling, 1948, 44).

Returning to Brooklyn, Wulling sent a letter to Millard and Northrop detailing the conditions he gave to Regent David Kiehle for accepting the job as dean of the College of Pharmacy. The conditions—demands really—included:

1. There would be adequate laboratory space for instruction in “practically every subject of the curriculum” and cooperation from other departments and colleges at the University “to whom pharmacy students would have to be sent for the present for such instruction.”

2. That the faculty and equipment would be increased as needed.

3. That the $5,000 appropriated by the Legislature be used only for equipment and not for buildings or salaries.

4. That $10,000 be appropriated at the next session of the Legislature for additional equipment.

5. That the degree program be expanded from a two- to a four-year program by the time the first class finished the two-year program.
The first home of the College of Pharmacy was called “Medical Chemistry Building” and was located where Johnston Hall now stands. In 1892 the College of Pharmacy was allocated 2,000 square feet in the center of the building, dubbed the Bowling Alley because of its shape. The College’s space is identified in Dean Wulling’s own handwriting. Later the building was occupied by the Chemistry Department, and then became the general storehouse before its demolition in 1924.

6. That the College not be subject to the medical college or any other college or department but answer directly to the Regents while given the latitude to administer its own affairs.

7. That the curriculum for the College be created exclusively by the pharmacy faculty.

8. That provisions be made for establishing a medicinal plant garden, a pharmacy library, and pharmacy museum to be housed in the College.

9. That two research fellowships be established in pharmacy.

10. That he have free hand to establish entrance exams and be supported in “the rapid development of the school.”

11. That pharmacy be a major leading to a doctorate.

12. That he be provided with an assistant right away and others as needed over time.
Other conditions included a provision that in short order he would receive a salary of about $6,000 to offset the income he had been earning from his “business, editorial work, private students, clinical microscopy, and college position” (Wulling Collection, letter to Dean Perry Millard, 1892).

Wulling never received an overt acceptance of his conditions from either Millard or Northrop. Nonetheless, he made up his mind to make the leap, and thus showed up in Minneapolis in August 1892, determined to have everything in order for when the new College opened its doors to students just two months later.

He immediately ran into obstacles that might have defeated a more faint-hearted individual. To begin with, Dean Millard proposed postponing the start of the College until the Legislature appropriated money for a new pharmacy building—a delay that in all likelihood would have doomed the whole enterprise for another decade or more. Realizing that he would not, in fact, be given space in Medical Hall, Wulling renewed his efforts to get into the Bowling Alley, lobbying faculty in physiology, histology, and medical chemistry, all of whom had space in the building. At first he met with refusal but eventually was able to wrest a small space—about 40 square feet for a laboratory—in the Bowling Alley but no space for a lecture hall or office. He ended up sharing a lecture room and office in Medical Hall with a faculty member who taught materia medica. Meanwhile, Dean Millard turned down his request for two additional pharmacy faculty members, a laboratory assistant, and a part-time office assistant, informing Wulling that he was expected to teach all the pharmacy coursework beyond what already existing departments were willing to supply.

The College of Pharmacy began life, then, as a one-person college, although the faculty for the College listed in that fall’s bulletin included Wulling, listed as “Professor of Theory of Pharmacy and Pharmacognosy,” H. M. Bracken, “Professor of Materia Medica, Toxicology, and Physiology,” C. J. Bell, “Professor of Chemistry,” and the aforementioned Conway McMillan, “Professor of Botany.” Among the courses Wulling taught those first years were classes in pharmaceutical chemistry.

Meanwhile, the course catalog, largely penned by Millard before Wulling had a chance to give his input, listed the new College of Pharmacy, as part of the “Department of Medicine.” Graduation requirements included four years of practical experience dispensing drugs, a provision sought by the state’s practicing pharmacists, even though Wulling objected to this provision because of “the inconsistency of a University diploma covering a requirement over which the University exercised no supervision,” as he later wrote. Eventually, both the University and the state pharmacy association ended up accepting the two years spent in the College of Pharmacy as counting toward the four-year requirement. In 1895, the Regents dropped the stipulation altogether when it became clear that it was impractical for the University to act as preceptor for in-store work experience.
The 1892 school year began with less than half of the 14 students entering pharmacy meeting the entry requirements that Wulling already felt were too low; the requirements did not even include a high school degree. The first student admitted was Arthur Von Rohr of Winona. The second was Lucy Blanchard of St. Paul. Tuition for the two-year program was $165. Classes commenced with a lecture by Wulling the morning of October 5, 1892. The average age of his students was 22. Wulling was 26. There were six students in all, each of them granted a Pharm.D. upon graduation in 1894.

It was a rigorous and, to Wulling’s mind, underpaid job that he’d taken on. That first year, he spent 21 hours a week in the classroom or laboratory with students, while also attending to the administrative tasks of running the College. His official title was Dean and Professor of Theory and Practice of Pharmacy and Pharmacognosy, teaching courses in physiology, pharmacy Latin, pharmacy theory, and pharmaceutical chemistry (medicinal chemistry), in short, everything except chemistry, materia medica, and botany.

In November 1892, Wulling received an unpleasant surprise when he discovered that his salary amounted to $1,800 a year, not the $3,500 he thought he was to receive. That spring when the Regents rejected a proposal to raise his salary to $2,500 per year, he turned in a letter of resignation—his first—which was rejected by President Northrop.

Laboratory of Medical Sciences Building, second home of the College of Pharmacy, 1894-1916. Pharmacy was accessed by the side entrance, the College of Dentistry via the main entrance. In 1912, the structure was renamed the Dentistry Building and in 1932 named Wesbrook Hall, which was demolished in 2011.
More unhappy news soon followed. Dean Millard tapped almost $2,000 of the paltry $5,000 legislative appropriation to help pay bills for the Department of Medicine. Confronted by Wulling, Millard refused to restore the money. Only two years later did President Northrop restore the lost funding.

The Board of Regents also “were cold to the idea,” as Wulling described it, of building a separate facility for pharmacy, even though this objective had been endorsed by the state pharmacy association. Eventually, the Legislature appropriated $40,000 for what did not become the pharmacy building but rather the Medical Science Building.

Eventually, the College of Pharmacy would be allotted about a quarter of that building’s space.

In the spring of 1894, the mystery of his salary was finally resolved when he was called to a meeting with then-Governor Knute Nelson, an ex-officio member of the Regents, to discuss his compensation. There he got the bad news—the $3,500 salary he’d been expecting had never been authorized, and the University representatives who initially contacted him had been under the misapprehension that the $5,000 the Legislature had appropriated for the College included money for his salary. He did, however, come out of that meeting with the governor with a commitment to a

A 1908 campus map shows the locations of the sites of the Medical Sciences, Medical Chemistry, and Millard Hall. These buildings housed the pharmacy program.
$200 a year raise, bringing his salary to $2,000 per year. It would not reach $3,500 a year until 1907, 15 years after he started at the University.

By the end of the 1895 school year, the original appropriation of $5,000 was exhausted and the Regents allocated about $1,000 for the following year’s operation. The next year, $1,820 was appropriated by the Regents to furnish space for pharmacy in the laboratory of the Medical Science Building.

For 1896-97, the Regents were even stingier, granting only $630 to pharmacy; Wulling had requested $2,000 for supplies and equipment. “Our stock was thin, and living from hand-to-mouth was not conducive to the best kind of work nor to happiness. We never had enough microscopes. They were expensive,” he complained. On the other hand, he wrote, “Medicine seemed able to get all they needed.” Indeed, the College would remain underfunded until 1911, when efforts by Wulling and the state pharmacy association resulted in a legislative appropriation he finally considered adequate (ibid., 116-29).

The laboratory of Medical Science Building opened early in 1896; the College of Pharmacy would remain there until it was moved to a reconstructed Millard Hall in 1913. Until that move, space would continue to be an issue. By 1898, pharmacy had 54 students enrolled and was bursting its seams when the Medical College threatened to boot the College of Pharmacy from the storage space it occupied in the basement of Medical Science. Wulling averted that crisis by agreeing to a humiliating compromise in which his College would physically vacate the disputed area for two months in the winter to make way for an animal surgery course; in return, pharmacy received portable storage cases that Wulling himself designed (ibid., 168-70).

Cultivating the Pharmacy Profession

Despite all the problems, Wulling soldiered on, slowly building up the College and laying the groundwork for the Department of Medicinal Chemistry.

He continued to work like a navvy, some days teaching five or six hours at a stretch, but in his second year on the job, he managed to acquire money to hire student assistants for $100 a year plus free tuition. In 1893, tired of the constant power struggles within the Medical Department, the Regents relented to Wulling’s repeated requests and turned pharmacy, along with homeopathy, dentistry, and medicine, into separate colleges reporting directly to the President. Late in 1895, the Regents approved the creation of a graduate program in pharmacy.

Two years later, the Regents acquiesced to his recommendation that the College no longer give out doctorates to students graduating with a two-year degree. A Masters of Pharmacy degree (Phm.M.) was created for students who completed an additional eight months of study beyond the basic two-year program, which now
granted a pharmaceutical chemist degree (Ph.C.). Students who completed yet another eight-month program beyond the masters’ requirement were granted a Doctor of Pharmacy (Phm.D.), although neither of these advanced degrees were under the auspices of the University’s Graduate School—that switch would not occur for another quarter century (Netz, 1971, 19). Meanwhile, in June 1898, entrance requirements for the College were finally raised to a point that met Wulling’s approval (Wulling Collection, autobiography, undated).

One of Wulling’s most important steps in advancing medicinal chemistry at the College was his creation of small medicinal plant gardens that he established on the property of his own home in South Minneapolis and on a small plot of land on the south side of the Bowling Alley, and then, later, on the south side of the Medical Sciences Building (Netz, 1971, 190).

The two initial plots included only some 20 species of medicinal plants, including digitalis, belladonna,aconite, stramonium, larkspur, peppermint, and ricinis. Nonetheless these medicinal gardens were, in Wulling’s mind, key to a deeper understanding of the substance and actions of pharmaceuticals. At the time the College of Pharmacy opened, most drugs were derived from plants. Sometimes, the actual plants—or the active parts (roots, stems, aerials, seeds, or berries)—were delivered in bundles to local dispensaries, sometimes ground up as dry powders or dissolved in tinctures. In any case, Wulling’s insistence on creating a garden was
inseparable from his belief that pharmacy students should have a practical, hands-on understanding of the natural sources of the drugs they would be prescribing (Anderson & Pennigton, 2005, 13).

As usual, though, development of the College’s medicinal gardens—and associated facilities needed to study the products of those gardens—did not follow an orderly process of development, but faced the kind of frustrating setbacks and delays Wulling encountered in almost every direction.

In 1900, he was granted a much larger space behind the Medical Sciences Building for growing medicinal plants—a 100 by 200 square-foot plot of land allotted for “a botanical garden provided no expense be incurred.” There was one big problem, however. That spring, when Wulling and several student volunteers began cultivating the site, they discovered that it had been used as a dumping ground for construction materials and needed to be restored with several feet of fresh topsoil before it could be planted. With no money appropriated for such an expenditure, development of the garden at that site was postponed a decade.

In 1909, the College’s permanent faculty was expanded by the addition of Dr. Edward Newcomb, hired to take over for Wulling as professor of pharmacognosy. Newcomb had previously taught at the Philadelphia College of Pharmacy. Although the new faculty member was younger and less experienced than Wulling had initially wanted, Wulling was attracted by Newcomb’s experience in horticulture and drug plant culture. It was, he wrote, just what was needed to develop “our drug garden nucleus into a representative garden.”

The Students Christian Association Building. This 1908 photograph shows the building with its new name, the YMCA Building. It is known in 2011 as the Music Education Building, but is not currently occupied.
Soon after joining the faculty, Newcomb took the lead role in transforming the medicinal plant gardens into a world-renowned facility widely considered one of the best in the country and internationally acclaimed for its great variety of medicinal plants under cultivation (ibid., 316).

In January 1926 Newcomb took a leave of absence to become general representative of the National Wholesale Druggists Association in New York City. He resigned his university position in 1927 to become secretary and vice president of that organization and was one of the founders of the American Foundation for Pharmaceutical Education (Netz, 1971, 64).
The next year, Wulling took $500 that the Regents finally granted for enlarging medicinal plantings—he originally had requested $24,000 for this purpose—and, matching the Regents’ money with $500 of his own, he spent most of the summer of 1911 touring medicinal plant gardens in the United States and Western Europe. On the voyage home from Europe, he drew up specifications for a new garden at the
University that would achieve his goal of becoming “representative.”

For some years, Wulling had been taking pharmacy students on spring botanical tours of Minnesota and Wisconsin. With the arrival of Newcomb, these tours began to emphasize the riparian environment along the Mississippi River from the University campus to Fort Snelling, a region particularly rife with plant species possessing medicinal value. Over time, plants from this stretch of the river were transplanted to the grounds of the University’s medicinal gardens.

Newcomb also took charge of planning and overseeing construction of a consolidated medicinal plant garden on a site where Northrop Auditorium now stands.

The medicinal plant laboratory adjoined the main pharmacy building by a tunnel, 1913. Its basement was used for drying, milling, and garbling. The upper floor was used to start plants from seeds in early February and March, which were then nursed for outdoor planting. Approximately 325 species and varieties of drug plants were developed from seeds in the greenhouse.

Students carried out the actual work of clearing and plotting the garden. Later a plant house with drying ovens, a drug mill, a facility for growing aquatic medical plants, and a heated tunnel connecting the facility to the building where the College was housed was built.

The new plot and plant house soon became the “representative garden” Wulling had dreamed of. By 1912, the College was offering assistance to a dozen other schools intent on setting up their own drug gardens, and, in addition to his other titles,
Wulling was named director of the University Medicinal Plant Gardens (Wulling, Collection, autobiography, undated).

Until then it had been widely assumed that growing conditions in the United States were not conducive to producing a wide enough array of medicinal plants and that the country had to rely on imports to fill its needs. Based upon his long study of botany and personal knowledge of the abundance of flora along the Mississippi, Wulling thought otherwise. Under his tutelage the University’s medicinal garden was responsible for a number of advances, including the discovery that plantain,
Students did most of the work of indoor and outdoor planting, harvesting, garbling, drying, milling, assaying, and converting plant parts into medicinal preparations.

Students extracting active ingredients from digitalis.
abundant in Minnesota, was a source for psyllium seed, and that wild rice, quack grass, and wheat could be a source of ergot.

Within four years, the medicinal plant garden was nationally recognized for the groundbreaking research emanating from it, especially in the study and development of digitalis. By 1916 it had a greenhouse, drug plant, and milling laboratory, and was recognized for its advances in digitalis research (College of Pharmacy, 1992).

By then, the outbreak of World War I had caused a steep decline in drug imports, leading to a scarcity of medicinal plants and consequently a rise in prices for products made from them. The price of belladonna, for example, increased 700 percent by the time the United States entered the war in April 1917. In response, the Department of Agriculture called for a concerted effort to increase the domestic production of all drugs, including those derived from plants (Worthen, 2007).

Wulling reacted to the call of war with characteristic energy, contacting the Surgeon General of the Army and offering the services of the College to back the war effort.
tional Research Council responded asking Wulling that the College be prepared to supply all the digitalis the army might need—a request that the University went on to fulfill, setting aside two acres of the medicinal plant gardens to the exclusive cultivation of foxglove—the plant from which digitalis is derived—and shipping, by
Northrop Hall under construction.

The neoclassical-style Northrop Hall building was completed in 1929.
Wulling’s reckoning, some 23,800 8-ounce bottles of tincture of digitalis and 2,000 capsules of digitalis powder to the American Expeditionary Forces before the war came to end (Wulling, 1948, 78).

By war’s end, the gardens comprised more than 300 named species and varieties of plant life, from *Atropa belladonna* to *Thymus vulgaris* to larkspur, peppermint and *Datura stramonium*. The garden also included century plants and banana and rubber trees—the last two transplanted to the site from President Northrop’s home. The College of Pharmacy’s leadership in medicinal plants led to the University’s first plant science seminar in 1921, and, eventually, the formation of the American Society of Pharmacognosy (Worthen, 2007, 656-7).

Despite the acclaim, the very next year, pharmacy was informed that the plant garden constructed only 10 years earlier was going to have to make way for the construction of Northrop Hall.

The garden was to be moved into an old garden and greenhouse space on University Avenue operated until then by the Department of Botany, which was building new greenhouse facilities elsewhere. Transfer of the pharmacy garden was completed in 1927 (Netz, 1971, 65-7).
Fires Bring Progress

During the first two decades of the 20th Century, the chronic space problem that had plagued the College of Pharmacy from the very beginning was also finally solved—but here again, not without major setbacks that included, improbably enough, not one, but two fires.

Frustrated by the Regents’ failure to provide adequate facilities for pharmacy, Wulling resorted to one of the tactics that he’d used before to break logjams. In 1909, he again submitted his resignation to President Northrop (himself on the verge of retirement) but withdrew it when, shortly thereafter, the Board of Regents voted to request funds from the state to construct two new medical buildings and to bequeath Millard Hall to the College of Pharmacy; in a twist of fate or perhaps poetic justice, Millard Hall would be renamed Wulling Hall in 1942.

Although Millard Hall did not have the layout or space pharmacy needed, Wulling accepted the arrangement, especially since it was considered to be a temporary fix until a new permanent facility could be constructed in the next few years. The move from Medical Sciences into Millard was set to go when a fire on Christmas Eve 1912 broke out in the building, causing extensive damage and gutting the top floor. A temporary metal roof was erected on top of Millard Hall. Then just three months later, another fire gutted the interior of the rest of the structure. Ironically, the “temporary” roof did not collapse, but during the conflagration all the inside floors collapsed into the basement, leaving behind nothing more than the shell of the four sandstone and brick exterior walls.

In the end, the successive fires were probably a godsend for the College. By now plans had already been announced.
to turn Millard Hall, whose interior floors were made of wood, into a fireproof building. Using a legislative appropriation of $75,000, plus $8,000 in insurance money from a fire that had destroyed yet another campus building, the Regents approved the idea of not only renovating Millard but also building a modern greenhouse and plant laboratory right next to it. The structures to be connected by a tunnel (Netz, 1971, 40-1).

Wulling Hall finally opened its doors to the College on September 17, 1913. It had begun as Medical Hall, underwent a name change to Millard Hall, and then called the Pharmacy Building before eventually being named after its most ardent supporter. The building featured four stories and a sub-basement. It was fireproof, with an outer shell of steel and concrete. Dedicated solely to pharmacy teaching and research, it was thoroughly modern and offered state-of-the-art features like equipment to produce distilled water, steam heat controlled by thermostats in every room, maps, charts, 5,500 microscope slides, prescription and analytical balances, compound microscopes for every student, centrifuges, refrigerators, drug-drying ovens, animal cages, sand and water baths, refractometers, and more. Connected by tunnel to the building was the medicinal plant laboratory where plants were propagated before transplantation to the outdoor garden. Both the medicinal garden and the new buildings made a splash, with articles appearing in American, European and Latin American drug journals (ibid., 31). Ultimately Pharmacy/Wulling Hall would serve as home for the College of Pharmacy until the 1960s.

The budget for the school likewise climbed. For the academic school year of 1898-99, the Regents appropriated a meager $1,500 for supplies and equipment; another $200 for books and...
journals and a stipend for a clerical assistant for Dean Wulling. A little more than a decade later, the school received $15,000, by which time, Wulling’s annual salary had finally reached the $3,500 that he’d been expecting to receive when he joined the University in 1892. From that time forward, appropriations for the College remained adequate to pharmacy’s needs (ibid., 446).

The College was advancing on other fronts as well. By 1907, the school had 99 students enrolled; about a third of them were women. During World War I, the percentage of female students would climb even higher as young men enlisted or were drafted into the military. By the middle of the 1920s, the number of students would climb to almost 150. New faculty members were added slowly, relieving some of the burden on Dean Wulling’s shoulders.

In addition to Professor Newcomb, perhaps the most significant new hire took place in 1913. John Handy, an instructor in pharmaceutical chemistry, resigned and was replaced by Charles Rogers. In 1936, Rogers would succeed Frederick Wulling as Dean of the College of the Pharmacy. In doing so, he would finally departmentalize the College—creating, for the first time at the University, a stand-alone department of Pharmaceutical Chemistry (College of Pharmacy, 1992).

Rogers joined the University as an instructor in 1913 and resigned in 1914 to accept a position as assistant professor at the University of West Virginia. He returned to Minnesota in 1917 as assistant professor of pharmaceutical chemistry and completed his doctorate in 1918.

By then, Rogers had already enhanced his own and the University’s reputation in pharmaceutical chemistry with publication of his textbook, *Inorganic Pharmaceutical Chemistry*, only the second textbook published by a member of the pharmacy faculty—the other being an earlier book on pharmaceutical chemistry written by Dean Wulling (Minnesota State Pharmaceutical Association, 1930-40).
A Graduate Program is Born

In 1915, pharmacy came out ahead on another bone of contention going all the way back to 1892, when, as Wulling had advocated from the very beginning, a high school diploma became a prerequisite for enrollment in pharmacy. The year before, the University had also instituted a system of optional three- and four-year programs—until then, students only had to go for two years to get their degree; two years later, the programs were no longer optional, but mandatory. Both the two- and three-year programs demonstrated the critical role of pharmaceutical chemistry at the College of Pharmacy; the three-year curriculum, for example, required students to take four quarters’ worth of pharmaceutical chemistry, for a total of 19 of 67 credits.

In 1926, the three-year program was eliminated and the University became only the second school in the country to adopt a mandatory four-year degree program. The move layed the groundwork for the next major advance for pharmaceutical chemistry at the University.

In 1923 the Minnesota State Pharmacy Association passed a resolution calling on the University to place graduate study in pharmacy under the auspices of the University’s Graduate School—a move that had long been pressed by Dean Wulling as well.

But for that to happen, it was necessary that the Regents first approve a minimum four-year course in pharmacy leading to a B.S. in pharmacy, which it did in 1926. The following year—1927—the Regents took the next logical step and approved graduate programs for both pharmacognosy and pharmaceutical chemistry to be offered through the University’s Graduate School (Netz, 1971). The first Master of Science in pharmaceutical chemistry was awarded only two years later, in 1929, to a student named Louis Maynard (ibid., 67).

Thus was a true graduate program in pharmaceutical chemistry born. The next big step would be the formation of the Department of Medicinal Chemistry. §