Perspectives on the Future of Graduate Education in Medicinal Chemistry and Pharmacognosy[1]

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INTRODUCTION

Graduate education in medicinal chemistry and pharmacognosy focus on the interdisciplinary application of chemical, biochemical, and molecular principles to the identification and development of therapeutic agents. Research and graduate education in medicinal chemistry emphasize drug design and include the synthesis of organic medicinal products, elucidation of the biochemistry and molecular biology of medicinal agents, examination of the relationship of chemical structure to biological activity, qualitative and quantitative analysis of drugs, and application of computational chemistry to drug design. Research and graduate education in pharmacognosy emphasize drug discovery and encompass isolation and structure elucidation of pharmacologically active natural products from plants and microbes, examination of the biosynthesis of natural products, and evaluation of the biochemical effects of these active constituents. The graduate and research program areas of drug macromolecule interactions, drug design based on biochemistry and biotechnology, and bioassay-directed drug discovery are examples of important growth areas for medicinal chemistry and pharmacognosy.

This perspective on the future of graduate education in medicinal chemistry and pharmacognosy addresses several issues. First, the impact of trends in Colleges of Pharmacy and in doctorate research universities on graduate programs in medicinal chemistry and pharmacognosy will be discussed. Secondly, the perspectives of the pharmaceutical industry and of academia will be summarized. Third, a training program for the PhD degree in medicinal chemistry and pharmacognosy will be discussed. Finally, personal perspectives on the importance of benchmarking and on

[1]Presented at the American Association of Colleges of Pharmacy Conference on the Future of Graduate Education in the Pharmaceutical Sciences, Snowmass Village, July 18, 1998, Aspen CO.

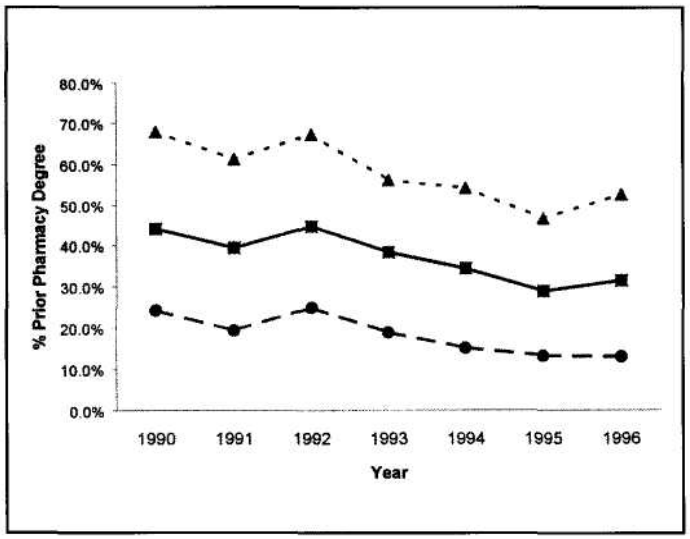

Fig. 1. Percentage of graduate students in medicinal chemistry and pharmacognosy programs with a prior pharmacy degree. The percentage of domestics students (•), international students (▲), and total students (■) with a prior pharmacy degree is decreasing steady during the past decade (10).

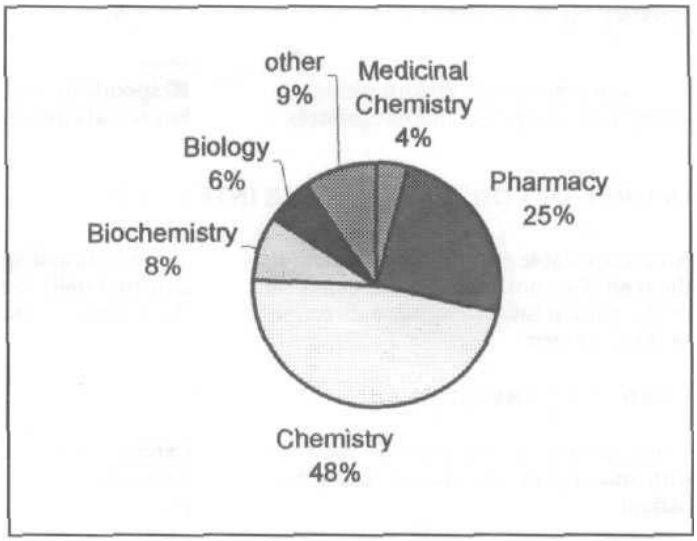

Fig. 2. BS degrees of current graduate students in medicinal chemistry and pharmacognosy programs. The distribution of prior degrees is represented for 533 students in 39 medicinal chemistry and pharmacognosy programs surveyed in 1996 (9).

the interdisciplinary nature of research and graduate education in the biomedical and life sciences will be presented. Several publications have served as a foundation for this perspective and/or review the status of graduate education in the sciences(1-3), in pharmaceutical sciences[2](4-6), and in medicinal chemistry(7-9).

IMPACT OF TRENDS IN PHARMACY

The emphasis and direction of professional pharmacy education has had a significant impact on graduate education in medicinal chemistry and pharmacognosy. This effect is particularly evident when one examines the enrollment of domestic students in graduate programs in medicinal chemistry. The percentage of domestic graduate students entering programs in medicinal chemistry and pharmacognosy with BS in Pharmacy or entry-level PharmD degrees has been steadily decreasing for many years. For example, over the past decade the percentage of domestic students with a prior Pharmacy degree has decreased from 24.2 to 12.3 percent (Figure 1) in all medicinal chemistry graduate programs reported by the AACP(10). Factors that may influence this trend are the significant financial incentives for students with a pharmacy degree to begin professional pharmacy careers, the lengthening of the professional pharmacy programs (particularly in the case of entry-level PharmD degrees), and the decreased number of intensive chemistry courses in the pharmacy curriculum. Most domestic applicants to graduate programs in medicinal chemistry and pharmacognosy have a BS degree in either chemistry or biochemistry. At the present time, the majority of international students entering these graduate programs have a BS in Pharmacy, although the percentage is also declining. The data collected in the recent survey of graduate programs in medicinal chemistry and pharmacognosy also reflect these trends, as shown in Figure 2, and indicate that the ratio of students entering with a chemistry degree vs. a pharmacy degree is approximately 2:1(9).

The prior training of incoming graduate students impacts significantly on the didactic courses enrolled in during the first year in a graduate program in medicinal chemistry and pharmacognosy. This problem in having an adequate undergraduate training occurs with both groups of students, *i.e.*, those students with a prior pharmacy degree and those students with a non-pharmacy degree. Incoming graduate students with a prior pharmacy degree often require additional courses in calculus and physical chemistry and have less experiences in laboratory courses. On the other hand, incoming graduate students with a non-pharmacy degree often require coursework in basic medicinal chemistry, pharmacognosy, and pharmacology. Possible solutions being examined by several graduate programs in medicinal chemistry and pharmacognosy are a new undergraduate major, the BS in pharmaceutical sciences, or providing elective courses in principles of medicinal chemistry, pharmacognosy, and pharmacology for BS chemistry and biochemistry majors.

IMPACT OF TRENDS IN RESEARCH UNIVERSITIES

The research universities in the U.S. are the major producers of science and engineering graduates and continue to be the major force in basic science research and scholarship. The changing environment at research universities is significantly impacting graduate programs in colleges of pharmacy. Enhanced focus on research and development (and the associated increased resources in direct costs, indirect costs, patent and licensing, etc.) is being emphasized at research universities. At the same time, public and political expectations for higher education are changing and are emphasizing increased public funding for K-12 education. The uncertainties of financing of academic health science centers are another factor impacting pharmacy graduate programs. Selective investment of new resources or reallocated funds

[2]Triggle, D.J. and Miller, K.W., *Interim Report*: *Commission on the Future of Graduate Education in the Pharmaceutical Sciences*, American Association of the Colleges of Pharmacy, Alexandria VA (1998).

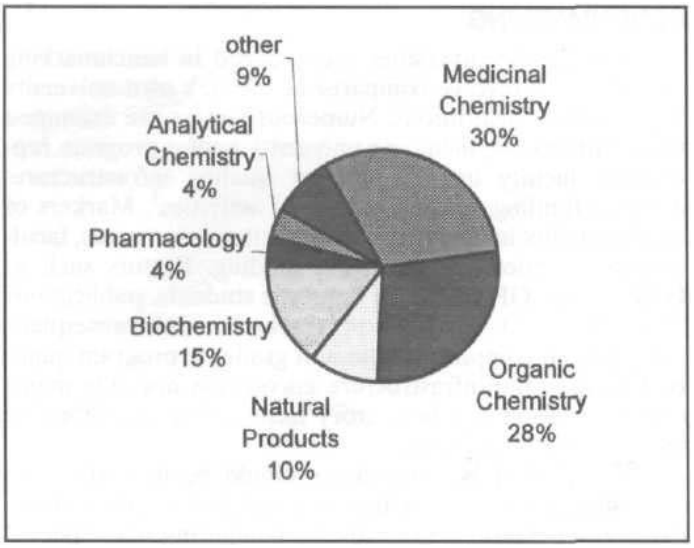

Fig. 3. Formal training of faculty in graduate programs in medicinal chemistry and pharmacognosy. The formal training for faculty is primarily distributed among medicinal chemistry, organic chemistry, pharmacognosy, and biochemistry. The data represent 216 faculty in 39 programs obtained from the 1996 survey (*9*).

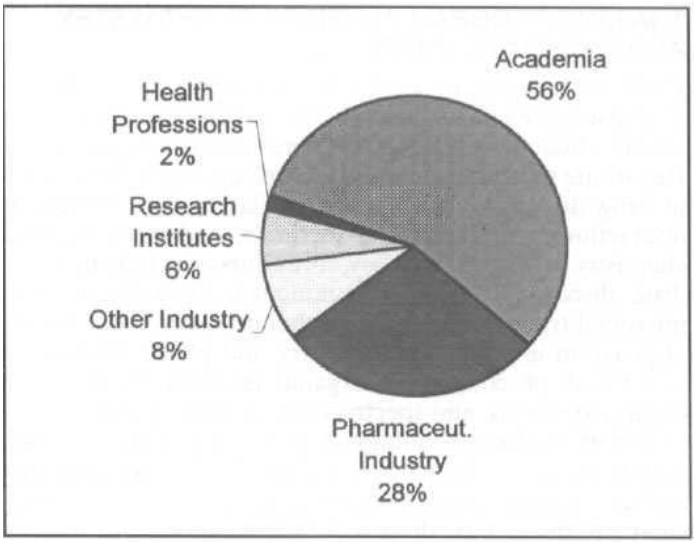

Fig. 4. Careers of PhD graduates from programs in medicinal chemistry and pharmacognosy. The majority of graduates with permanent positions are found in academia or the pharmaceutical industry. The data was obtained from reports on 649 graduates in last ten years from 39 programs (*9*).

to top departments within the university are often based upon external rankings, such as those of the National Research Council published in 1995(11). Pharmacy PhD programs are not evaluated by the NRC and are clearly at a disadvantage when competing for such selective funding. Furthermore, graduate programs in medicinal chemistry and pharmacognosy, and in pharmacy in general, are small compared to other graduate programs at research universities. Finally, the fields of medicinal chemistry and pharmacognosy are no longer the sole purview of pharmacy graduate programs. Increasingly, chemistry departments are expanding into medicinal chemistry and related areas with new thrusts in "chemistry of life processes," "chemistry at the biology interface," and "chemical biology."

VIEWS FROM PHARMACEUTICAL INDUSTRY

In 1992-1993, the Medicinal Chemistry Section of International Union of Pure and Applied Chemistry (IUPAC) conducted a survey on the training of graduate students for medicinal chemistry. The surveys were sent to research directors of medicinal chemistry in major pharmaceutical companies in US, Europe, and Japan. The summation was published in two manuscripts(7,8), and the results of this survey were both provocative and startling. Pharmaceutical departments in medicinal chemistry or drug discovery tend to focus on hiring organic chemists, often from a small number of highly select universities. Additionally, the commonly held view is that these chemists "can learn their medicinal chemistry and pharmacology on the job." The authors of the manuscripts do point out several caveats of this survey. First, the majority of the respondents received their formal training in organic chemistry and have industrial experiences ranging from 10 to 25 years. Secondly, the focus of the preamble and the survey itself was only on the synthesis of new molecules. Third, significant national differences were observed. Finally, smaller pharmaceutical firms and biotechnology companies were not generally contacted. These smaller firms are more interested in scientists with increased breadth.

VIEWS FROM ACADEMIA

In 1996, the same authors conducted a more comprehensive survey of graduate training programs of medicinal chemistry departments and recently published the results in early 1998(9). First, medicinal chemistry has a much broader definition in academia. The focus is still on the synthesis of novel agents for therapeutic purposes, but increasingly, research is also directed towards biochemistry, enzymology, molecular biology, and other related topics. This emphasis reflects the formal training of faculty in graduate programs in medicinal chemistry and pharmacognosy, with a nearly equal distribution among medicinal chemistry, organic chemistry, and pharmacognosy/biochemistry (Figure 3).

Furthermore, greater diversity in training also exists among various graduate programs. One area where diversity is clearly evident is the varied list of subjects included in medicinal chemistry training programs. Common core courses are medicinal chemistry, organic chemistry, and biochemistry, while elective courses range widely from areas of anatomy and cell biology to microbiology, genetic engineering, and toxicology. One aspect that influences the training programs in medicinal chemistry and pharmacognosy is the task of preparing graduate students for diverse potential occupations. Figure 4 illustrates the distribution of careers for PhD graduates from programs in medicinal chemistry and pharmacognosy. Not surprisingly, greater than 50 percent of graduates with a permanent position (not a postdoctoral position) are employed in academia. Another 28 percent of graduates are employed in the pharmaceutical industry, with some of these graduates not necessarily involved in organic synthesis. The remaining graduates are employed in other industrial settings such as the biotechnology industry, in research institutes, or in the health profession.

TRAINING PROGRAM IN MEDICINAL CHEMISTRY AND PHARMACOGNOSY

Doctoral training programs in medicinal chemistry and pharmacognosy have several critical components. First, a strong didactic program of core courses is essential. Regarding medicinal chemistry, core courses include topics in drug design, structure-activity relationships, molecular interactions, computational methods, and combinatorial chemistry. In pharmacognosy, core courses include topics of drug discovery, isolation techniques, biosynthesis, and microbial transformations. The chemistry core of a doctoral program in medicinal chemistry and pharmacognosy is comprised of courses in organic reaction mechanisms, organic synthesis, and spectroscopy. A biology core of biochemistry, molecular biology, and/or pharmacology courses is also essential. Topics covered in this biology core can include enzymes and enzyme mechanisms, receptors, molecular pharmacology, drug metabolism, molecular targets, genomics, gene therapy, or bioinformatics. The curriculum course list concludes with one or more special topics courses, often focused on the research dissertation project of the student.

The PhD dissertation is the critical component of the PhD degree. The dissertation project involves in-depth, state-of-the-art research, and the research should be original, substantial, significant, and independently accomplished(2). Increasingly, graduate students are engaged in collaborative, multidisciplinary research with other colleagues (faculty collaborators, graduate students), and this "team approach" clearly has advantages in preparing the PhD student for one's subsequent career. It is crucial that the student's contribution to the collaborative research be clearly delineated and demonstrate originality and significance.

The doctoral education of students in medicinal chemistry and pharmacognosy must include additional breadth of experiences. Communication skills are increasingly important. Graduate students need to develop excellence in both written and verbal communication. Furthermore, experiences in accessing and exploiting the vast computer information network are equally important for successful research and teaching careers. One additional area for selective enhancement of doctoral student training is internship opportunities. The development of internships, particularly in the pharmaceutical industry, is more difficult to arrange during the PhD program, and often internships are established on a one-on-one basis.

Finally, the training of a scientist in medicinal chemistry and pharmacognosy does not conclude with the receipt of the PhD degree. The vast majority of new PhD graduates continue their training through a postdoctoral research position. The key is to select a postdoctoral research position that complements research experiences from the dissertation and enhances training beyond the PhD. Often, this is accomplished by undertaking a postdoctoral position in a related scientific area, such as organic chemistry, biochemistry, or molecular biology. Further, the postdoctoral position often broadens scientific contacts and perspectives on research and scholarship.

[3]OSU Research Commission, *A Report on Findings and Recommendations*, The Ohio State University, Columbus, Ohio, 1998

BENCHMARKING

Many research universities are engaged in benchmarking activities that involve comparisons of one's own university to other peer institutions. Numerous factors are examined in benchmarking, including university and/or program reputation, faculty quality, student quality, infrastructure, external funding, and development activities[3]. Markers of faculty quality include publications, citations, awards, faculty/student ratios, and research funding. Factors such as GRE scores, GPA, percent domestic students, publications from the PhD dissertation research, and subsequent employment comprise markers of graduate program quality. Facilities and infrastructure encompass not only major instrumentation and laboratory facilities but also libraries and computers facilities.

The goal of benchmarking should be to understand one's situation and to use this information for setting objectives. The purpose is not only for comparing with "peers" but also for identifying areas for improvement. The need for reliable databases for benchmarking and willingness to share information are essential in any quality benchmarking activity. Often, data gathered by external organizations such as the National Research Council, U.S. News & World Report, and the Association of American Universities are utilized in benchmarking activities. Some benchmarking data is imperfect by nature, such as opinion survey data and information from differing interpretations of questions. Despite these limitations, important lessons can be learned that aid in assessment and planning. Particular problems that graduate programs in pharmacy face are that pharmacy PhD programs are not evaluated by some organizations (such as the National Research Council), no centralized database of reliable and consistent information is available, and survey data often does not separate professional pharmacy education from doctorate graduate programs in colleges of pharmacy. These issues must be addressed before reliable benchmarking for pharmacy graduate programs can be accomplished.

INTERSCIPLINARY NATURE

Universities are dominated by departments that maintain the discipline and meet educational missions. Increasingly, research and graduate education transcend these departmental barriers. Furthermore, many outstanding faculty and students are involved in research and graduate education programs that are situated at the interface of traditional disciplines. From my perspective, medicinal chemistry is such an interdisciplinary field (chemistry, biochemistry, pharmacology, and molecular biology).

The demand for interdisciplinary activities continues to increase as groups of faculty and students cluster around new problems and the interfaces between current disciplines. As a result, interdisciplinary graduate education is a faculty driven effort that represents the cutting edge of scholarship and research. Graduate programs must be responsive to the development of these new directions without the constraints of traditional structure. To primarily emphasize one aspect of medicinal chemistry graduate training (*e.g.*, synthetic organic chemistry) ignores the vital contributions of other areas such as biochemistry, pharmacology, and molecular biology in the training of graduate students. Such a singular emphasis would not only be a disservice to our graduate students, future researchers, and

future scholars but also to the interdisciplinary science of medicinal chemistry and pharmacognosy.

Am. J. Pharm. Educ., **62**, 463-67(1998); received 10/19/98.

References

(1) National Research Council, Committee on Science, Engineering, and Public Policy (COSEPUP), *Reshaping the Graduate Education of Scientists and Engineers*, National Academy Press, Washington DC (1995).
(2) Council of Graduate Students, *The Role and Nature of the Doctoral Dissertation*, Washington DC (1991).
(3) Lapidus, J.B., "Doctoral education: Preparing for the future," Council of Graduate Students, Washington DC (1997).
(4) Borchardt, R.T., "Are graduate programs training pharmaceutical scientists to function effectively in the new, highly integrated and globalized pharmaceutical industry?" *Pharm. Res.*, **14**, 554-555(1997).
(5) Till, A.E., "Graduate education in the pharmaceutical sciences: How can it better meet the needs of the generic pharmaceutical industry?" *ibid.*, **14**, 837-838(1997).
(6) Serajuddin, A.T.M., "Education in pharmaceutical sciences needs a brand new direction to meet the challenges of drug research and development," *ibid.*, **15**, 8-10(1997).
(7) Ganellin, C.R., Mitscher, L.A., Topliss, J.G., "Educating medicinal chemists," *Ann. Rep. Med. Chem.*, **30**, 329-338(1995).
(8) Ganellin, C.R., Mitscher, L.A. and Topliss, J.G., "Vocational training for medicinal chemists: views from industry," *Eur. J. Med. Chem.*, **31**, 747-760(1996).
(9) Ganellin, C.R., Mitscher, L.A. and Topliss, J.G., "Education of medicinal chemists in departments of medicinal chemistry," *Medicinal Res. Rev.*, **18**, 121-137(1998).
(10) Data compiled from annual statistics reported in the *Amer. J. Pharm. Educ.*, Winter Supplements, 1990-1997.
(11) Goldberger, M.L., Maher, B.A. and Flatteau, P.E., (edits.), *Research-Doctorate Programs in the United States: Continuity and Change*, National Research Council, Washington DC (1995).