Title	Shaping future medicinal chemists: Perspectives from European schools of pharmacy within the GP2A Network
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Publication date	2025-01-28
Original Citation	Bayraktar, G., Carro, L., Decker, M., Giuntini, F., Helesbeux, J. J., Marchand, P., Matthews, S. E., McCarthy, F. O., Mistry, S. N., Moreira, V. M. and O'Boyle, N. M. (2025) 'Shaping future medicinal chemists: Perspectives from European schools of pharmacy within the GP2A Network', Journal of Medicinal Chemistry. https://doi.org/10.1021/acs.jmedchem.4c03103
Type of publication	Article (non peer-reviewed)
Link to publisher's version	10.1021/acs.jmedchem.4c03103
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Download date	2026-09-19 09:33:19
Item downloaded from	https://hdl.handle.net/10468/17063

Shaping Future Medicinal Chemists: Perspectives from European Schools of Pharmacy within the GP_2A network

ACCESS

Medicinal Chemistry in Pharmacy Education. Training in medicinal chemistry at Schools of Pharmacy in Europe has undergone rapid change in the past 30 years. This editorial sets out to map the progression of change at our institutions and reflect on future teaching of the discipline.

Across the European Union (EU), Directive 2005/36/EC of the European Parliament and of the Council (amended June 2024) common legislation underpins the foundation of degrees in pharmacy.[1] These minimum training requirements specify that a Pharmacist has acquired adequate knowledge of medicines and the substances used in the manufacture of medicines, and of pharmaceutical technology and the physical, chemical, biological and microbiological testing of medicinal products, and the metabolism and effects of medicinal products. Annex V stipulates that courses of training for pharmacists must include general and inorganic chemistry, organic chemistry, analytical chemistry, and pharmaceutical chemistry (including the analysis of medicinal products). Outside of the EU, other countries within Europe follow their own regulations, similar in content to Directive 2005/36/EC.

Despite this directive and outwardly common approach, national landscapes and individual state regulation of pharmacy influence course structure, syllabus and curriculum. Over the past 30 years, this has significantly impacted the teaching of medicinal chemistry in Schools of Pharmacy across Europe.

What is GP_2A? GP_2A (Group for the Promotion of Pharmaceutical Chemistry in Academia) is a member-led network of pharmaceutical and medicinal chemists from across Europe.[2] For over 30 years since its inception in 1992, the goal of the network has been to strengthen medicinal and pharmaceutical chemistry in Schools of Pharmacy, facilitate dissemination by early career researchers through our annual conference and promote innovative teaching of chemistry to inspire the next generation of scientists. Originally formed by academics from France, Portugal, Spain and the UK as the Groupement des Pharmacochimistes de l'Arc Atlantique, GP_2A expanded to include members from Germany, Ireland, Italy, Romania, Sweden and Turkey and rebranded in 2019 to reflect this (Figure 1). GP_2A members have shaped the teaching of medicinal chemistry in our institutions across diverse cultural backgrounds and regulations. This commentary emanates from annual discussions within our network over 30 years.

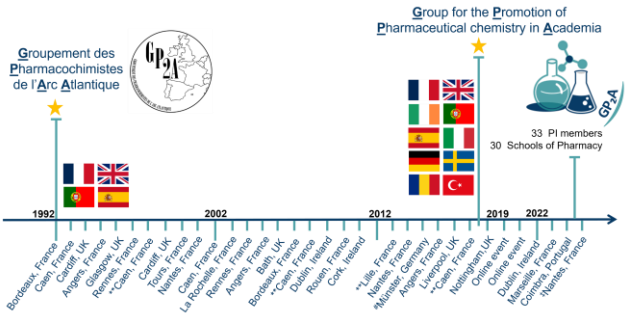

Figure 1. Evolution of the GP_2A network over the past 30 years and annual conference locations. ** In combination Journées Franco-Belges de Pharmacochimie. # In combination with ChemBioInteractions. ‡ In combination with Paul Ehrlich MedChem Network.

Medicinal Chemistry Teaching in Our Institutions – Past and Present. Historically, medicinal chemistry was more commonly known as pharmaceutical chemistry and indeed, this very journal was titled Journal of Pharmaceutical and Medicinal Chemistry until 1963. Looking back, a pharmacist (more commonly known as a chemist or druggist) was associated with a white coat, shelves full of exotic bottles holding exciting concoctions and the practice of compounding medicines on-site. Education was by apprenticeship and required knowledge of drug synthesis and properties, suitable excipients and formulation, exacting skills in measurement and analysis even to the point of taste and smell. Pharmacists were, and continue to be, the experts in medicines and their delivery.

The teaching of medicinal chemistry evolved from pharmacognosy and natural product synthesis to drug discovery and development, chemical analysis and how chemical structure results in molecular target engagement. The emergence of what we consider a contemporary syllabus of medicinal chemistry in the 1990's, developed from a strong foundation in organic chemistry to explore the molecular proof of how medicines work, incorporating design, synthesis and structure-activity relationships (SAR) of drug molecules, and physicochemical features that impact pharmacokinetic and pharmacodynamic behavior. Advances in biochemistry and pharmacology revealed detailed druggable targets at the molecular level and shaped new perspectives. As such, there is now a much stronger interaction with interfacing disciplines, especially pharmacology and drug metabolism and pharmacokinetics (DMPK), but also

toxicology, pharmaceutical biology and pharmaceutics. This mirrors real life, as pharmacy (and indeed medicinal chemistry) is multidisciplinary and collaborative by definition and ultimately, has led to the introduction of integrated MPharm courses in many countries. The results are modules defined by pathology with medicinal chemistry taught alongside pharmacology, pharmaceutics, clinical pharmacy and other topics in pharmacy curricula.[3] The integrative approach has been adopted widely and has benefits and drawbacks from scientific, curricular and learning perspectives.

Degrees of Difference Across Europe. Despite the common framework, teaching at our institutions varies widely with differences in entry points and student backgrounds, in the curriculum, in the chronology of teaching and the outputs expected on a national basis. For example, across Europe some teach chemistry every year (1-5) and others only in years 1-4, 2-4, 3-5, etc. of the degree. In some institutions, pharmacy students can choose to specialize in medicinal chemistry and yet others offer a common syllabus without specialization. For those with an integrated curriculum, medicinal chemistry is placed within each integrated module but the overall competency achieved is not necessarily cohesive. Looking across our institutions, the syllabus varies noticeably towards the final years with for example, advanced organic synthesis, molecular modelling, biopharmaceuticals, advanced spectroscopic analysis, precision medicine or gene therapy taught in some while in others, subsets of students can access these through optional modules or engagement with a research team. Thus, the medicinal chemistry knowledge of graduate pharmacists is not uniform.

Compounding this, pharmacy graduates are employed in several sectors, from community, hospital, pharmaceutical industry, academia, and increasingly public health such as pharmacoeconomics and pharmacovigilance. These many different faces now compete within our syllabus and ever-increasing training for the workplace which has resulted in a reduction in basic science in the curriculum (Figure 2).[4,5] The net result for pharmacy graduates is a barrier to some careers in basic science due to differences in competencies achieved and implementation across Europe, with consequences on standardization of the degree and international mobility.[6] This has important ramifications for the recruitment of pharmacists as future medicinal chemists in Europe and has been identified by our network and others who support postgraduate studies in medicinal and pharmaceutical chemistry.

Relevance of Medicinal Chemistry to Pharmacists. Aside from "is it on the exam?" the question of relevance is often asked when teaching chemistry in applied settings, especially those with patient focused careers. Chemistry is regarded as the "central science" and usually a requirement on entry to pharmacy programmes so any reduction in content has profound consequences. The fact that the pharmacist is the only tangible link to active molecular structure in the clinical chain depends on this and medicinal chemistry is critical to understanding where a drug has come from and what it will do. For those working in clinical pharmacy and hospital settings, knowledge of medicinal chemistry is key as a differentiating factor from other health professionals and there is significant potential to grow this. Further emphasis and integration of medicinal chemistry into clinical pharmacy can demonstrate this relevance. Many examples exist of the chemical basis for clinical decisions and science as the evidence base but perhaps as educators we must reinforce the importance of chemistry in each.

The demographic of pharmacy careers is shifting as seen by the increasingly diverse careers of our graduates and in the expansion from the WHO identified seven professional roles to ten.[7,8,9] These newer roles in common require keen analytical skills as well as the ability to thrive in multidisciplinary environments and as such a foundation in medicinal chemistry with its many different inputs is of great benefit. Indeed, almost 60% of German pharmacy students at a representative university, consider medicinal chemistry to be moderately to very important for their professional career.[10]

Shaping the Future. Fundamental medicinal and pharmaceutical chemistry is vital to ensure that the pharmacist truly understands the drugs that are dispensed to their patients. The future will involve change, from being experts across a wider range of drugs to expanded roles in patient care and personalized medicine at the heart of communities and beyond. Small molecules have had a tremendous impact on human health and longevity, but newer therapies such as biologicals and gene therapy have considerably increased the portfolio requiring medicinal chemistry for development.[11] Virtual screening, artificial intelligence (AI) and the use of technology is prolific in medicinal chemistry. Just as the advent of molecular modelling, space for new and emerging technologies will need to be incorporated in evolving curricula to ensure our graduates can use these tools effectively but without reduction in the foundation of basic science.

In the pharmaceutical industry, sustainability is already having a profound effect on manufacturing campaigns and it is imperative to strengthen green chemistry in our curricula. The drive to make pharmaceuticals more eco-friendly has led to design of greener synthesis with technologies such as biocatalysis and flow chemistry becoming mainstream. These and other technologies will deliver many drugs of the future.

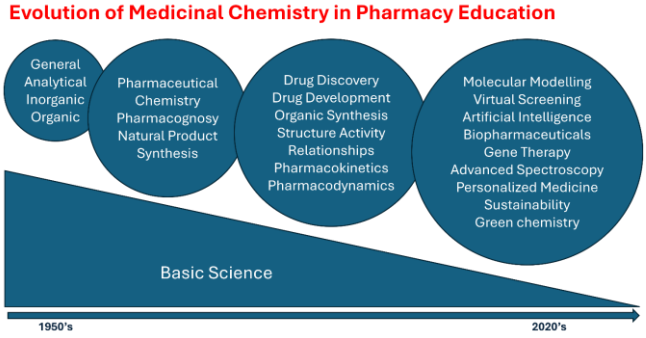

Figure 2. The evolution of medicinal chemistry and concomitant reduction of basic science in pharmacy curricula.

From the teaching perspective, in any given pharmacy syllabus the depth of medicinal chemistry knowledge varies. It must be accepted that defining the core concepts and extent of competencies the pharmacy student achieves in medicinal chemistry is the first step to achieving a standard.[12,13] Adopting a consistent undergraduate framework has the potential to realign and synchronise pharmacy programmes across Europe, promote mobility and foster career specialization via postgraduate study. Taught postgraduate courses and micro-credentialing will be integral in the future education of pharmacists and already, many institutions offer successful postgraduate options in medicinal chemistry.

In recent years, the use of technology in teaching has seen integration of the virtual laboratory alongside traditional experiments in organic synthesis, natural products, qualitative and quantitative pharmacopeial analysis with generally positive feedback from students. The expansion of this field has allowed a much broader scope of experiments with increasingly complex, visual and life-like scenarios and is certain to be part of the future teaching landscape. The recent COVID-19 pandemic also presented challenges and opportunities from both a pedagogical and scientific perspective. This is evident in our ability to pivot to online teaching and the legacy of this in our current teaching practice. The experience enforced remote learning and deeper consideration of universal design for learning, opening the door to education for students where options were limited. It is important that this flexibility and student-centered approach be maintained into the future.

Conclusion. Education in medicinal chemistry has undergone dynamic change in the past 30 years. However, while some things change, many remain the same. Initial perceived threats such as the emergence of new techniques and technology and the use of computation have only strengthened the discipline. The use of technology in teaching has led to better engagement with the principles of universal design for learning and better opportunities for marginalized students. Harmonization of medicinal chemistry education in the pharmacy degree and further integration of the topic into clinical pharmacy should be encouraged with the aim that the first thought of every pharmacist should revolve around structural properties. Maintaining the emphasis on real-world relevance to both patients and industry will continue to underpin future careers and further embed the field and basic science into pharmacy. The development of dedicated postgraduate options with medicinal chemistry specialization enables pharmacists to develop further skills through research and careers in the pharma industry. Though the graduate profile changes, as teachers, as a network and as a discipline, we continue to introduce and implement pedagogical changes to engage, inspire and shape future pharmacists and medicinal chemists.

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Notes

Views expressed in this editorial are those of the authors and not necessarily the views of the ACS. The authors declare no competing financial interest

Author Contributions

The manuscript was written through contributions of all authors and all authors have given approval to the final version of the manuscript.

ACKNOWLEDGMENT

We would like to formally acknowledge past and current members of the group for discussions over the years. These include (but are not limited to) Olivier Duval, Thierry Besson, Sylvain Rault, Pascal Berthelot, Roger Waigh, Guillaume Le Baut, Marc Le Borgne, Frederic Fabis, Mary Meegan and many more. We are very grateful for their support and encouragement.

ABBREVIATIONS

AI, Artificial Intelligence; DMPK, Drug Metabolism and Pharmacokinetics; GP_2A, Group for the Promotion of Pharmaceutical Chemistry in Academia; SAR, Structure Activity Relationship; WHO, World Health Organization.

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