
Medicinal Chemistry in IUPAC

Accomplishments During the Past Decade and Relationships With Industry

by *Robin Ganellin*

Medicinal chemistry is a key discipline vitally important to the pharmaceutical industry. Medicinal chemists are involved in new drug discovery and solving the problem of designing molecules to optimize their biological properties. In the past decade the Medicinal Chemistry Section of IUPAC has been very active, meeting twice yearly and providing a forum for the exchange of knowledge and views among medicinal chemists from different countries who are in academia and the pharmaceutical industry. This cross fertilization of ideas has been stimulating and invaluable to the chemists involved and has without doubt benefited the wider community of medicinal chemists. For the industrially advanced countries these meetings have provided useful information sources and improved understanding of the subject. For the less industrialized countries they have helped further the establishment of medicinal chemistry in their respective societies.



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The tangible output of the Medicinal Chemistry Section is seen in the publication of books and articles, the organization of international meetings and educational schools, the presentation of lectures, and in the formation of the Asian Federation of Medicinal Chemistry (AFMC), as detailed below.

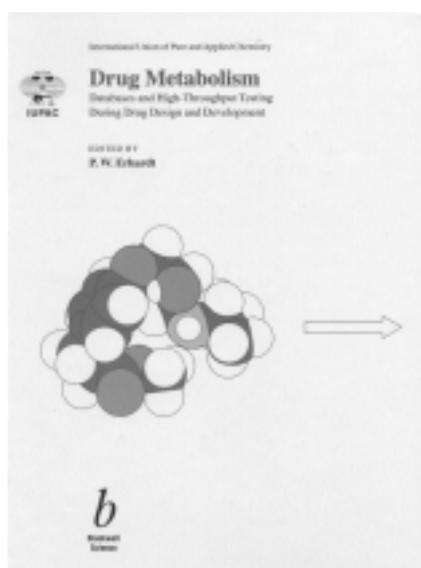
Books

Three important books have been published by the Medicinal Chemistry Section. *Medicinal Chemistry for the 21st Century*,¹ published in 1992, forms part of the IUPAC series "Chemistry for the 21st Century Monographs" and contains 24 chapters by eminent scientists from industry and academia. It is organized into four parts: new lead discovery, protein structure-function relationships, pharmacophore studies, and bioavail-

ability manipulations. It contains many thought-provoking suggestions about the future of drug discovery.

More recently, *Drug Metabolism: Databases and High Throughput Testing During Drug Design and Development* was published.² It deals with the issue of predicting the likely metabolic transformations of candidate drugs, a critical problem for pharmaceutical companies engaged in the development of new medicines. Knowledge of likely metabolism is valuable for prediction of the likely half-life of drug duration and for assessing potential side effects that may have adverse toxicological consequences. What then is predictable from structure-mechanism relationships? Past experience has not been well publicized so that databases of compilations of experimental information or predictive modelling would be very useful. Current models are, however, of limited applicability and this book identifies their potential uses and limitations. The book describes how a joint project with the International Union of Pharmacology, IUPHAR, is being conducted that aims to establish a human metabolism database that can be accessed around the world for specific applications that directly affect human welfare. The availability of such a searchable database would be potentially very valuable in the design and development of new therapeutic substances. The book also provides some case studies by various practitioners from the pharmaceutical industry.

The Section has also scored a real hit by producing this year the *IUPAC Handbook of Pharmaceutically Acceptable Salts*.³ Because many drug substances are acids or bases it is convenient to convert them into salts to improve stability and increase water solubility. Of course the counter ion must be suitable and non-toxic



and must not interfere with the desired biological action of the drug. This aspect of drug presentation is of fundamental importance for drug development and yet there is very little helpful literature for guidance. Preparation of the optimal pharmaceutically acceptable salt form of a new drug substance is a problem frequently faced by medicinal chemists who could greatly benefit from a convenient, comprehensive, and authoritative source of information concerning the full range of possibilities including the more unusual salts. This book reviews the literature and generates a critical compilation of information in this subject area. It is definitive and will doubtless be the source book for the future.

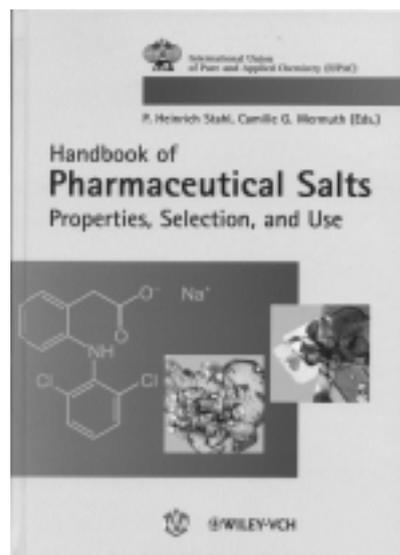
Glossaries

A "Glossary of Terms Used in Medicinal Chemistry" was compiled with the aim of providing concise definitions to those for whom the usage and meaning may not always be clear.^{4a} This is probably especially helpful to chemists whose native language is not English. The glossary was published in the *Annual Report on Medicinal Chemistry*,^{4b} which is distributed by the American Chemical Society to over 10 000 medicinal chemists, and also made available on the Web.^{4c}

Computational drug design is a continuously developing field which is now a very important component in the discipline of medicinal chemistry. At the same time, many medicinal chemists lack significant formal training in the field and may not have a clear understanding of the terminology used. Furthermore, there is the possibility that in different countries certain terms may not have the same meaning, a fact that gives added value to the establishment of a standard international definition. This led to production and publication of a "Glossary of Terms Used in Computational Drug Design."⁵

Combinatorial chemistry—involving the rapid synthetic assembly of structural building blocks in various possible combinations to produce large libraries of compounds for drug screening purposes—is a rapidly expanding field of medicinal chemistry. It is also generating a new vocabulary to describe the various operations and components. To assist medicinal chemists in their understanding of this field and to help with the acceptance of a universally understood language, a "Glossary of Combinatorial Chemistry Terms"⁶ was published in *Pure and Applied Chemistry* and subsequently, in the *Journal of Combinatorial Chemistry*. This ensures its use within the American Chemical Society as a standard glossary of terms. Further work is focused on producing an opinion document on the legal implications of patenting virtual libraries. This is a very important issue which has profound implications for research and development in the pharmaceutical industry.

Other glossaries of terms are being prepared, including a Glossary of Drug Metabolism Terms, Glossary of Terms in Pharmaceutical Process Chemistry, and Glossary of Terms in Pharmaceutical Technology.



A recent project has been approved to publish as a book, a compilation of the glossaries pertinent to chemistry and drug development that have been published in *Pure and Applied Chemistry* during the past decade, i.e., since 1992. See the Web site at <www.iupac.org/projects/2002/2002-001-1-700.html>.

Training of Medicinal Chemists

Medicinal chemists are critical in the design, discovery, and synthesis of new chemical entities in the pharmaceutical industry. Without them there would be no successful research for new medicines. The path for chemists to become medicinal chemists is, however, often indirect and training is commonly "on the job." As a contribution to the discussion about suitable formal training, the Medicinal Chemistry Section has published between 1993 and 2001 a series of papers on this subject.⁷⁻¹³ The series is based on the information received in answers to questionnaires sent to leading pharmaceutical research companies and universities that teach medicinal chemistry in Europe, Japan, and the USA. The results have also been presented at international symposia in the Netherlands (1993), Italy (1994), and Egypt (1998). A syllabus for a short course on medicinal chemistry has also been published,¹⁴ and courses have been initiated in some Latin American countries.

Guidelines for Natural Product Collaborations

Scientists in many countries throughout the world are interested in collaborating with companies for the study and evaluation of natural products as potential sources or leads to new medicinal agents. At the same time, there is concern—particularly from scientists in developing countries who typically have had little experience in this field—regarding how to proceed in such matters and how to handle related intellectual property issues. The collaboration between pharmaceutical research companies in the developed countries and natural products scientists in developing countries is often hindered

by suspicion on the part of the latter that they are not being treated fairly. This can lead to protracted negotiations, which may well founder because of the lack of understanding among all concerned parties. To facilitate such collaborations, the Medicinal Chemistry Section prepared a document of guidelines, which was published in 1996 as IUPAC Recommendations entitled "Preservation and utilization of natural biodiversity in context of the search for economically valuable medicinal biota."¹⁵ This article is independent from the Manila Declaration and Melaka Accord and describes general topics and potential issues to be considered in a collaboration on natural products. The Section also produced two other documents on the subject: a technical report¹⁶ intended to help with drawing up contracts and an article titled "Medicinal Chemistry in the Development of Societies."¹⁷

Formation of the Asian Federation of Medicinal Chemistry

Under the leadership of Dr. Naofumi Koga, the Section facilitated the formation of the Asian Federation of Medicinal Chemistry (AFMC). An inaugural meeting was held at the Pharmaceutical Society of Japan's Nagai Memorial Hall on 11 May 1992. The members include nine societies from four countries: Australia (1), China (2), Japan (4) and Korea (2). The AFMC has been very active in sponsoring symposia between countries (e.g., The Fourth Korea-Japan Joint Symposium on Drug Design and Development, April 1994 in Tokushima, Japan and The First Australia-Japan Symposium on Drug Design and Development, May 1994, Coolom, Australia). The first AFMC Symposium on Medicinal Chemistry was held in Tokyo, September 1995 (AIMECS 95); subsequent meetings have been held in Seoul, Korea (1997), Beijing, China (1999), and Brisbane, Australia (2001). The next meetings will be in Kyoto in 2003 (AIMECS 03). The proceedings of the first meeting were published in a book.¹⁸

Future Representation of Medicinal Chemistry in IUPAC

With the restructuring of the divisions in IUPAC, the Medicinal Chemistry Section was combined in 1996 with the Division of Clinical Chemistry to form Division VII, Chemistry and Human Health. The medicinal chemistry interest is now represented by a Subcommittee on Drug Discovery and Development. It is anticipated that it will continue to support the activities of medicinal chemists in the future and contribute to the technical success of the pharmaceutical industry. New members to the subcommittee are always welcome.

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www.iupac.org/divisions/VII