

# JOURNAL OF MEDICINAL CHEMISTRY

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## EDITORIAL

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### Medicinal Chemistry: 1989 and Beyond

Undoubtedly you have noticed the new cover design for the *Journal of Medicinal Chemistry*. As this is the first significant design change in the 26 year history of the Journal, such an occasion deserves editorial comment. Although the cover underwent only minor modification prior to this issue, the contents of the Journal have changed significantly to reflect major advances in the field. When the American Chemical Society first published this Journal in 1963 under the editorship of Professor Alfred Burger, the name "Medicinal Chemistry" was barely established and the rationale employed for developing new drugs was minimal at best. During the ensuing 26 years, a critical mass of knowledge pertaining to the relationship between molecular structure and biological activity has firmly established medicinal chemistry as a full-fledged discipline.

But what about the future? Where is medicinal chemistry headed? Developments in four major areas are having a profound impact on the field. These are (1) computers and software design, (2) instrumentation, (3) computational chemistry, and (4) recombinant DNA technology. Interlocking applications in these areas will be synergistic in providing medicinal chemists with new tools and concepts for their research.

The electronic revolution has barely scratched the surface of its potential in drug research. Inexpensive and powerful personal computers have become affordable to nearly all medicinal chemists. Like its predecessor, the hand-held calculator, the personal computer will become essential to research in medicinal chemistry. Moreover, the accessibility of supercomputers and emergence of computer neural network systems will open new avenues to rational drug design.

Similarly, advances in instrumentation such as X-ray diffractometers and NMR spectrometers have set the stage for their use as standard tools in medicinal chemistry research. Now it is possible to determine the X-ray crystal structure of an enzyme within 1 week. This is rapid enough to provide feedback to guide the medicinal chemist in designing more potent and selective inhibitors. Together

with multidimensional NMR techniques, these physical methods of analysis are almost as rapid as the biological assay. Thus, inhibitor molecules will be more deliberately designed on the basis of specific interactions with groups at the active site.

Today, scientists are exploring the structure-activity relationships of enzymes and the structure-function relationships of receptors. Unthinkable just a dozen years ago, recombinant DNA technology has made this possible. This technology will have profound impact on understanding the chain of events starting from ligand-receptor binding and ending in a biological effect. Advances in computational chemistry will play an important role in sorting out the dynamics of these events. Such advances include the development of improved models for the folding of polypeptide chains and for predicting ligand-induced conformational changes in proteins.

Within the next 20 years a majority of receptor proteins will be sequenced and synthesized by recombinant DNA techniques. In this context, supercomputer neural networks may be of assistance in the design of small molecules that are recognized by these receptors. Thus, non-peptide small molecules that mimic or antagonize endogenous oligopeptides or protein guest molecules will be designed de novo from a knowledge of the molecular architecture of the host molecules (receptors).

Medicinal chemists of the future will be a more diverse group of scientists. Expertise in organic synthesis will still be important, but many more subspecialties will contribute to molecularly focused research in medicinal chemistry. Moreover, interdisciplinary research activities will be more important, if not essential, to drug design in the future.

I see an exciting future for medicinal chemistry and I believe that the advances during the next decade will far exceed those made during the past 26 year history of this Journal.

Philip S. Portoghese  
*Editor*