Annual Review of Pharmacology and Toxicology 1997. Annual Reviews Inc., 4139, El Camino Way, Palo Alto, CA 94303-0139, USA. Vol. 37. 571 pp. Price: Individuals, US$ 65; Institution, US$ 130.

Drug discovery in recent years has been based on an understanding of molecular details of the cellular targets for newly identified drugs. This has resulted in adoption of the phrase 'rational drug design' by pharmaceutical companies, as opposed to an admission from them that, perhaps, earlier drug discovery programmes could have been 'irrational' or serendipitous in their approach! With the explosion of information in recent years resulting from molecular biology approaches to understanding the mechanisms of cellular responses to various hormones, toxins and drugs, it has become necessary to provide an overview of current trends in the area of pharmacology and toxicology. This particular *Annual Review of Pharmacology and Toxicology, 1997*, could meet the needs of a variety of investigators in both academic and pharmaceutical environments. Twenty chapters on a wide variety of topics including the tissue renin–angiotensin system, the use of transgenic animals as a new approach in pharmacology, farnesyltransferase inhibitors, as cancer chemotherapeutics, and the pharmacology of neurotrophic factors provide a broad and detailed description of current areas of research. Perhaps a major disappointment in the volume, however, is that many of the chapters are extensive descriptions covering practically all the recent developments in a particular area, with only a few lines indicating future trends in a broad perspective. Perhaps this is the role that the Annual Reviews Inc, sees for itself, with the explosion of information available in every field nowadays.

The detailed characterization of receptors and subsequent signal transduction pathways has allowed pharmacology to proceed to analysis of drug action at the molecular level. The importance of obtaining crystal structures of various components in any signalling pathways cannot be overemphasized, and information obtained from the structures of a number of receptors, kinases, docking molecules and enzymes has allowed the investigator to design molecules that could interact with active sites of these molecules. The article on 'Structure based drug design', by McCammon and others concisely summarizes the computational advances that have been made in the areas of molecular visualization, molecular modelling, docking, 3-D database techniques and free-energy perturbation. A number of instructive examples have been provided where structure-based design has been used for compounds of pharmacological interest, and include the design of inhibitors for HIV protease, possible new inhibitors for thymidylate synthase, acetylcholinesterase and elastase. The chapter is a very good introduction to the power of computational methods in the analysis of 3-D structures and the ability to design new molecules utilizing structural information, and highlights areas of future development in 'computational alchemy'.

As mentioned earlier, pharmacological studies in recent years utilize information obtained from the molecular characterization of receptors and ion channels, as well as down-stream effectors of a signal transduction pathway. Three chapters on G protein $\beta\gamma$ subunits, metabotrophic glutamate receptors and the structure and function of the β_3-adrenergic receptor provide up-to-date information on current thinking arising out of studies on these model systems using molecular biological and structural approaches. Eva Neer has contributed significantly to the realization that the $\beta\gamma$ subunits of G proteins themselves act in regulating a variety of cellular responses. The article describes the various downstream effectors, which are regulated by the $\beta\gamma$ subunits which include the potassium channel, phospholipases, adenylyl cyclases, tyrosine kinases and Ras. The crystal structures of the trimeric $G\alpha\beta\gamma$ subunits described this year will now direct investigators towards studies on structure–function relationships, though it must be mentioned that a number of earlier studies through site-directed mutagenesis, have already provided valuable information which can now be looked at in structural detail.

Glutamate receptors were initially characterized as ligand-gated cation channels, but in recent years, a number of receptors for glutamate have been identified that mediate their action through G-proteins. The article by Conn and Pin summarizes recent information on the cloning and characterization of genes for a number of metabotropic glutamate receptors and their splice variants. Emphasis is also placed on the discovery of agonists and antagonists with receptor subtype specificity, opening up the possibility of using some of these compounds as drugs in regulating glutamate receptor activity in the brain. Studies have been carried out in rats using both agonists and antagonists to investigate the role of these receptors in inducing limbic convulsions in rats, and in the regulation of hypertension, providing promising leads in the treatment of similar disorders in the human.

While pharmacology is able to analyse the actions of drugs at the molecular level, toxicology is still largely dependent on performing experiments in whole animals and deriving somewhat empirical conclusions. There is a contrast, therefore, in the detail provided in chapters devoted to the toxicology of environmental tobacco smoke, medication compliance as a feature in drug development and perfusion injury after liver preservation for transplantation. For the general reader, however, these chapters are interesting. If a smoker were to read the chapter by Witschi *et al.* on the effects of smoke on the developing foetus and new born babies, just by the mother inhaling sidestream smoke, surely a change in smoking habits would take place! The whole scenario seems to be one of deriving a transient and personal pleasure at the expense of a possibly penalty on a totally innocent party!

The human genome sequencing project has the potential to revolutionize the method and practice of science, if tools are available to sift through the data that are likely to be spewed out! Therefore, an article by Meyer and Zanger on the molecular mechanisms of genetic polymorphism of drug metabolism is interesting in that it initiates thoughts on including genetic screens to test the efficacy of drugs in different populations. It was interesting to read that certain polymorphisms have been identified in drug-metabolizing enzymes, such as cytochrome P450 genes

and *N*-acetyltransferase genes, which occur in a relatively high frequency, and simple DNA tests are available to predict the phenotype. Could this be the advent of drug therapy only after studying the individual's genetic background? Would this provide greater efficacy and fewer complications resulting from drug toxicity? The future beckons us all.

But the past must and will continue to influence the present. The first, and usual article in the *Annual Reviews*, is written by a leader in the field and this particular volume begins with the reminiscences of Avram Goldstein, whose contributions span the realms of pharmacology and biochemistry. The account is a very personal glimpse of the scientific life of Goldstein, touching on anti-Semitism feelings that were rampant in the US in the 1940s, his establishing the Department of Pharmacology at Stanford, his productive scientific collaboration with his wife of 50 years, Dora Benedict, and his interaction with industries in California. He hints at the changes that have occurred in pharmacology in recent years, especially the emphasis being given in teaching programmes to applications of molecular biology, with a consequent decline in the importance being placed in bioassays, dose–response relationships, spare receptor theory and other aspects considered an integral part of pharmacology. Goldstein warns against this trend and urges current pharmacology departments to have a more classical approach to the discipline of drug action. While we hear pleas these days that science now should be holistic in its practice and cross barriers of individual disciplines, Goldstein's warning that such ideas may dilute and eventually abolish specialists in a particular field, should be considered with due respect.

SANDHYA S. VISWESWARIAH

Department of Molecular Reproduction, Development and Genetics, Indian Institute of Science, Bangalore 560 012, India

MEETINGS/SYMPOSIA/SEMINARS

XXVI International Ethological Conference

Date: 2–9 August 1999
Place: Bangalore

The International Ethological Conferences have been, so far held only in European and American Universities with the exception of Kyoto, Japan in 1991. The main factors include the scientific programme and other discussions.

Suggestions are invited for good scientific programmes.

Contact: Ms Shakunthala Sridhara
Secretary, General XXVI IEC
Ethological Society of India
University of Agricultural Sciences
Department of Vertebrate Biology
GKVK, Bangalore 560 065, India
Fax: 91-080-3330277, 91-080-3339998
Ph: 91-080-3330153, Extn. 366;
91-080-3339998