

Microsomes, Drug Oxidations, and Drug Toxicity

Edited by

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Microsomes,
Drug Oxidations,
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Drug Toxicity



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Dr. Minor J. Coon

The symposium provided a timely and appropriate occasion for all participants to join in honoring Professor Coon on his 60th birthday for his outstanding contributions to biochemistry and pharmacology. He was particularly recognized and lauded for his important achievements and leadership in the field of cytochrome P-450 and related microsomal enzymes.

Preface

The electron transfer system and related enzymes localized in microsomal membranes play a pivotal role in attenuation, and in many instances also in potentiation, of the pharmacological effects of a large variety of xenobiotics ingested by human and other organisms. These enzymes are also functioning in the metabolism of certain lipids such as fatty acids and steroids. A better understanding of the nature, reaction mechanisms, and functions of these microsomal enzymes is, therefore, highly desirable not only for promoting basic biomedical research but also for protecting human beings from hazardous effects of foreign chemicals such as drugs, food additives, pesticides, carcinogens, and environmental pollutants. The recognition of the importance of these enzymes provided the impetus for four international symposia dealing with the microsomal enzymes and their functions which were held in 1968 (Bethesda, Maryland), 1972 (Palo Alto, California), 1976 (Berlin, West Germany), and 1979 (Ann Arbor, Michigan). The very rapid growth of information in this field, however, called for another meeting and the Fifth International Symposium on Microsomes and Drug Oxidations was held in Tokyo, Japan, on July 26-29, 1981. In this volume is compiled the scientific information presented at that meeting.

In this symposium, as in the preceding meetings of the series, an effort was made to encourage interdisciplinary discussions which are surely needed to draw a clearer picture of the area covered. It was also the intention of the Organizing Committee to invite, as far as possible, active workers of younger ages to present their fresh data and to ask senior scientists of established reputation to open each session by introducing the significance and problems related to that session. At the end of the symposium, a 7-membered panel discussion was held to evaluate the outcome of the meeting, especially concerning the multiplicity of mammalian cytochrome P-450. A summary of this discussion, kindly prepared by panel chairman Dr. R. W. Estabrook, as well as a plenary lecture given by Dr. M. J. Coon are included in this volume. Because of the limitation of

space, only two pages are allotted to each paper presented by poster, but these short papers, we believe, are also of great value in assessing recent research advances in the field.

The topics emphasized in this symposium include the characterization and mechanisms of action of cytochrome P-450 and related enzymes, microsomal metabolism of endogenous substrates, regulation of microsomal metabolism, and metabolic activation and drug toxicity. A session entitled "Newer Aspects of Microsomal Drug Metabolism" covered recent developments achieved by new techniques and ideas. It is our hope that the information contained in this volume will be of help in furthering our knowledge concerning the important and complex microsomal enzymes and their metabolic implications.

Finally, on behalf of the other members of the Organizing Committee (Drs. Y. Aso, Y. Ishimura, M. Katagiri, H. Kitagawa, Y. Omori, T. Omura, E. Takabatake, T. Yamano, and H. Yoshimura) we should like to express our sincere gratitude to the speakers, chairpersons, and participants for their friendly cooperation which so contributed to the success of the meeting. Our special thanks are due to the International Advisory Board composed of Drs. A. H. Conney, M. J. Coon, R. W. Estabrook, J. R. Gillette, S. Orrenius, D. V. Parke, and V. Ullrich for their kind assistance and advice in organization. We also wish to acknowledge with gratitude the generous financial support of a number of pharmaceutical companies in Japan, from the International Union of Biochemistry in particular, and from Hoffmann-La Roche Inc., Merck & Co., Schering Corp., Burroughs-Wellcome Co., and G. D. Searle Corp., all of the United States.

Osaka and Tokyo
April, 1982

Ryo Sato
Ryuichi Kato

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