Insecticide Biochemistry and Physiology

Edited by

C. F. Wilkinson

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Preface

Only four short decades ago, the control of insect pests by means of chemicals was in its early infancy. The pioneers in the area consisted largely of a group of dedicated applied entomologists working to the best of their abilities with a very limited arsenal of chemicals that included inorganics (arsenicals, fluorides, etc.), some botanicals (nicotine), and a few synthetic organics (dinitro-*o*-cresol, organothiocyanates). Much of the early research was devoted to solving practical problems associated with the formulation and application of the few existing materials, and although the discovery of new types of insecticidal chemicals was undoubtedly a pipe dream in the minds of some, little or no basic research effort was expended in this direction.

The discovery of the insecticidal properties of DDT by Paul Müller in 1939 has to be viewed as the event which marked the birth of modern insecticide chemistry and which has served as the cornerstone for its subsequent developement. DDT clearly demonstrated for the first time the dramatic potential of synthetic organic chemicals for insect control and provided the initial stimulus which has caused insecticide chemistry to become a field not only of immense agricultural and public health importance but also one that has had remarkable and unforseeable repercussions in broad areas of the physical, biological, and social sciences.

Indeed, there can be few other synthetic chemicals which will be judged in history to have had such a broad and telling impact on mankind as has DDT. Initially, of course, its discovery signaled the beginning of the intensive search for new insecticides that continues unabated to this day and that has led in part to the successful development and use of the other chlorinated hydrocarbons, the organophosphorus compounds, the carbamates, and the additional materials currently in use. The widespread use of these compounds during the last 20 years has played a major role in the development of our own modern agricultural system and is an integral component of the "green revolution" which it is hoped will serve to partially alleviate the nutritional needs of the rapidly expanding populations in other areas of the world. In addition, insecticides have brought spectacular social and economic gains to large areas of the world as a result of their role in the eradication of malaria and other arthropod-borne diseases. But in spite of these benefits the widespread use of

insecticides, like so many other modern technological advances, has created some serious problems that were not immediately obvious.

Early optimism regarding the practical potential of DDT and other materials has been tempered to some extent by the emergence of insect resistance to insecticides as a real threat to continued control, and more recently there has been increasing recognition of the potentially deleterious effects of persistent insecticides on wildlife and other nontarget species in the environment. Furthermore, concern continues to be voiced over the possible toxicological hazards to man of chronic exposure to trace residues of insecticides in the food supply. As a result of these and other problems, many insecticides such as DDT, which initially proved so successful, are no longer considered acceptable and have been or are being phased out. The search for new replacements has been intensified since, despite frequent statements to the contrary, it seems clear that chemicals will continue to represent our major means of insect control in the foreseeable future. It is equally clear that in order to discover and develop these insecticides of the future a much greater degree of sophistication will be required than has hitherto been the case.

In recognition of this need, basic research in all aspects of the field has expanded by leaps and bounds during the last decade and has assumed many new dimensions with respect to the disciplines that it now encompasses. Indeed, the entire area of insect control with chemicals has come a long way from its rudimentary beginnings as a branch of applied entomology and is extremely difficult to define. It now reaches into almost every corner of the biological, physical, and life sciences and includes such disciplines as physiology, biochemistry, pharmacology, toxicology, organic and physical chemistry, and environmental studies as well as economic entomology. The current overall level of sophistication in the field closely reflects that of the individual disciplines of which it is composed.

The decision to prepare this book was in itself not arrived at lightly. The enormous breadth and diversity of the field and the voluminous literature with which it is now associated should be sufficient to give serious pause to any would-be author. Furthermore, in the last few years we have been bombarded with a plethora of volumes (books, monographs, symposia proceedings, committee reports, etc.) covering most major areas of the pesticide field. Among these are books dealing with specific groups of insecticides such as the pyrethroids (Casida, 1973), naturally occurring insecticides (Jacobson and Crosby, 1971), chlorinated hydrocarbons (Brooks, 1974), organophosphorus compounds (Eto, 1974), and chemosterilants (LaBrecque and Smith, 1968).[1]

[1]Casida, J. E. (ed.), 1973, *Pyrethrum, the Natural Insecticide*, Academic Press, New York. Jacobson, M., and Crosby, D. J. (eds.), 1971, *Naturally Occurring Insecticides*, Dekker, New York. Brooks, G. T., 1974, *Chlorinated Insecticides*, Vols. I and II, CRC Press, Cleveland. Eto, M., 1974, *Organophosphorus Pesticides: Organic and Biological Chemistry*, CRC Press, Cleveland. LaBrecque, G. C., and Smith, C. N. (eds.), 1968, *Principles of Insect Chemosterilization*, Appleton-Century-Crofts, New York.

Other recently published volumes include those on the chemistry (Melnikov, 1971), metabolism (Menzie, 1969), mode of action (Corbett, 1974; Aldridge and Reiner, 1972), formulation (Van Valkenberg, 1973), and environmental aspects (White-Stevens, 1971) of pesticides, and there are books on the so-called third generation pesticides, the insect hormones (Menn and Beroza, 1971; Sláma *et al.*, 1974).[2] Add to this incomplete list the numerous symposia proceedings (O'Brien and Yamamoto, 1970; Gillett, 1970; Metcalf and McKelvey, 1975)[3] and pesticide-related chapters in other texts and it is clear that the field cannot by any stretch of the imagination be said to suffer from underexposure. Consequently it is perhaps necessary from the outset to provide some justification (or apology) for yet another volume.

Many of the volumes referred to offer excellent and comprehensive coverage of the subject areas with which they are concerned, but in keeping with the evolution of the field and following the common trend of contemporary scientific literature they are frequently of a narrow, highly specialized nature. As a result, they often appear isolated from and out of context with the broader aspects and more general principles of the field of which they are a part. For this reason, it was decided to attempt to reverse the trend toward specialization and prepare a volume which would provide a broad (though admittedly selective) coverage of the basic interactions of insecticides with living organisms.

Although several excellent general texts are available (Martin, 1964; Metcalf, 1955; O'Brien, 1967; Hassall, 1969),[4] most are to some extent outdated, and there seems a notable reluctance on the part of the authors to revise them. Indeed, with one recent exception (Matsumura, 1975)[5] the task of compiling a general text seems to be rapidly passing the point at which it can be adequately accomplished by a single person. Consequently, in ascertaining the need for this book it was decided to adopt the now common format of a

[2]Melnikov, N. N., 1971, *Chemistry of Pesticides*, Springer-Verlag, New York. Menzie, C. M., 1969, *Metabolism of Pesticides*, Bureau of Sport Fisheries and Wildlife, Special Scientific Report—Wildlife No. 27, Washington, D.C. Corbett, J. R., 1974, *The Biochemical Mode of Action of Pesticides*, Academic Press, New York. Aldridge, W. W., and Reiner, E., 1972, *Enzyme Inhibitors as Substrates*, North-Holland, Amsterdam. Van Valkenberg, W., 1973, *Pesticide Formulations*, Dekker, New York. White-Stevens, R. (ed.), 1971, *Pesticides in the Environment*, Vols. I and II, Dekker, New York. Menn, J. J., and Beroza, M. (eds.), 1971, *Insect Juvenile Hormones: Chemistry and Action*, Academic Press, New York. Sláma, K., Romañuk, M., and Šorm, F., 1974, *Insect Hormones and Bioanalogues*, Springer-Verlag, New York.

[3]O'Brien, R. D., and Yamamoto, I. (eds.), 1970, *Biochemical Toxicology of Insecticides*, Academic Press, New York. Gillett, J. W. (ed.), 1970, *The Biological Impact of Pesticides in the Environment*, Oregon State University, Corvallis. Metcalf, R. L., and McKelvey, J. (eds.), 1975, *Insecticides for the Future: Needs and Prospects*, Wiley, New York.

[4]Martin, H., 1964, *Scientific Principles of Crop Protection*, Metcalf, R. L., 1955, *Organic Insecticides*, Interscience, New York. O'Brien, R. D., 1967, *Insecticides: Action and Metabolism*, Academic Press, New York. Hassall, K., 1969, *World Crop Protection*, Vol. 2, CRC Press, Cleveland.

[5]Matsumura, F., 1975, *Toxicology of Insecticides*, Plenum Press, New York.

multiauthor volume written by outstanding authorities in the various areas to be included.

This cannot truly be considered a general text since it is concerned primarily with the basic biochemical and physiological events that determine the biological activity of an insecticide once it has reached the outer surface of an organism. In contrast to most of the existing books in the area, which are divided according to the various groups of insecticides discussed, (chlorinated hydrocarbons, carbamates, etc.), the first ten chapters of this volume are organized on a functional basis that emphasizes in the approximate order in which they occur the physiological processes and biochemical events taking place from the time the insecticide is administered to an organism to the time of its arrival and interaction at the target site; wherever possible an attempt has been made to stress the comparative aspects of the area under consideration.

As a logical consequence of the organization employed, the first chapter is concerned with the *Penetration and Distribution of Insecticides.* This is followed by a section consisting of four chapters that discuss the major biochemical mechanisms and pathways by which organisms metabolize a large variety of insecticides and other foreign compounds and thus afford themselves some degree of protection from the potentially hazardous effects of such compounds. Included here are chapters on *Microsomal Oxidation and Insecticide Metabolism, Cytochrome P450 Interactions, Extramicrosomal Metabolism of Insecticides,* and *Enzymatic Conjugation and Insecticide Metabolism.*

The next section of the book deals with the actual interactions of insecticides with their targets. Since most known insecticides are neurotoxicants, it is hoped that inclusion of the chapter on *The Nervous System: Comparative Physiology and Pharmacology* will provide a useful background for the subsequent discussions on *Acetylcholinesterase and Its Inhibition, The Acetylcholine Receptor and Its Interactions with Insecticides,* and the *Effects of Insecticides on Nervous Conduction and Synaptic Transmission.* The only other major insecticide target is covered in the chapter on *Insecticides as Inhibitors of Respiration.* An additional chapter on the *Physicochemical Aspects of Insecticidal Action* is included to emphasize the importance of physicochemical parameters in studies of structure–activity relationships and in the rational design of insecticides.

No book of this type would be complete without inclusion of the extremely important areas of insect resistance to insecticides and selective toxicity. These large and complex areas are discussed at length in chapters entitled *The Biochemical and Physiological Basis of Selective Toxicity* and *The Biochemistry and Physiology of Resistance,* both of which contain a complete cross-section of the material appearing in previous chapters.

The last section of the book contains selected topics of toxicological interest and importance and emphasizes the effects of insecticides on mammals. The evaluation of potentially hazardous chronic effects which occupies a central role in modern toxicology is discussed in *Teratogenic, Mutagenic, and Carcinogenic Effects of Insecticides,* and the various mechanisms by which the

toxic effects of insecticides may be modified through combination with other insecticides or drugs are outlined in the chapter on *Insecticide Interactions*. The following chapter on the *Treatment of Insecticide Poisoning* is one not often found in books of this type. Its inclusion reflects the growing concern over the occupational exposure of agricultural workers to insecticide residues in the environment, a subject which among others is given additional attention in the final chapter on *Environmental Toxicology*.

Several other topics could have usefully been included in the book and there may be some disappointment over the arbitrary limits which were established as a basis for selection. As previously discussed, however, the field is large, and it is clear that some focus was required. With one or two notable exceptions, all chapters which were initially planned have been included, and the book represents a comprehensive account of the current status of basic biochemical and physiological research in the insecticide field. We hope that it will prove useful as a fairly advanced text for students in the field and become a well-used reference source for many others whose interests or professions are in this important area.

Thanks are owed to numerous individuals who have played an active role in the preparation of the book. These include Rona Springer, for patient and valuable secretarial assistance, and the editorial staff at Plenum, particularly Seymour Weingarten, Senior Editor, and Evelyn Grossberg. Of course, the book could not have been prepared without the expert cooperation of the various contributing authors, and I wish to express to them my sincere gratitude for their enthusiastic participation in this venture.

C. F. Wilkinson

Ithaca

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