SYMPOSIUM ON METABOLISM

Introduction

Currently, a controversy rages in regard to the wisdom of the continued use of pesticide chemicals, especially the persistent ones being used for insect control. Many people urge that the persistent ones be minimized by replacing them with nonpersistent ones, by using nonchemical means of control, or by banning their use.

The persistence of pesticide chemicals is related to their volatility, their solubility, and their chemical stability on surfaces to which they are applied, in or on organisms which encounter them and in the environment. Also, the use of certain of these chemicals, in combination, often changes the degradation characteristics of one or more components of such mixtures. In recognition of these attributes and for certain other reasons, regulatory agencies now demand more and more complete information on the chemical fate of pesticide chemicals in or on plants and animals, and in the environment. Such data importantly relate to the acceptance and use of chemicals for pest control.

All organic pesticide chemicals, to a varying degree, are metabolized in living organisms and/or are photodecomposed in sunlight. The extent and nature of the transformations vary with the agent causing them and with the chemical in question, time and structure being important factors. The transformation of some of these chemicals takes place in a matter of minutes, while that of others requires months or years. The chemical reactions involved include hydrolysis, hydroxylation, oxidation, reduction, dehalogenation and desulfurization, ring opening, isomerization, and/or conjugation.

In the past two decades, much effort has been expended in a number of laboratories on the metabolism of insecticide chemicals and, especially in recent years, on the elucidation of the role played by enzymes in the metabolism reactions. An important part of this effort has been the work of John Casida and coworkers in regard to organophosphorus compounds, carbamates, and, more recently, rotenone, pyrethroids, and methylenedioxyphenyl synergists. This symposium recognizes this fact by the involvement of several former coworkers of Dr. Casida and by the inclusion of papers in the areas of research associated with him.

The papers presented at this symposium will be published in two parts. The first part—the address by John E. Casida after receiving the International Award for Research in Pesticide Chemistry at the Joint CIC-ACS Meeting in Toronto—appears in this issue. The other papers will appear in the November-December issue.

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Mixed-Function Oxidase Involvement in the Biochemistry of Insecticide Synergists

John E. Casida

Methylenedioxyphenyl (1,3-benzodioxole) compounds enhance insecticide chemical toxicity by inhibiting the mixed-function oxidase (mfo) system of microsomes. This synergist action is very important because it minimizes the amount of insecticide chemical necessary for insect control. The toxicity of pyrethrum, other pyrethroids, and certain methylcarbamates, organophosphates, and chlorinated hydrocarbons is synergized by such compounds, particularly when resistant housefly strains are involved. 2-Propynyl ethers and esters, benzothiadiazoles, and other new compounds of high synergistic activity probably also act as mfo inhibitors. Most of these compounds are mfo substrates as well as inhibitors, and it appears that they act by either serving as alternative substrates, sparing the insecticide chemical from detoxification, or by reacting with another site in the mfo system, preventing oxidative insecticide detoxification. Interactions with other toxicants or drugs metabolized by the mfo system sometimes occur in mammals treated with piperonyl butoxide or other insecticide synergists; however, these interactions in mammals are evident only at high synergist doses and the effect is of short duration. There is a need for synergists of increased effectiveness and safety, and it is important to include tests of mfo inhibition in mammals, along with the usual toxicological parameters, in evaluating the safety of such compounds.

Pesticide chemistry is a relatively new scientific discipline which has, in the main, been developed in the past three decades. Nevertheless, this field of chemistry is now a mature science and is contributing importantly to man's welfare. Not all of the studies in this area pertain to chemicals that are, by themselves, inherently toxic to the pest(s) being controlled; many deal with pesticide synergists which are compounds that are nontoxic or negligibly toxic alone, but which serve to enhance the toxicity of a pesticide chemical when they are combined. The development of synergists for use in pest control stems from the premise, common to all research in pesticide chemistry, that individual chemicals or combinations can be found that selectively and preferentially control pests without harm to man and useful species.

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