

Chapter 1

Pest Management with Natural Products

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Natural products for pest control is not a new concept – products from nature have been used to control pests since the early beginning of agriculture circa 8000 B.C. to repel or kill biting arthropods. Throughout the years, natural products have played a direct role in controlling weeds, insects, plant pathogens and nematodes in the field, or indirectly as leads for development of modern pesticides through chemical syntheses. In addition to classic natural products chemistries for pest management there has been increased interest in the use of volatile natural products for pest management in agriculture. Hence, the two-day symposium of Natural Products for Pest Management honoring the work and contributions of the late Dr. Horace (Hank) Cutler as part of the Agrochemicals Division (AGRO) program at the ACS national meeting in Philadelphia in 2012, was very timely and provided an excellent opportunity to learn about past and present projects of natural products chemistry laboratories in academia, government, and industry. This introduction provides a brief and informative look at the varying topics discussed at the AGRO division symposium on natural

products. The compilations range from current research on hot topics and glimpses into past discoveries, to in-depth reviews on important topics in natural products. More importantly, this ACS symposium series book provides researchers of all disciplines with a practical approach for the management of pests, urban or agricultural, using natural products.

Introduction

Natural products for pest control is not a new concept – products from nature have been used to control pests since the early beginning of agriculture circa 8000 B.C. to repel or kill biting arthropods. Throughout the years, natural products have played an important role either directly by controlling weeds, insects, plant pathogens and nematodes in the field, or indirectly as leads that have been used to create modern pesticides through chemical synthesis. Due to the continuous use of products with identical or similar modes of action there has been a rapid increase in pesticide resistance among targeted pests. With their complex and diverse chemistries natural products have generated new interest in the development of commercial pesticides with novel modes of action. At the same time, public awareness of potential short- and long-term health effects connected to pesticides has guided pesticide manufacturers to develop so-called green chemistries with less potential for residues and harmful effects on non-target organisms.

Since the turn of the millennium, increased interest in natural products as pest control agents for both agricultural and urban pests has opened the market to biopesticides, and the modern tools provided by natural products chemistry and biotechnology have facilitated fast development of new pesticide products entering the competitive market place. Hence, the two-day symposium of Natural Products for Pest Management honoring the work and contributions of the late Dr. Horace (Hank) Cutler as part of the Agrochemicals Division (AGRO) program at the ACS national meeting in Philadelphia in 2012, was very timely and gave us an excellent opportunity to learn about past and present projects of natural products chemistry laboratories in academia, government, and industry. Chapter 2 in this book authored by Dr. Stephen Cutler highlights the legacy and achievements of his father, Dr. Hank Cutler, that helped lay the foundation for natural products chemistry as a resource for agrochemical product development.

Biopesticides are quickly advancing to the forefront of crop protection. The U.S. Environmental Protection Agency (EPA) defines biopesticides as pesticides derived from natural materials such as animals, plants, microbes, and certain minerals. The importance of natural product pesticides is highlighted in the recent statistics that valued the global pesticide market at \$49.9 billion in 2012. Total market value of pesticides is expected to reach nearly \$67.5 billion in 2017 after increasing at a five-year compound annual growth rate of 6.2%. As a segment, biopesticides were expected to total \$2.1 billion in 2012, and surpass \$3.7 billion in 2017, with an annual growth rate of 12%. This suggests that natural product pesticides are slowly achieving mainstream status, demonstrated by a large number of licensing agreements and acquisitions in this sector. These topics,

discussed in Chapter 3 by Asolkar *et al.*, substantiate the growing interest in new chemistries derived from natural sources. Instead of using these chemistries as leads for synthesis, more emphasis is placed on understanding the function of individual compounds and the positive combination effects that occur in complex natural matrices. Natural products played an important role in pest control during the early years of agriculture and crop husbandry and may well become a major component of future pest management. The ACS-AGRO symposium presentations, captured here as outstanding and informative chapters, clearly indicate a renewed interest in natural products research and development, and emphasize the value of natural product chemistries in modern pest control.

An additional tool for management of insect pests in agricultural settings has been the use of volatile natural products, which are more commonly identified as either host plant volatiles (e.g., kairomones) or pheromones. These volatile chemical signals between plants and insects often play a significant role in communicating to the insect an appropriate food source, a safe ovipositional site, or the identity of a non-host plant. Researchers have utilized this form of communication between plants and insects and gone on to develop blends of volatiles that attract insect pests or to enhance the attractiveness of a pheromone by mixing kairomones with these pheromones. Several presentations at the 244th ACS-AGRO symposium highlighted the use of host plant volatiles or pheromones to control or monitor insect pests.

Chapters 4, 5, and 6 in *Pest Management with Natural Products* directly address the multiple uses of volatiles for manipulating insect behavior, monitoring an insect pest, or even diagnosing plant health. In Chapter 4 Mafra-Neto *et al.* provide a nice example of formulating semiochemicals into an emulsion for the controlled-release of semiochemicals for use in mating disruption, attract and kill, and repellent treatments. Chapter 5 provides an overview on the use of host plant volatiles and pheromones for monitoring or control of an agricultural insect pest. And finally, the use of volatiles in agriculture and their relation to the development of in-field instruments for the detection of pathogens, fungi, or other forms of plant distress is discussed at length; the review by Aksenov *et al.* in Chapter 6 provides an in-depth look at the collection, analysis, and data processing of plant volatiles.

In Chapter 7, Gross *et al.* report on a quantitative structure-activity relationship (QSAR) study that uses an insect octopamine receptor expressed in a yeast strain. It investigates the structural parameters of monoterpenoids that are optimal for their binding at that receptor. Research by Patt *et al.* reported in Chapter 8 focuses on natural and synthetic compounds that influence the feeding responses of the insidious Asian citrus psyllid; the work reveals that some synthetic ligands were capable of enhancing the effects of a natural feeding stimulant. Chapter 9 from Zou *et al.* addresses pheromone chemistry of mealybugs and scale insects. It provides valuable detailed pathways for synthesis of a series of irregular terpenoids that serve roles in chemical communication for those plant-sucking insect pests. Chapter 10 by Miresmailli presents work on characterizing the differential volatilization of individual compounds in a natural insect repellent after it is applied to human skin. A portable gas chromatograph was used to track the evaporation of multiple monoterpenoids in the air above the

treated skin. Chapters 7, 8, 9, and 10 illustrate the importance of understanding the physical, chemical and biological properties of natural products, with emphasis on several terpenoids, which can manipulate the behavior of pests to our advantage or kill them.

One of the biggest pesticide needs is new herbicides with new modes of action, as there has been no new herbicide mode of action introduced in over 20 years. Chapter 11 by Evidente *et al.* outlines the work of these authors in discovery of microbial metabolites with novel structures that might be useful in fighting parasitic weeds, and Chapter 12 deals with efforts by Macias *et al.* to discover new herbicides, based on phytochemical phytotoxins. In both cases, the structures of the phytotoxins discovered are unlike any commercial herbicides, making a new mode of action likely. Using metabolomic methods, Pederson *et al.* in Chapter 13 provides evidence to support the view that clover is producing allelochemicals that have effects on other plants much like those of some commercial herbicides. These chapters illustrate the potential of natural sources for new herbicide discovery.

Natural product pesticides of today serve the same purpose as the products our ancestors used to control weeds, insects, plant pathogens or nematodes. However, thanks to the advancement in the field of natural product chemistry, we now know more about the detailed chemical composition of products that originate from plants and microbes. We appreciate nature's ability to adjust to ever-changing environmental conditions, and we no longer assume that everything that comes from nature is non-toxic or benign. Also, we have methods to identify and quantify active compounds in natural sources, and use the information as clues to develop pesticides with novel modes of action as discussed in Chapter 14 by Duke and Dayan. And finally, what would the science of natural product chemistry be without attempts to manipulate the metabolic pathways in plants and microbes capable of producing compounds that can be used to control agricultural and urban pests? Chapter 15 by Hahn discusses the art of using microbes as production plants for active pesticide chemistries.