NATURAL PRODUCTS FROM PLANTS AS INSECTICIDES

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Contents

Summary

Botanical insecticides are reviewed, with an emphasis on natural products that have received regulatory approval. Traditionally used products including nicotine, rotenone, sabadilla and ryania are now little used or being phased out by regulatory authorities, but use of pyrethrum is increasing. Despite major research interest a decade ago, antifeedants, especially neem and azadirachtin based products have made a relatively modest impact in the field. Essential oil products have recently emerged as the most important botanical insecticides. Research has demonstrated the potential of a number of other experimental plant natural products as botanical insecticides including piperamides, acetogenins, thiophenes, and limonoids.

1. Introduction

Botanical pesticides have a proven track record and long use as simple extractives for pest control and have spun off important groups of synthetic pesticides from phytochemical leads such as pyrethroids and neonicotinoids. While botanicals are now a small part of the overall pesticide market due to replacement by synthetics, the new environmental movement has provided a favorable environment for the rebirth of botanical insecticides. Public concern over use of synthetic insecticides is growing. This has led to the large growth in organic agriculture where the industry self-regulates the use of products restricting synthetics but allowing some botanical pest control. In many cities in Europe and North America, cosmetic use of synthetics is now banned in urban areas. Public resistance to adoption of Genetically Modified Organisms is another factor favoring alternative control measures such as biopesticides, biocontrol and other methodologies.

In reality, however, botanicals have certain advantages but an equal number of drawbacks in practical use. The advantages of botanical pesticides lie in their rapid degradation and lack of persistence and bioaccumulation in the environment, which have been major problems in synthetic use. For example DDT residues are still present in some sandy soils in Ontario decades after use was discontinued and contaminate some medicinal crops, grown in these soils to levels which are a barrier to their export. Our research with a number of experimental botanical pesticides such as piperamides and alpha terthienyl, shows they are degraded in the environment in hours or days. A long history of safe use for some plant natural products provides also some confidence about low risk, although this cannot be assumed for new products. The diversity and redundancy of phytochemicals in botanical extracts is also useful. Redundancy, which is the presence of numerous analogs of one compound, is known to increase the efficacy of extractives through analog synergism, reduce the rate of metabolism of the compounds and prevent the evolution of pesticide resistance when selection occurs over several generations .From a research discovery point of view, the number of insect deterrents derived from plants seems endless as co-adaptation appears to have produced a huge diversity of novel compounds across the plant kingdom and a remarkable redundancy of plant defenses within each plant species. Research activities have provided application for behavior modifying antifeedants, essential oils with repellant fumigant and insecticidal action and a large number of agents with novel modes of action.

Despite many advantages, the botanical pesticide market has a number of major challenges and although there has been growth, it has not grown in a comparable way to botanical medicine market in recent years. Some of these challenges have been reviewed. The major hurdle is costly toxicology testing for new products which may have limited Intellectual Property (IP) protection and a relatively small market size. Other challenges include economical supply of plant product, quality control and lack of stability. There is, as well, competition from other biopesticide and biocontrol agents. The Environmental Protection Agency (EPA) has granted reduced registration requirements to a variety of traditionally used insecticide products on its 25B exempt list in the USA. This is the main area where there has been growth in botanicals in developed countries, but some new products are also emerging from developing countries.

In the present chapter a concise review is provided of botanical insecticides, with an emphasis on plant natural products that have received regulatory approval. We consider some of the products that have been on the market for a long time, as well as new materials and research trends. Other available reviews provide comprehensive coverage of all natural products as pesticide leads by Dyan et al, and research on botanical insecticides by Isman.

2. Traditionally used Botanical Insecticide Products

Traditionally used botanical insecticide products include nicotine, rotenone, ryania, sabadilla and pyrethrum. Although nicotine (Figure 1) and tobacco have a long history of use and are effective contact and ingested insecticides they also have extremely high mammalian toxicity and are candidates for regulatory phase out. Tobacco is still used in some greenhouse applications. Rotenone is the trade name of the insecticide derived from extracts of the tropical legumes *Derris* and *Lonchocarpus.* The main active principle, the isoflavonoid rotenone (Figure 1), is moderately toxic to mammals due to poor absorption and rapid metabolism, but is highly toxic to insects and fish, due to its rapid uptake and inhibition of respiratory electron transport at site 1. Rotenone has been widely available as plant extract at reasonable cost and used as a dust on horticultural and ornamental crops, but its use has been phased out recently in the US and Canada during regular re-evaluation. It continues to be used in other countries.

Sabadilla is the seed extract of the neotropical lily *Schoenocaulon officinale* which contains veratridine alkaloids which have a neurotoxic mode of action. The extract has low mammalian toxicity and is a useful contact insecticide against a number of agricultural insects such as lepidoptera, leafhoppers, and thrips. Ryania is an extract of from the South America shrub *Ryania sp.* containing the diterpene alkaloid ryanodine (Figure 1), which is a contact and ingested insecticide against horticultural and ornamental crop pests. It exerts its toxicity by blocking Ca^{++} ion channels. The market for these botanicals is relatively small.

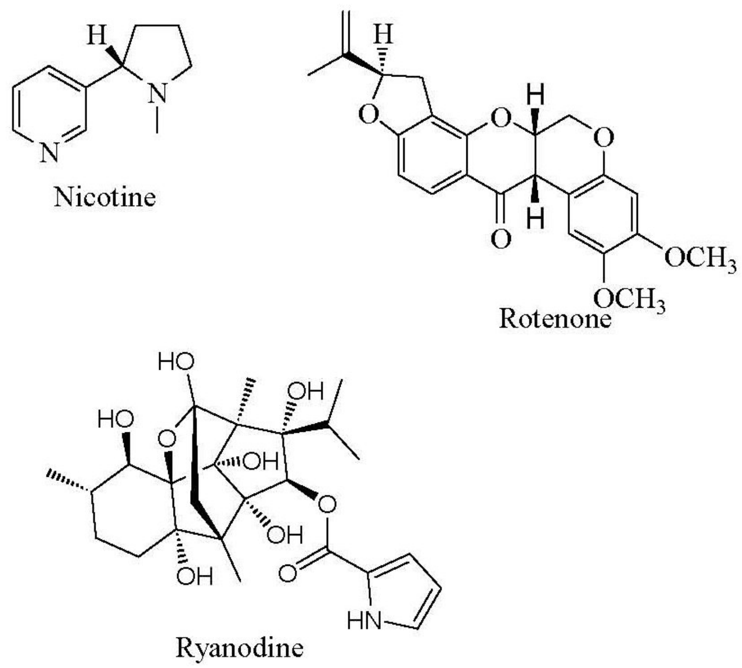

Figure 1 Traditional botanical insecticides

Pyrethrum is now the most important traditional botanical insecticide on the market. It is derived from the African daisy, *Chrysanthemum pyrethrum,* which produces an insecticidal oleoresin that can be extracted with organic solvents and pyrethrum extract contains six major pyrethrin compounds: pyrethrin I and II, jasmolin I and II and cinerin I and II (Figure 2). These compounds are monoterpenes derived from IPP and DMAP in which an unusual cyclopropane ring is formed, while the jasmolone functionality is derived from cyclization of fatty acid derivatives. The extracts are analyzed by HPLC for preparation of a standardized pyrethrin product. Pyrethrin is valued for its quick knockdown of flying insects especially of mosquitoes and houseflies, but is effective against a wide variety of home and garden and nuisance insects, due to its action on the insect nervous system at the Na^+ channels. It has low mammalian toxicity but does have significant toxicity to fish and aquatic invertebrates. With the development of more stable and effective synthetic pyrethroids during recent decades, the market for natural pyrethrum declined, while synthetic pyrethroids have become major commercial products. Natural pyrethrin is now showing revival again due to the interest in natural pest-control methods.

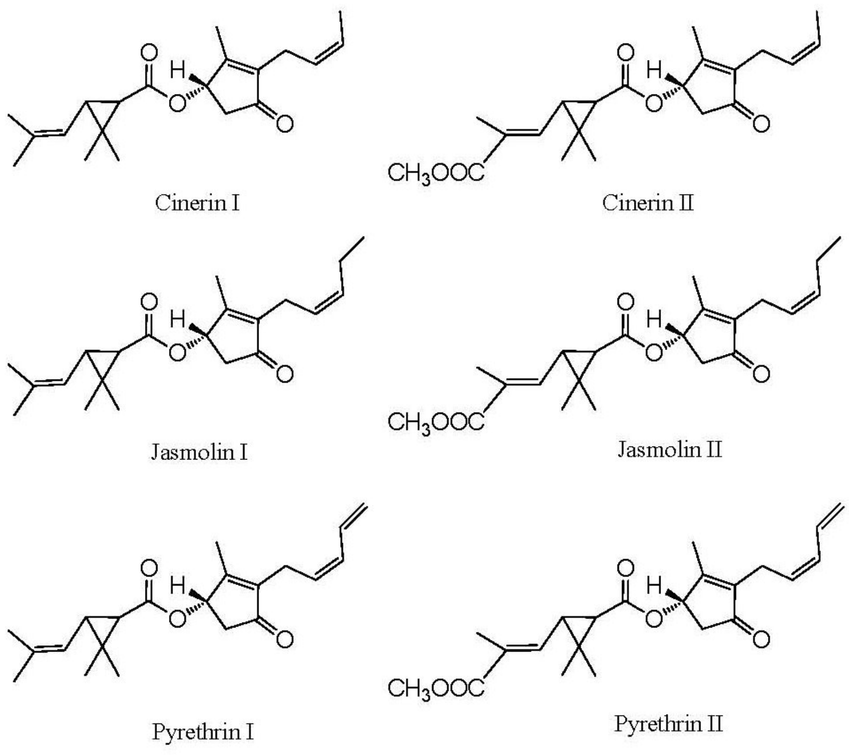

Figure 2. Pyrethrins from Chrysanthemum pyrethrum

The potential use of pyrethrum in organic agriculture has created new issues for the pyrethroid industry. Although the oleoresin is a natural product, its extraction in producing countries such as Kenya and Indonesia involves the use of undesirable solvents for organic agriculture such as petroleum ether and hexane. In order to avoid solvent residues left during this extractions for the organic pesticide market supercritical CO_2 extraction (SCE) has been proposed as a means to prepare a cleaner oleoresin product. SCE is a high efficiency process that has exceptional solvent properties due to the supercritical phase. The oleoresin can be obtained in good yield directly by SCE from pyrethrum flowers but the developing countries where the product is produced lack these expensive industrial installations. An alternate procedure is to clean up the oleoresin product using supercritical extraction after export. This has been achieved successfully optimized on both lab and pilot scale in recent experiments by Kramp. The SCE process at 40 C and 10 Mpa yields 0.51g/g pyrethrin concentration as a highly pure solvent free oil for commercial application as an insecticide. The oil is of high enough quality to be introduced directly into a preparative HPLC for the rapid separation of pure pyrethrins, cinerins and jasmolins in good yield for standardization purposes. Significant levels of hexane found in the crude oleoresin, fell below detectable levels in the SCE extract.

Another issue in developing pyrethrum products for the organic market is the need to use synergists in pyrethrum products. Synergists are required because pyrethrum is quickly metabolized and rapidly loses activity against insects without them. Conventionally the synergist piperonyl butoxide (PBO) has been used which enhances pyrethrin activity about 4 times through the inhibition of cytochrome P450 enzymes. PBO is a synthetic compound and therefore not suitable for use in organic agriculture. There are naturally occurring cytochrome P450 inhibitors which could replace PPO in botanical insecticide formulations, including historically used naturally occurring lignans such as sessamolin, tryptophan derived alkaloids and a large number of medicinal plant extracts. An exceptional synergist that has been investigated recently is the extract of black pepper. Like PBO black pepper extract has a potent activity as inhibitors of cytochrome P450 enzymes, but also inhibits Na^+ channels. In trials with fruit flies a remarkable synergy ratio of 11.6 times was observed with pyrethrum and pepper combinations whereas the synergism ratio with pyrethin and PBO is 4-5 times.

Taking advantage of recent advances in transcriptomics, the mode of action and response of insects to a pyrethrum and pyrethrum pepper combination has been studied. Using a fruit fly microchip the dysregulation of genes in treated fruitflies showed that pyrethrin upregulated 70 genes and downregulated 25 genes. Several of these genes were phase one and two metabolism genes that provide a robust biochemical response to metabolize and excrete toxins like pyrethrin. Addition of the pepper synergist led to upregulation of only 5 of these genes and downregulation of 2.

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