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The future of pest control and the pesticides industry

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Abstract - The pesticides industry needs to look differently from the existing basis that toxic materials are required in order to eliminate pests and weeds from food crops. New generation of pesticides will be motivated by a knowledge of metabolic pathways. The article reviews the effectiveness of several classes of natural pest control agents such as: pheromones, allelopathic chemicals, toxicants from tropical and desert plants, naturally occurring hormonal agents from insects and plants, microbial agents, plant growth regulators, and natural products as inducers of insect resistance.

The word 'Pesticides' is a broad term which covers a large number of more accurate names such as: Insecticides, Herbicides, Fungicides, Rodenticides, Miticides, Algicides, Nematicides etc. The term pesticides also applies to compounds used as repellants, attractants and insects sterilants or chemosterilants.

Pesticides are classed as 'economic poisons' and are defined as "any substance used for controlling, preventing, destroying, repelling or mitigating any pests". A group of chemicals are included in the word pesticides that do not actually kill pests but due to the fact that they fit into the broader umbrella of pesticides in a practical sense. Among these are chemical compounds that stimulate or retard growth of plants and sometimes insects growth regulators, those that remove leaves, defoliants or speed the drying of plants, desiccants and are used for mechanizing the work in harvesting cotton, soybeans, potatoes and other crops.

THE WORLD PESTICIDE MARKETS

The world pesticides sales are estimated at the user's level to be about $ 13.8 billion, in the year 1985. Looking ahead 5 years the experts are predicting sales of $15.7 billion, a rise in sales of $2 billion.

A survey conducted by a journal of agrichemicals reveals that, on an average 9% of sales are being returned to research and development.

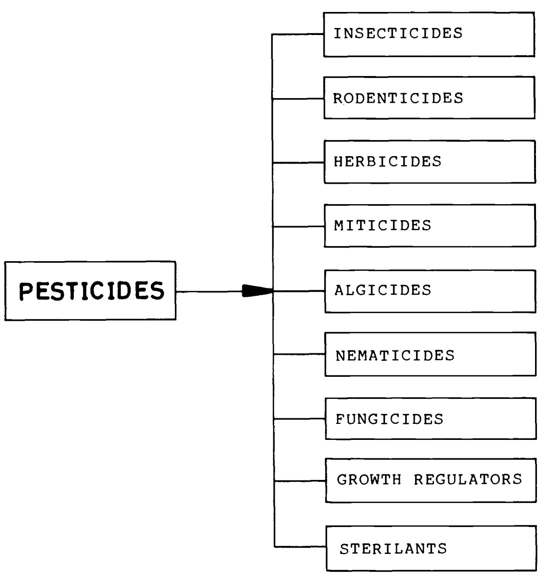


Table 1 The World Pesticide Markets (Incl. USA) (User's Level) (Million of US 1984 Dollars)

Pesticide	1980	1985	1990
Herbicide	4,891	6,331	7,183
Insecticide	3,916	4,268	4,815
Fungicide	2,199	2,537	2,947
Other	559	642	804
TOTAL	11,565	13,778	15,749

Genetic engineering/biotechnology is attracting considerable amount of money for R & D.

Despite the tragedy at Bhopal (India), developing countries will continue to demand local production and formulation of agrichemicals particularly in East Europe, Asia and the Middle East.

The main problems to be confronted are:

(i) Increasing negative attitude against the use of agricultural chemicals in food, feed and fibre production.

(ii) Registration delays for new compounds.

(iii) Environmental restraints.

(iv) Lack of national financial resources and infrastructure and extension support for farmers, in the developing world.

NEW TRENDS

The pesticide industry has evolved on the basis that toxic materials are required in order to eliminate pests and weeds that detract markedly from yield of food products. The toxicity of pesticides and their damage to the human species has long been recognised. The problem was brought to a head by Bhopal.

There is no question that the proper use of the existing pesticides has made them, along with fertilizers, the major factor in the preservation of the human race. Although exact figures are difficult to provide, starvation would ensue in the world were it not for the green revolution with its dependence, in part at least, on pesticides.

Is it possible to accomplish in the future what pesticides have been able to do for us in the past fifty years with materials which are much less toxic ? The answer appears to be yes, although the point cannot be stressed too much that intensive and expensive development will be required.It is encouraging however, that non-toxic pesticide materials have been earmarked for development.

New pesticides will be motivated by knowledge of metabolic pathways. There is nothing new about this. Sulfanilamide and penicillin work because they interfere with the metabolic pathways of microorganisms. Knowledge of metabolic pathways, however, has multiplied manyfold since the development of these simple antibiotics. It is this knowledge which is being put to work in the synthesis of pesticides that are toxic to harmful organisms but not to higher species.

Several classes of material, most of them natural pest control agents, are being investigated. These include:

Pheromones
Allelopathic chemicals
Toxicants from tropical and desert plants
Naturally occuring hormonal agents from insects and plants
Microbial agents
Plant growth regulators
Natural products as inducers of insect resistance.

SERIOUS PROBLEMS IN PEST CONTROL

Following are some of the most serious problems in the pest control:

(i) Persistence: Persistence is a hazard that is exemplified by chlorinated hydrocarbons, which have been found in areas as remote as north and south poles.

(ii) Lack of Specificity

(iii) Broad Spectrum activity has advantages, but also concomitant dangers, such as effects on non-target organisms including beneficial insects, microorganisms, birds, wild life and other animals.

(iv) Build up of resistance in a number of insects, diseases of crop plants and animals including man.

(v) Reliance on too few pesticides hastens the natural selection of resistant strains. Larger and larger quantities of pesticide is required when resistance is already built up.

(vi) Distribution of pesticides is a problem most encountered in developing countries.

RESEARCH OPPORTUNITIES FOR PEST CONTROL IN FUTURE

In view of the Bhopal tragedy, safety and efficiency measures have become very stringent. Fewer pesticides may be available due to this. After 1990, third and fourth generation pesticides are not likely to get a large market share. Pesticides with novel and specific action will be in great demand. Maximization of yield will be needed to feed the increased world population.

Evaluation of the effects of pesticides on the environment will receive more attention. Research data will have to be generated so as to convince the people about the minimization of the side effects of the pesticides.

Pest control will include techniques of new food production systems and preservation technologies. Food production systems will be Computer controlled which will combine remote sensing devices and field treatments.

There will be a greater integration of insecticide, herbicide and fungicide strategies.

In addition to chemists, scientists of different disciplines such as physiology, toxicology etc. will be needed for the pest control programme. Chemists will be required to study genetics and computer science.

Improved knowledge of genetic engineering will provide the technology for introducing lethal genes into pests and protective genes into crop plants and animals. Pesticides will be used at a submicrogram level to control specific processes such as behaviour, development and reproduction. They will be target specific and have limited or no carcinogenic activity.

A brief description of the new trends in a few different areas under the term pesticides is given herewith.

Insecticides

The first organophosphate insecticide was synthesized by Schreder in 1940 by the trade name, Bladen. Many other Organophosphates were introduced in 1950s. One of the most important of these Organophosphates was Malathion introduced by American Cyanamide in 1950. Malathion was followed by Imidan, Dyfonate, Diazinon, Supracide, Azodrin, Eldrin and Phosdrin etc. gained importance all round the world for almost all the important crops such as rice, corn, potatoes, fruits, grapes, in sugar beets and other crops.

In addition to the agricultural market Carbamates gained outstanding importance as public health insecticides. For example Baygon was found to be an excellent insecticide against almost all species of household pests. It activates the pest insects in their hiding places and causes them to emerge and thus come in intensive contact with the active material. This is an excellent example of combination of behavioral and insecticidal action.

In the 1960s "environmentally" more acceptable compounds were discovered. The first investigation was the insect hormone mimics and the second was the development of light stable pyrethroid insecticides. Further devlopments gave rise to the insect growth regulator and biological insecticides incorporating other modes of action. The development of pyrethroids has achieved the greatest acceptance in crop protection. Permethrin and Pydrin are used at approximately one-tenth the rate of Organophosphates and Carbamates. Following these several other pyrethroids were developed such as Pay-off, Mavrik, Cypermethrin, Baythroid and Scout that are highly effective.

Fungicides

The history of fungicide development can be divided into four distinct areas, based on kinds of chemistry or mode of action of the fungicide utilized:

(i) Sulphur Era (Ancient times to 1880s)
(ii) Copper Era (1880s to 1950s)
(iii) Organic Protectants Era (1950 to present)
(iv) Systemic Era (1970 to present).

The classical copper, sulphur and mercury based fungicides are still in great use in the form of Bordeaux mixture. Copper based fungicides are valuable for use in such crops as coffee, cocoa and tea. Their use for control of potato, late blight and vine downy mildew has been somewhat reduced by the newer organic fungicides.

Spraying with organo- mercurial fungicides has greatly declined although aryl mercurial compounds are still widely applied as cereal seed dressings to combat seed borne fungal diseases. Due to dangers of environmental pollutions use of organo-mercurial seed dressings has been severely restricted in several countries.

New developments in fungicides, both surface and systemic, which may be substituted for organo mercurials as cereal seed dressings, are mainly the heterocyclic derivatives. Among fungicides without hetero atoms there are several derivatives containing cyclopropane rings, some of which are analogous to the new synthetic pyrethroid insecticides.

Plant growth regulators

The use of plant growth regulators in agriculture started from a very small base in the early '30s with the use of a number of different synthetic auxins for the rooting of cuttings. Growth retardant compounds such as chlorphonium, chlormequat chloride, and maleic hydrazide were developed for use in floriculture and nursery crop production.

Perhaps the greatest research effort in PGR's is the search for compounds to specifically enhance crop yields. Some success has already been achieved in this area.

The yield of rubber from Hevea rubber trees has been increased 200 - 300% by the use of ethephon. The yield of pineapple plants has been greatly increased by the use of 3-CPA [Sodium 2 (3-chlorophenoxy) propionate].

Almost all major agronomic crops now benefit from the use of PGR's at some stage of their development.

During the past few years there has been a considerable increase in the research effort devoted to plant growth regulation. A large part of this effort has been devoted to basic studies, for we need to understand the basic physiology and biochemistry processes in the plant if we are to develop chemicals to control these processes. Many of these controls will eventually be built into the plant by genetic engineering processes presently under study by biotechnologists in both the public and private sector.

The future research in plant growth regulators will be mainly in the following areas:

Resistance to herbicidal injury and stress conditions.
Direct enhancement of yield.
Control of transpirational losses.
Regulation of chemical composition of the crop.
Broad spectrum growth inhibition.
Control of flowering (initiation and inhibition).
Delay of inhibition of senescence.
Control of dormancy in woody plants.

Biotechnology

Pesticide chemists are shifting the emphasis from 'kill' to 'control'. It is time to get rid of the '-cide'. Focus on new concepts is control of insect growth and control of pests with natural products. The approach is more subtle: stop them from feeding, stop them from breeding, prolong their adolescence, hasten their senility, mess with their brains.

Insect hormones and pheromones are important parts of the picture, but it is the brain activity that controls their production and also the insects response to them. Therefore, the insect brain is a likely place to look for clues on developing efficient new insect control substances.

Not much is known of the biosynthetic mechanisms by which the substances are produced or of the endogenous factors that control their timely release, or of the elfactory chemoreceptive process that enables the signals to be received. All these areas present promising avenues for research. Researchers should work to identify insect neurotransmitters, then look for receptor antagonists to develop new insecticides.

Inhibition of the key enzymes being the approach to pest control, inhibitors of juvenile hormone esterase have been developed.

Pheromones have also played a vital role in this new era of crop protection. Their use as sex attractants to monitor for possible pests outbreaks has allowed us to better target our insecticide applications. Pheromones are compounds released as signals by organisms of a species that after reception or uptake by other members of the same species provoke certain rections in latter. Pheromones serve as sex attractants, stimulants and sedatives, congregation scents, alarm signals, tracking and marking signs, and social signals. The specific effect of minute quantities on the target organism is characteristic of this class of compounds. Pheromones have low toxicities and seldom cause any side effects.

Various methods are available for influencing and controlling pest population, e.g. by attracting the insect to a site where it can be destroyed. The protracted exposure to the sex pheromones can send the insects into a hyperactive phase that is followed by an inactive phase. With an excessive supply of attractant sources in the form of pieces of paper or cork particles soaked in pheromone, it is possible to provoke insects into numerous unproductive populations.

A new sex pheromone was discovered from the azuki bean weevil and was named as 'Erectin'. It is not a long distance sex attractant. It is a synergistic mixture of C_{26} to C_{35} hydrocarbons and (E)-3,7-dimethyl-2-octene-1,3-dioic acid. Neither the hydrocarbon nor the acid works by itself. In this case a glass rod or aluminium foil or any other surrogate has been dosed with the pheromone. Male will be attracted towards it and try to copulate. In other words it is the apparent reversal of the sterilized male technique which may become a new population control approach. Of all the potential developments, pheromones are closest to the marketplace.

Genetic engineering is basically a method to cross-breed or hybridise different organisms. Half of the heredity comes from male and half from female, each contributing half of the thousands of genes to the hybrid seed and the hybrid plant that grows from it.

With genetic engineering scientists can take just one or several genes from one organism - a corn plant, a bacterium or a cow - and grant these genes to completely different organisms to produce a hybrid with new properties.

Through genetic engineering it is possible to achieve rapid plant breeding and confer desirable traits on important crops. One such trait is resistance to insect attack. Scientists are learning how to genetically engineer genes into crops that make the crops naturally resistant to insects. Further work is to make them resistant to attack by fungi, bacteria and nematodes.

By 1990s it is expected that some major crops resistant to insects and other pests will be available through the plant genetic engineering. It will result in the decreased dependence on pesticides. The central thrust of plant protection will get shifted from treatment to prevention. It will enhance the productivity per acre and also enable to bring non-cultivated land under use.

Herbicide resistance is also of commercial importance and should increase the spread of minimum-till agriculture. Monsanto have recently disclosed a genetic engineering technique to make plant cells and whole plants resistant to the herbicide glyphosate. Robert T. Fraley and Dilip Shah of the Biological Sciences Group (at Monsanto) inserted a modified gene that codes for 5-enol pyruvyl shikimate-3-phosphate synthase (EPSP Synthase) into petunia or tobacco plant cells to yield plants resistant to the herbicide Glyphosphate. Monsanto plans to field test a soil microbe named as pseudomonas fluorescens that has been genetically engineered to make a protein insecticide.

Another aspect of biotechnology which is potentially important to agriculture is the development of genetically engineered soil bacteria to enhance crop yields. These genetically modified bacteria would be added to the soil or to the seed. Bacteria that invade the roots of soybeans and "fix" nitrogen there to the benefit of soybean plants are familiar examples.

Soil microbes can also be used for protecting the roots of plants from insects, disease or viral attack. This development will lead to biological control of plant pests.

In near future genetically engineered soil microbes that produce specific and naturally occurring pesticidal chemicals, will be developed and their environmental impact will also be carefully studied. These will be of great value to both developed and developing countries, where highly mechanised and high performance agriculture is practised or not.

Microbial pesticides will be less capital intensive than many of the present traditionally used products. This will enable the farmers to use them particularly in developing countries. Many discoveries are needed for further development in this area.

Biology can control the pests by many alternative routes such as:

(i) By male sterility. Large number of insects are sterilized through radiation and then released to compete with normal males for the females in their natural environment. In this autocidal campaign the insect spreads sterility and eventually eradication through its own population.

(ii) Derivatives of anacardic acid when injected to female cricket, it failed to lay eggs after mating with male crickets. This method may become useful for pest control for cockroaches if it can be fed to the insects. Anacardic acid, extracted from the root bark of the african msimbwi tree, strongly inhibits a complex of enzymes called prostaglandin synthetase. Thus inhibiting the enzymes, the eggs are not released.

NATURAL PRODUCTS

Allelopathic chemicals

Allelopathy means mutual harm, the emitting species generally gain some advantage and recipient is harmed.

Allelochemicals are attractive because they are natural products made by plants or microbes. One can either manipulate the producing organism in the field or use them as a factory for batch production of chemicals.

Chung-Shin Tang and Chin-Chung Young at the University of Hawaii, recently developed a simple system that allows the recovery of toxic root exudates from plants into the rock and sand media. The continuously circulated nutrient solution elutes allelopathic substance from the media, this then passes through an AD-4 adsorptive resin which traps the allelochemicals.

It is also found that addition of chlorine to these molecules produces greater herbicidal activity and soil persistence.

Mode of action of allelopathic chemicals is as follows:

(i) Allelopathics can alter the rate of ion uptake of plants and thereby affect the intake of magnesium, potassium, calcium, manganese and iron. This will affect the growth of the plant.

(ii) Allelopathics inhibit mitosis in plant root and divisions of bacterial species due to the break down of Indole acetic acid (IAA).

(iii) Allelopathics act as photosynthetic inhibitors.

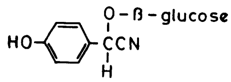
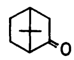
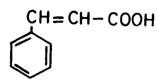
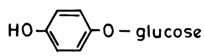
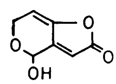
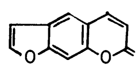
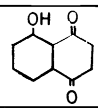
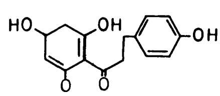
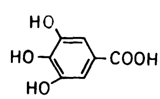
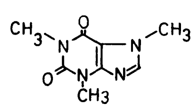
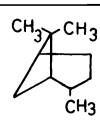
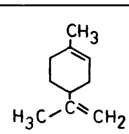
(iv) Inhibit or stimulate respiration of plants.

(v) Inhibit protein synthesis and production of enzymes by altering membrane permeability.

(vi) Allelopathics produced by cover crops inhibit seed germination of weeds.

Table 2 gives the list of some important allelopathic compounds, isolated from plants, microbes and soils. The natural plants or microbial products can be modified slightly to give them greater activity, selectivity or persistence.

TABLE 2: ALLELOPATHIC COMPOUNDS ISOLATED FROM PLANTS, MICROBES, AND SOILS

Chemical name	Class	Structural formula	Natural source	Effects
Dhurrin	Cyanogenic glucoside		Sorghum plants	Inhibit seed germination, seedling growth
Allylisothio-cyanate	Thiocyanate	$CH_2=CHCH_2NCS$	Mustard plants	Inhibitors of seed germination
Camphor	Monoterpene		Salvia shrubs	Formation of zone of inhibition inhibit growth of annual plan
Acetic Acid	Aliphatic acid	CH_3COOH	Decomposing straw	Inhibit seed germination
Cinnamic acid	Aromatic acid		Guayule plants	Insecticides, fungicides, growth control
Arbutin	Phenolic compound		Manzanita shrubs	Antimicrobial agent
Bialphos	Amino acid derivative	$CH_3-\overset{O}{\overset{\Vert}{P}}-CH_2CH_2-\underset{NH_2}{\overset{H}{C}}-\overset{O}{\overset{\Vert}{C}}-NH-\underset{H}{\overset{CH_3}{C}}-\overset{O}{\overset{\Vert}{C}}NH-\underset{H}{\overset{CH_3}{C}}-COOH$	Micro-organisms	Herbicides
Patulin	Simple lactone		Penicilium fungus on wheat straw	Inhibitors of seed germination
Psoralen	Furano-coumarin		Psoralea plants	Inhibit seed germination
Juglone	Quinone		Black walnut trees	Causes wilt to the crop
Citric acid	Aliphatic acid	$HO-\underset{CH_2COOH}{\overset{CH_2COOH}{C}}-COOH$	Grape and	Inhibit seed germination
Phlorizin	Flavonoid		Apple roots	Toxic to young apple trees, insecticide
Gallic acid	Tannin		Spurge plants	Inhibit seed germination, nitrogen fixing and nitrifying bacteria and plant growth
Caffeine	Alkaloid		Coffee plants	Kills several weeds
α-pinene	Terpenoids		Salvia shrubs	Insecticide
Malic Acid	Aliphatic acid	$HO-\underset{CH_2COOH}{CH}COOH$	Apple and tomato fruit	Inhibits seed germination
d-limonene	Terpene		Orange and mandarin peel	Insecticide

Natural defences of the plants

Plants produce a wide variety of secondary metabolites as defensive weapons. These include alkaloids, cyanogenic and triterpenoid glycosides, non-protein amino acids, phenols and flavonoids. Such natural chemical defences are 'far superior' to the synthetic pesticides chemists have deployed against plant predators during the past 40 years.

If we can isolate the protective chemicals produced by plants and determine their chemical structure, this could provide valuable pointers to the development of new pesticides and novel methods of pest control.

The ultimate in natural resistance seems to have been bestowed on the Neem tree, which is a sub-tropical tree in the arid regions of India, Pakistan, Sri Lanka and parts of South East Asia and Africa. For centuries it's been known in these areas as being virtually free of insects, nematodes and diseases. All parts of the Neem tree appear to be resistant, although the seeds are especially blessed in this regard. During the past decade scientists have shown that extracts and formulations of the seeds are highly effective against at least 128 species of crop pests.

Chemists have isolated and identified several active compounds in Neem seeds. The most important one is the complex triterpenoid called "Azadirachtin"after the genus of the tree azadirachta. Azadirachtin itself is effective against atleast 40 species of insects in the U.S. It works at concentration as low as 0.1 ppm. The molecular structure of azadirachtin is so complicated that it is highly unlikely that it will be synthesized for commercial production. These Neem formulations have been shown to be biodegradable, non-mutagenic, non-toxic to warm blooded animals, fish and birds. EPA of U.S. has recently approved the marketing of Neem formulation as a pesticide for limited use on non-food crop.

These expectations reflect scientist's growing realization that beyond merely emulating nature they can in fact improve on it.

ALTERNATIVE ROUTES TO AVOID HAZARDS

Pesticide Chemistry is concerned with the protection of humans and live-stock as well as plants. In addition to the environmental effects of the existing pesticides, the manufacture of these pesticides involves hazardous chemicals.

Bhopal was one of the greatest tragedies in this respect. At Union Carbide, Bhopal ,Carbamates were manufactured. Compared to Organo-phosphates the volume required of carbamates is much less. Most carbamates are manufactured by the interaction of methyl isocyanate (MIC) with the hydroxyl group of phenol, heterocyclic compounds or oxime. Isocyanate results from reaction of phosgene with methyl amine:

$$CH_3NH_2 + \underset{\text{phosgene}}{COCl_2} \longrightarrow \underset{\text{methyl isocyanate}}{CH_3NCO} + 2HCl$$

Alternative routes must be explored for manufacturing methyl isocyanate, which do not require the use of hazardous chemicals like phosgene. One of the alternatives proposed can be interaction between methyl chloride with sodium cyanate. A better method is said to have been offered by DuPont and possibly by others, involves the interaction of oxygen from air with N-methyl formamide:

$$\underset{\text{N-methyl formamide}}{2HCONHCH_3} + \underset{\text{(air)}}{O_2} \longrightarrow \underset{\text{methyl isocyanate}}{2CH_3NCO} + 2H_2O$$

Although the use of phosgene for making methyl isocyanate is avoided, and the manufacturing hazards are decreased, the problem of toxicity is still not eliminated.