ORGANOPHOSPHORUS INSECTICIDES - A REVIEW

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Introduction

Prior to the 1960's, organophosphorus insecticides (OP's) were not very popular. Organohalogen compounds like the now famous DDT were regarded like "magic". These were used in bulk and added to the environment without anyone thinking about the effect that this would have on health and the environment. During the 1970's all American adults had detectable levels of DDT in their fat. Bioaccumulation, bio-magnification and the excessively long half-life eventually led to the ban of most of them and nowadays the production is almost nil except for a few compounds with a short half-life. The place of the organochlorines was eventually taken by the organophosphates, carbamates and recently by the synthetic pyrethroids.

OP's were developed in Germany during World War II as a substitute for nicotine, which was in short supply. These insecticides work by inhibiting acetyl cholinesterase, the enzyme which destroys acetyl choline at synapses. For this reason more powerful agents were synthesized in Nazi Germany during World War II to be used as chemical warfare agents namely Sarin, Tabun and Soman.

The first OP's used in agriculture were very toxic, non selective and unstable especially as regards to hydrolysis. However nowadays OP's, although still toxic agents, are more selective. OP's have a relatively short half life both in vivo and in environment, however they are acutely toxic when compared to other insecticides (Table 1).

Due to their short half life and rapid rate of metabolism in vivo, OP's have a low potential of chronicity, although continued, low level exposure may inhibit acetyl cholinesterose to low dangerous levels.

Toxicity of OP's

A review of the toxicology of OP's is presented in Chapter 1. OP's are absorbed readily from all routes of exposure i.e. dermal, oral or respiratory routes. They may cause sensitization on contact with the skin.

Systemically OP's are potent, irreversible inhibitors of acetyl cholinesterase. Consequently after acute intoxication there is accumulation of acetylcholine at nerve endings. The result of this are nicotinic and muscarinic effects. The muscarinic effects are observed in the smooth muscles of the lungs, GIT, and exocrine glands like salivary, lachcymal and sudorific glands.

Table 1: Toxicology of some insecticides

Insecticides	Class	(a)	(b)	(c)
malathion	organophosphate	>4444	1375	0.02
dichloruos	organophosphate	107	80	0.004
lindone	organochlorine	1000	88	0.008
carboyl	carbamate	>4000	850	0.01
	Pyrethroids	>5000$^{\Delta}$	200-1500$^{\Delta}$	0.07*

(a) LD 50 $mgkg^{-1}$ Dermal
(b) LD 50 $mgKg^{-1}$ Oral
(c) ADI^{+} $mgKg^{-1}$
\+ ADI - "allowed daily intake" values are obtained from Toxicity evaluations performed by the Joint FAO/WHO meeting on pesticides residues (JMPR) through 1990.
Δ Data obtained from "Toxicity of pyrethrins and its constituents to mammals", William F. Barthel. Pyrethrum the natural pesticide. Academic press pp. 124-141 App..X.
* Value for phenothrin a synthetic pyrethroid. N.B. Pyrethrum is a natural product extracted from species of chrysanthemum while pyrethroids are synthetic, modified analogues.

Cardiac effects are observed due to both nicotinic and muscarinic receptors. The nicotinic effects are observed in the autonomic nervous system and skeletal muscles.

The summation of muscarinic and nicotinic effects result in a "cholinergic crisis". If this remains untreated the patient will perish from respiratory failure and possibly from cardiac block. If the patient survives there is a probability of developing organophosphate induced delayed polyneuropathy (OPIDP). This is a phenomenon which is seen with some OP's and is independent of anti cholinerterase activity. Tri orthocresyl phosphate (TOCP) and leptophos are two OP's causing such delayed symptoms. Such phenomenon is usually observed 2-4 weeks after intoxication and exacerbates during the next few weeks to months.

Paralysis and wasting of the distal muscles of the limbs are the characteristics of this delayed phenomenon. Sensory disturbances may also be present and are the first to disappear. However recovery takes months or even years and is seldom complete.

Organophosphates are also immunosuppressive, carcinogenic and teratogenic in animals.

Table 2: Comparison of potential for chronic intoxication of some chemicals*

Compound	Class	C.I.
Dieldrin	Organochlorine	12.8
DDT	Organochlorine	5.4
Warfarin	Coumonin	20.8
Paraquat	Bipyridyl	5.4
Potassium Cyanide	/	<0.04
Dichloruos	Organophosphate	<0.80
Azinophosmethly	Organophosphate	0.64

C.I. Chronicity Index
* Edited from Toxicology of Pesticides, Wayland J. Hayes. Jr. pp. 47. 1975.

Clinical aspects of organophosphates

The second chapter concerns clinical applications of organophosphates, since some of these agents are useful clinically. A review of clinical treatment of intoxication is also presented.

One of the uses of these agents is as ectoporasiticides. Malathion is the agent used in this field. It is safe and effective and is quite effective against scabies, pediculosis etc.

Another agent used clinically is Metrifonate. This is an anthelminitic used against the fluke, Schistosoma haematobium.

Primary glaucoma, both acute congestive and chronic simple are amenable to treatment with anti cholinerterase agents. These act by decreasing the resistance to the outflow of aqueous humoue. For this reason echothiophate and isofluorophosphate, two OP's, are used.

OP's have also received attention for the treatment of Myasthenia gravis but with little results. OP's show also a variety of interactions with a number of drugs.

Clinical management of OP acute intoxication relies upon pharmacological treatment with drugs and supportive therapy. Effectiveness depends much on early and drastic treatment. Atropine in relatively high doses is used to combat the muscarinic effects of OP's. Nicotinic effects are reversed. Antidotal therapy is available, effective and used in conjunction with atropine. Pralidoxine and other oximes are the antidotes. Other agents are used to accelerate elimination of OP's namely cathartics, emetic and activated charcoal.

The effect of OP's on the environment

Soil composition has an important effect on the half-life of the OP's. OP's are absorbed on clay and organic matter and hence the higher the concentration of these two components the longer is the persistence. However toxicity is greatly reduced since they are not bioavailable.

Another important factor in soil and in water is the pH. OP's are relatively unstable in the presence of water and this instability is greatly enhanced at high pH's. However, one exception to this is diazinon.

Table 4: Persistence of Trichlorfon (hrs) at different pH's

pH	1	3	5	7	9
Persistence (hours)	32	33	15.3	0.7	0.1

Table 5: Persistence of Parathion (days) at different temperatures in solution

Temperature	10	20	30	40	50	60	70
Persistence (days)	3000	690	180	50	15	4.75	1.65

Another factor common to both water and soil is the microflora and fauna present. Certain organisms namely *Bacillus cereus, Pseudomonas melophthora* and the fungus *Trichoderma viride* can metabolise OP's and certain organisms can utilise these as an energy source.

Light increases degradation of OP's in air, water and at the surface of soils. Photolysis and photoxidation is a serious problem in the absence of moisture since the oxygen analogue of the OP may be produced. This is known as the oxon. These compounds are generally much more toxic than the original OP.

OP's are not found naturally. Hence contamination of the environment occurs through agriculture practice and from industrial plants producing such compounds.

The stability of Malathion in normal well water versus rabbit faeces contaminated well water

Methodology and Results

In this study the rate of decomposition of malathion in well water was compared to that in well water contaminated with faeces and urine. Two water samples, containing the same volume of well water with the same malathion concentration were used, but to one of these a quantity of rabbit faeces and urine were added. The samples were stored in a cupboard in the dark at ambient temperature and analyzed weekly. The technique used was extraction with dichloromethane. The extract was concentrated and than transferred into methanol. A Gas chromatographer equipped with a nitrogen phosphorus detection.

The samples were cultured for the bacteria present. In the first sample ('clean') pseudomonas were isolated. In the second, there were pseudomonas together with a large variety of other organisms. As already stated, pseudomonas can degrade OP's. The pH of the samples was also taken.

Table 6: pH values of samples tested

Sample	pH
Clean water	6.95
Contaminated	5.80

Conclusion

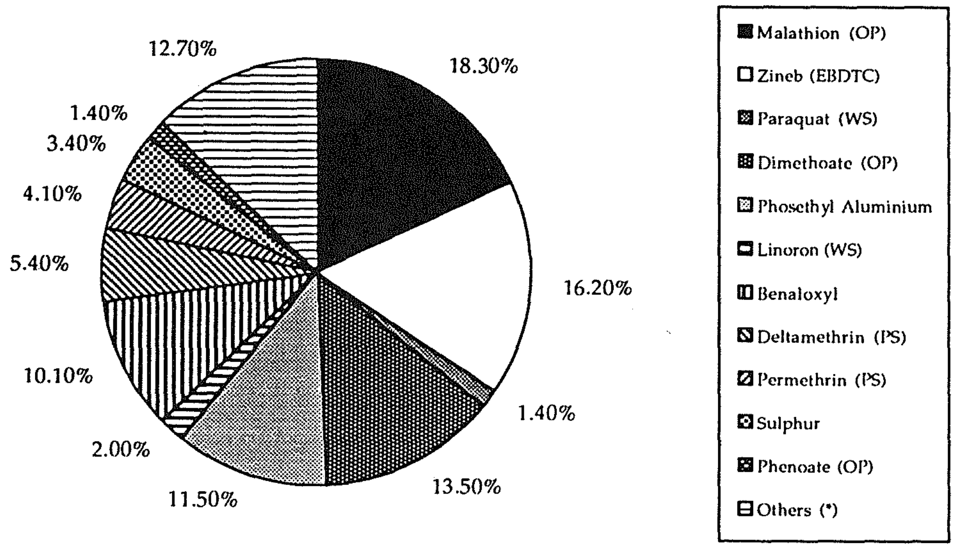
In both samples a heavy bacterial population was present, more significant in the second. On the other hand the pH was significantly more acidic in the contaminated sample, probably due to organic acids. Bacterial degradation was assumed to be very similar in both samples. Since there was no light present and the temperature was never higher than 30°C chemical hydrolysis was very low. Since the pH was lower in the second, therefore the rate of chemical degradation was lower here.

Pesticide use in Malta

A survey was carried out to investigate the use of pesticides in Malta. The factors investigated were the environment, safety precaution taken by the farmers and knowledge of the use of the pesticides by the farmers.

A total of 51 farmers were interviewed from every part of Malta. The total number of pesticides used by these farmers amounted to 27. These included insecticides, fungicides and herbicides (See Pie Chart 1).

The total percentage of OP's used is 34.5% of all pesticides. Climatic and physical composition of soil in Malta are ideal for eliminating the toxic potential of the large majority of pesticides. Bright sunshine, warm weather and high humidity, virtually all year round, are factors accelerating decomposition of pesticides. From the survey it was found that 12.3% of soils are clay, 86.0% loamy and just 1.7% sandy. Apart from this 93.8% of farmers use organic manure to fertilise their land either alone or in combination with chemical fertilizers. These factors as already mentioned sequester not only OP's but most pesticides and hence make them non bioavailable.



Pie chart 1.
OP = Organophosphates
EBDTC = Ethylene bisdithiocarbamates
PS = Pyrethroids
WS = Weed killers (general, NOT a class)
Others = Icluded are Ziram, Maneb, Triform, Glyphosphate and others making up a total of 18 pesticides

From a series of questions asked to assess knowledge about health and safety, it is clear that education is really necessary. 50.9% of farmers do not use a face m,ask or any protection routinely. 23.8% smoke or drink while applying pesticides and 52.9% do not have a clear idea why they use a particular pesticide. Some believe that pesticides are actually fertilizers, others do not distinguish between fungicides and insecticides and use them interchangeably.

In another series of questions concerning the actual use of pesticides, an excessive rate of application was noted. In fact 52.9% apply pesticides twice weekly or more. The time interval, usually of 28 days, between the last spraying and crop harvesting is not respected by 88.3% and 7.8% pick the crop within a few days after the last application.

Farmers lack the knowledge both for the correct use of pesticides and the health hazards associated with their use. For this reason an educational pamphlet has been prepared highlighting the most important points.