

12/10/95

**The toxic effect of long term administration
of some insecticides in cucumber
and squash on rats**

Thesis submitted for partial fulfilment
of
M.S. degree in Clinical Toxicology
by



Yaser Amin Khalifa Okasha
M.B.,B.Ch.

615.954
Y. A

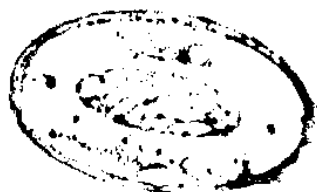
5/11/95

supervised by

Prof. Dr. Ahmed Kamel Mashhour
Professor of Forensic Medicine and Clinical Toxicology
Faculty of Medicine, Ain Shams University

Prof. Dr. Zidan Hendi Abdul Hamid
Professor of Pesticides, Vice Dean ,
Faculty of Agriculture, Ain Shams University

Dr. Asmaa Ahmed Fawzy
Lecturer of Forensic Medicine and Clinical Toxicology
Faculty of Medicine, Ain Shams University



1995

بسم الله الرحمن الرحيم

و قل ربى زدنى علما

صدق الله العظيم.



Acknowledgement

First and foremost thanks to God, I would like to express my deep gratitude and appreciation to Prof.Dr. Ahmed Kamel Mashhour professor of Forensic Medicine and Toxicology, Faculty of Medicine, Ain Shams University for his guidance, patience, and for giving me much of his precious time.

I am also extremely grateful to Prof.Dr. Zidan Hendi Abdul Hamid professor of Pesticides & Vice Dean of Faculty of Agriculture, Ain Shams University, for all the knowledge and research facilities that he supplied me with.

Many thanks to Dr. Asmaa Ahmed Fawzy lecturer of Forensic Medicine and Toxicology, Faculty of Medicine Ain Shams University

My deepest gratitude goes also to Prof. Dr. Abdul Hamid Zidan professor of Pesticides , Faculty of Agriculture, Ain Shams University for the tips and guidance that he gave me through my experiment.

My thanks also goes to Assist.Prof Tarek Mohamed Hashem assistant professor of Pathology, Faculty of Medicine , Ain Shams University.

Many thanks to my intimate colleague Taymour M. Khorshid who helped me through editing this work.

Words will never be enough to describe the support and encouragement that I had from my Mother and my Father to whom I will be always owed the matter what I ever do.

Finally, I would like to dedicate this work to My Wife and My Daughter , my source of light and inspiration.

Table of contents

<i>Introduction.....</i>	<i>1</i>
<i>Reveiw of literature.....</i>	<i>4</i>
<i>Aim of the work.....</i>	<i>36</i>
<i>Materials and methods.....</i>	<i>37</i>
<i>Results.....</i>	<i>49</i>
<i>Discussion.....</i>	<i>94</i>
<i>Conclusion.....</i>	<i>100</i>
<i>Recommendations.....</i>	<i>102</i>
<i>Summary.....</i>	<i>105</i>
<i>References.....</i>	<i>108</i>
<i>Arabic summary.....</i>	<i>121</i>

INTRODUCTION

INTRODUCTION

The wide use of pesticides in the agriculture field, either individually or in different combinations, although it improved the quantity of the harvests, its quality regarding the remnants of the pesticides (residues) in the fruits, leaves or any other part of the plant is really threatening the health of its consumers.

Numerous concerns have been raised as the interests in pesticides food safety issues have increased. These include an awareness of the existence of toxicology data gaps for a large number of pesticides, the potential for “inert” ingredients of potential toxicological significance to leave residues in food, the questionable reliability of food consumption estimates used in dietary pesticides risk assessments, and health concerns for infants and children as particularly sensitive population subgroups, (Winter, 1992)

However, the increase in the world population and in demand for food and economical crops, has put a pesticide burden on man and environment. Pesticide residues from vector control and from agricultural uses contaminate the terrestrial and aquatic surrounding and contribute to the pollution problem of the environment. Various human toxicosis have resulted from pesticides use. With careful and enlightened use of pesticide,

hazards to both man and environment could be significantly reduced (*Iyaniwura, 1992*).

Pesticides represent a good example for the risk/profit equation. Owing to their pest-destroying properties, they are required in the mondial food, but remain inevitably present as residues in food originating from both animal, and vegetables treated with pesticides. Therefore, due to biological activity a problem arises in public health and environmental toxicology fields (*Periquet.etal.,1991*).

Prior to being introduced into the market place, a pesticide is required to undergo a battery of tests in animals which are designed to identify the kinds of adverse effects that can be anticipated following acute or chronic exposure. Tests are also carried out to determine whether the pesticide is a carcinogen, a mutagen, or a teratogen. If the pesticide is an organophosphorus compound, it must be tested for delayed neurotoxicity. All new pesticides must be tested for its effect on fish, water, and wild life.

Detailed guidelines and protocols for the conduct of these studies are provided under the FIFRA regulations in the USA, and in similar guidelines, such as the OECD recommendations in Europe.

The US EPA FIFRA guidelines for example, contain sections dealing specifically with each of the following subjects:

1. Product chemistry.
 2. Fish and wild life effects.
-

2. Fish and wild life effects.
3. Effects on humans and domestic animals.
4. Product performance.
5. Labeling.
6. Experimental use permits.
7. Non-target plant effects.
8. Re-entry studies.
9. Non-target insect effects.
10. Biorationals.
11. Environmental chemistry studies.
12. good laboratory practice requirements.

The purpose of this elaborated system of chemical and biological testing in animals is to insure that there is sufficient information about the potential adverse effects of the pesticide to reliably predict whether it can be used safely for its intended purposes.

There is no doubt that the cost of toxicological assessment of pesticides are a rate limiting step in the development of new compounds. Biochemistry is now finding its way into several aspects of toxicology of pesticides by : a) routine examination of blood chemistry and other biochemical parameters, b) metabolic fate and its distribution (toxicokinetics), c) measurements which define at an early stage, changes which indicate effects on the functions of particular organs, d) studies to elucidate mechanism of toxicity.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

1- Toxicity of Insecticides Residues :

Two types of residues can be expected in food prepared from animals or plants treated with pesticides. The first type is represented by the pesticide itself and/or its primary metabolites as free or conjugated forms. Except for highly lipophilic compounds, these metabolites generally appear early and are non cumulative, since they are metabolized and eliminated rapidly. These substances may have toxic properties and may be metabolized to highly reactive electrophilic intermediates. They are considered to be potentially toxic for its consumers. The second type includes covalently bound metabolites that appear later. Their presence can indicate a potential toxic effect in the target species, although these transformed products have lost their pesticidal toxicity. They therefore probably represent low toxicity for its consumers specially considering their low bioavailability, which has been demonstrated for many pesticides (*Rico, 1990*). On the other hand, (*Neskovic et al., 1990*) treated wheat grains with labeled 14-C Chlorpyrifos-methyl (an organophosphorus compound) to generate bound residues for determining their bioavailability to rats. In a parallel experiment, bound residues were prepared with non-labeled Chlorpyrifos-methyl to determine possible adverse effects in rats fed with grain bound residues for 28 and 90 days. Two

dose levels of 10 and 50 ppm were initially used on the grains. The 10 ppm dose led to the formation of 25.1% bound residues (2.51 ppm) after 6 months as determined by radiomeasurements. The higher dose (50 ppm) was assumed to form 12.55 ppm bound residues. When the ¹⁴C bound residues were fed to male rats for 24 hours, the animals eliminated ; 75 % of the radioactivity in urine, 7% in expired air and 8% in feces after 3 days, indicating that the residues were highly bioavailable. A further *bioavailable* amount (4%) was found in selected organs.

The amount of residues permitted in food prepared from plants treated with pesticides, should not exceed a certain limit called *the Maximal Residual Limit* or (MRL) which should be monitored by a supervising committee. Plants exceeding the MRL for certain pesticide should be eliminated .

Following an investigational study of the relation ship between pesticides tolerance and safety by *Winter (1992)*, it was concluded that pesticide tolerances are not relevantly as regard for safety standards. This conclusion is based on the findings that theoretical exposure to legal levels of pesticides (at / below their MRL) may pose greater than negligible risks, while exposure to most illegal residues level (above their MRL) are of apparent toxicological significance. Thus, the common and logical views that legal residues are safe while illegal residues are not; are not supported by any scientific evidences. *Neskovic et al.(1991)* tested the subchronic toxic effect of bound malathion residues in rats It

induced effects to some extent in organs weight (spleen and adrenals), and blood cholinesterase activity. In both males and females there was an increase in serum alanine transaminase (ALT), and alkaline phosphatase. Hematological showed only changes in hemoglobin (Hb) concentration in males.

2- Toxicity of Organophosphorus Insecticides:

2.1 General overview :

Toxicity of organophosphates has prompted extensive investigations because of their established value and widespread use as an agricultural pesticide unfortunately, in an improper manner.

Bagatelle et al. (1969), found that extensive damage to epithelium of all organs has resulted in rats treated with Cantharidin insecticide. Also, they noticed injury to cell membranes as early as 5, 10 and 15 minutes after parenteral administration of the insecticide.

At the same year, *Boyed and Dobs* fed albino rats on diet treated with Monuron herbicide at LD₅₀. They noticed that, autopsy had revealed local gastroenteric irritation accompanied by degenerative changes in liver and kidneys, in addition to stress reaction and loss of weight with significant alteration in water content of most body organs.

In 1971, *Sherman et al.* studied the comparative toxicity of 4 halogenated organophosphorus insecticides on chicks and Japanese quails. They found no difference in susceptibility between males and females of the quail. Except for higher dose (800 ppm) little inhibition of cholinesterase was detected.
