Current Perspective on Pesticides: Their Classification, Behaviour, Potential Use and Toxic Effects

Adil Ahamad[1*], Javed Ahamad[2], Mohd. Javed Naim[2]

Abstract

The employment of extensive range of chemical to save their crops from disastrous effects of pests is an important aspect worldwide in order to increase the crop yields and minimizing post-harvest losses. It is estimated that approximately 1.8 billion people are engaged in agriculture and majority of them use pesticides to protect food and commercial products they produce. Pesticides are indispensable in agricultural production. The intensive use of toxic and remanent pesticides in agriculture has prompted research into novel performant, yet cost-effective and fast analytical tools to control the pesticide residue levels in the environment and food; because of the raised concern about their potential adverse effects on human health with farm workers being more prone to them. Also, lack of information among the farm workers and unregulated quantities usage leads to further raised their presence to toxic levels among the crops and finally to humans leading to several diseases like cancer, immunological disorders, and reproductive disorders etc. Synthetic organic pesticides (i.e., man-made, carbon-containing chemicals) includes chlorinated hydrocarbons, organophosphates, carbamates, pyrethroids, phenoxy herbicides etc. Pesticides are classified on the basis of different classification terms such as chemical classes, functional groups, modes of action and toxicity. This review proposes an overview of recent advances in the use of pesticide and their possible toxic profile.

Keywords: Pesticides, Pest control, Herbicides, Insecticides, Fungicides.

Significance | Monitoring the use of pesticide and analyzing their acceptable levels for human health.

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1. Introduction

Nowadays, to achieve high productivity in agriculture, pest control is managed using variety of toxic chemical compounds (pesticides) that are released into the environment leading to serious consequences (Isman, 2006). The group of substances known as pesticides pertains to substances used as insecticides, fungicides, herbicides, rodenticides, molluscicides, and nematicides. Nowadays, more than 1100 pesticides are possibly being used in various combinations, at different stages of cultivation and during postharvest storage to protect crops against a range of pests and fungi and/or to provide quality preservation (Zanella et al., 2012). Pesticides include substances that are used to prevent, destroy, or control any pests in plants and animals, including humans. Pesticides have contributed to increased agricultural yields and food security (Akhtar et al., 2009; Cooper and Dobson, 2007; Towson, 1992; Anees, 1974). International regulatory agencies have emphasized the control of pesticides such that shall not contain residues of individual pesticides at levels exceeding maximum residue limits (MRLs), for example, 10 μg/kg.

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Analyzing a large number of pesticides in various food commodities consistently remains a challenge for analytical chemists (Wang and Leung, 2009). It is generally accepted that pesticides play an important role in agricultural development because they can reduce the losses to agricultural products and improve the affordable yield and quality of food (Aktar et al., 2009; Fenik et al., 2011). Moreover, worldwide pesticide production increased at a rate of about 11% per year, from 0.2 million tons in the 1950s to more than 5 million tons by 2000, while only 1% of total pesticides are effectively used to control pests on target plants (Carvalho, 2017; Bernardes et al. 2017).

The application of pesticides has led to an increase in agricultural production worldwide. However, the widespread and excessive use of pesticides also exposes humans and animals who are non-target species. Some pesticides are considered a type of environmental pollutant and are frequently found in terrestrial and aquatic ecosystems. In many countries, pesticides can be purchased for personal and professional use; hence, restrictions on use are often neglected and pesticides are easily exposed to the ecosystem. In recent years, epidemiological investigations have been conducted on pesticide poisoning in livestock, wildlife, and agricultural workers in several countries (Munoz et al., 2017; Di Bilasio et al., 2020; Grilo et al., 2021). Infants and young children are particularly vulnerable to the hazards associated with exposure to pesticide residues due to their high food intake/body weight ratio and their metabolic pathways responsible for detoxification and excretion of toxins. Early-life exposure could easily disturb development processes if occurs at critical points, leading to the development of diseases (Freeman et al., 2016; Nougadere et al., 2020). Worldwide it is estimated that approximately 1.8 billion people are engaged in agriculture and most of them use pesticides to protect the food and commercial products that they produce. Others use pesticides occupationally for public health programs, and in commercial applications, while many others use pesticides for lawn and garden applications (Atwood and Paisley, 2017; Repitto and Baliga, 1996). Over 1 billion pounds of pesticides is used in the USA each year and approximately 5.6 billion pounds used worldwide. In a large prospective study of pesticide users in the USA, it was estimated that 16% of the cohort had at least one pesticide poisoning or an unusually high pesticide exposure episode in their lifetime (Alvanja et al., 2001). The U.S. Environmental Protection Agency (EPA) is responsible for regulating the production and use of pesticides in the United States under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and the Federal Food, Drug, and Cosmetic Act (FFDCA) (Atwood and Paisley, 2017). The US Department of Agriculture has estimated that 50 million people in the USA obtain their drinking water from groundwater that is potentially contaminated by pesticides and other agricultural chemicals (Ward et al., 2000; Nielsen, 1987).

As a result; several steps must be taken with immediate effect to minimize the health risk caused by various classes of pesticides and restrictions must be imposed to limit their usage beyond acceptable limits. Furthermore; some organochlorine pesticides like DDT, Dieldrin and Eldrin have been banned in this connection (Azmi and Naqvi, 2011).

1. Classification of Pesticides

Any substance or mixture of substances intended for preventing, destroying, repelling, or mitigating any insects, rodents, nematodes, fungi or weeds, or any other forms of life declared to be pests are called pesticides. Pests are those organisms that harms us and our belongings. Pesticides are used globally and extensively for the control of pests. Plant growth regulators, which are used to influence particular growth processes in plants, are also regulated as pesticides. Pesticide can be divided into different classes (**Box 1**) Toxicity of formulated chemical products as classified according to WHO hazard classes are mentioned in Table 1 & 2. Pesticide belonging to WHO class 1a are extremely hazardous, class 1b is highly hazardous, class 11 moderately hazardous, class 111 is slightly hazardous and class 1V is unlikely to present serious hazards in normal use. Nearly 90 % of the banned pesticides fall into category 1a/ 1b/11 of the WHO hazard grades (WHO, 2010).

(B) Pesticides can also be grouped on the basis of chemical compounds:

Since the 1940s, pesticide use has expanded because of the development of synthetic organic compounds. Synthetic organic pesticides (i.e., man-made, carbon-containing chemicals) includes chlorinated hydrocarbons, organophosphates, carbamates, pyrethroids, phenoxy herbicides etc. Groups with similar chemical structures tend to be similar in their mode of action, fate in the environment, and pest control properties, but not necessarily in their level of toxicity. Though pesticides may have different chemical structures, they can have similar modes of action. Their activity tends to be highly specific, and they are often harmless to non-target species (Trautmann, 1985).

(1) Chlorinated hydrocarbons (CH):

They include DDT, BHC (Lindane), Heptachlor, Aldrin, Dieldrin, Endrin, etc. In addition, PCBs are also hydrocarbons but not used as insecticides. They were commonly used in the past, but many have been removed from the market due to their health and environmental effects and their persistence (e.g., DDT and chlordane). This group came into general use in 1940. It is persistent and has a long half-life (i.e., 15-30 years). Some of them are very toxic e.g., Endrin (LD_{50} 10-15 mg/kg) (Abubakar et al., 2020).

(2) Organophosphates (OP):

Table 1. Toxicity of formulated chemical products as classified according to WHO hazard classes.

Pesticide Brand	Chemical Class	Active Ingredient	Toxicological Grade	Use
BASUDIN	Organophosphates	Diazinon	II	Insecticide
HERBOXONE	Chlorophenoxy acids	2,4-D	II	Herbicide
TOPIK	Aryloxyphenoxy-propionics	Clodinafop-propargyl	III	Herbicide
AATREX	Triazines	Atrazine q	U	Herbicide
MACHETE	Chloroacetanilides	Butachlor	U	Herbicide
CERTAINTY	Sulfonylureas	Sulfosulfuron	U	Herbicide
ERADICANE	Carbamides	EPTC	II	Herbicide
LASSO	Chloroacetanilides	Alachlor	III	Herbicide
DECIS	Pyrethroids	Deltamethrin	II	Herbicide
ALTO	Triazoles	Cyproconazole	III	Fungicide
SENCOR	Triazines	Metribuzin	II	Herbicide
CONFIDOR	Neonicotinoids	Imidacloprid	II	Insecticide
GRANSTAR	Sulfonylureas	Tribenuron-methyl	U	Herbicide

* Ia = Extremely hazardous; Ib = Highly hazardous; II = Moderately hazardous; III = Slightly hazardous; U = Unlikely to present acute hazard in normal use.

Table 2. Classification of pesticides based on toxicity criteria (WHO, 2010).

Type	Toxicity Level	LD_{50} For the Rat (mg/kg Body weight) *	
		Oral	Dermal
Ia	Extremely hazardous	<5	<50
Ib	Highly hazardous	5–50	50-200
II	Moderately hazardous	50–2000	200–2000
III	Slightly hazardous	Over 2000	Over 2000
U	Unlikely to present acute hazard	5000 or higher	5000 or higher

*LD_{50} is the amount of the substance required to kill 50% of the test population.

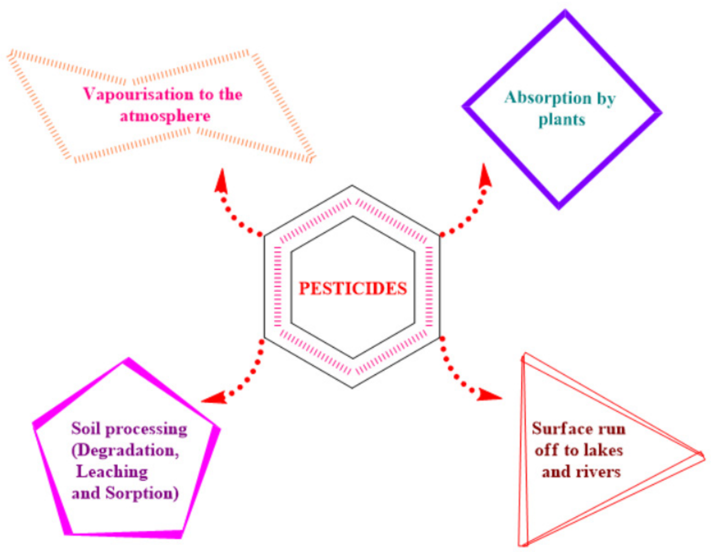

Figure 1. Pesticide behavior in the natural environment

Box 1

Pesticide is a general term that may be classified according to the pests:

- Insecticides: Kills or destroy insects
- Acaricides: Kills ticks and mites cause seabiasis (Acarines)
- Rodenticides: Kills rodents (Rats etc.)
- Fungicides: Kills fungi
- Algaecides: Kills algae
- Weedicides: Kills weeds
- Bactericides: Kills bacteria
- Molluscicides: Kills slugs or snails
- Nematicides: Kills nematodes

Box 2

- Malaria is caused by the protozoan Plasmodium and is spread to people by Anopheles mosquitoes.
- Yellow fever, encephalitis, and West Nile virus are caused by viruses and spread by mosquitoes.
- Sleeping sickness is caused by the protozoan Trypanosoma and spread by the tsetse fly Glossina.
- Plague or black death, caused by the bacterium Yersinia pestis and transmitted by the rat flea *Xenopsylla cheops.*
- Typhoid is caused by the bacterium Rickettsia prowazeki and transmitted by the louse *Pediculus humanus.*
- Schistosomiasis or bilharziasis is caused by the blood fluke Schistosoma, with freshwater snails as the alternate host (Rivero et al., 2010).

Box 3

Health effects of Pesticides

- Oxidative stress
- Carcinogenesis
- Chronic toxicity
- Nephrotoxic effects
- Hepatic dysfunctions

They were developed during the early 19th century, but their effects on insects, which were like their effects on humans, were discovered in 1932. Organophosphates came into general use as pesticides in 1950 because of the development of resistance against OC, DDT, etc. They are more toxic to mammals, but they are degraded in 2-4 weeks. Some are very poisonous (they were used in World War II as nerve agents). They are generally highly lipid soluble and may be classified as direct or indirect acetylcholinesterase (AchE) inhibitors. The common insecticides are malathion (comparatively safer for mammals), parathion, methyl parathion, dimecron, diazinon, dimethoate, chlorpyriphos, DDVP or dichlorvos, TTEP, etc. However, they usually do not persist in the environment. The organophosphates (OPs), because of their widespread use and frequently high acute toxicity, are involved in more pesticide poisonings than any other class of pesticides. They are compounds of phosphorus and Sulphur and are acetylcholine esterase inhibitors. Among them, TEPP is the most toxic i.e., LD_{50} 1 mg/kg while malathion is the least toxic i.e., LD_{50} 1500 mg/kg. The organophosphates interfere with the activity of cholinesterase. When the cholinesterase enzyme cannot perform its normal function, the nerves in the body send "messages" to the muscles continuously leading to muscle twitching and weakness. If the poisoning is severe, the victim may have "fits" or convulsions and may even die. Organophosphates are irreversible cholinesterase inhibitors and in the absence of medical treatment; the level of enzyme activity will return to normal only after several days, weeks, or even months. Additive effects of small, repeated doses over time, such as in a spraying season, may finally cause poisoning. The effects of mild poisoning include fatigue, headache, and dizziness. Moderate poisoning leads to the inability to walk, weakness and chest discomfort. In severe cases, there will be unconsciousness, severe constriction of pupils and muscle twitching ultimately resulting in death (Rusyniak and Nanagas, 2004).

(3) Chlorophenoxy acids (2,4-D):

They are being used since 1930 as herbicides and include 2,4-dichlorophenoxy acetic acid. They are toxic to plants especially broad leaf plants or weeds and mimic plant hormones. They are less toxic to animals but may produce eye irritation and GIT disorder. They are degraded in nearly two weeks, but regular exposure may be teratogenic in animals (Bradberry and Vale, 2017).

(4) Methamidophos:

It is classified by Environmental Protection Agency (EPA) as a class I compound. Methamidophos is a highly active, systemic, residual organophosphate insecticide/acaricide/avicide with contact and stomach action. Methamidophos; a potent acetylcholinesterase inhibitor, is highly toxic via oral, dermal, and inhalation routes. Early symptoms of acute organophosphate poisoning are dependent on the route of exposure and usually develop during or shortly after exposure (within 12 hours). Weakness, shakiness, blurred vision, tightness in the chest, sweating, confusion, changes in heart rate, convulsions, coma, and cessation of breathing may occur with significant inhalation, ingestion, or dermal exposure. The Allowable Daily Intake (ADI) level of methamidophos is 0.0003 mg/kg (do Nascimento et al., 2017).

(5) Carbamates (CB):

They are esters of carbonic acid and were first developed in Nigeria by U.K. scientists. The effects of carbamates and organophosphates are similar because they both inhibit cholinesterase. They include propoxur (Baygon), carbaryl (Sevin), Temik, and Zectran. They are also less persistent and degrade in about 4 weeks. They are also acetylcholinesterase inhibitors. Some are less toxic while some are more toxic e.g., propoxur LD_{50} 30 mg/kg. Thus, carbamates can cause severe poisoning, but they do not normally produce long-term, cumulative poisoning. The symptoms of acute carbamate and organophosphate poisoning are essentially the same (Dhouib et al., 2016).

(6) Methomyl:

Methomyl is a carbamate insecticide. It is a broad-spectrum fast-acting anti-cholinesterase agent. It is a direct contact and stomach poison. It is non-cumulative and rapidly metabolized in both plants and animals to substances of lower toxicity. Methomyl is particularly effective against organophosphorus-resistant pests. Methomyl may be absorbed from the gastrointestinal tract, through the intact skin, and, by inhalation of spray mist and dust. The ADI levels of methomyl are 0.01mg/kg (Liang et al., 2023).

(7) Thiodicarb:

It is a carbamate pesticide and belongs to class II, a moderately hazardous pesticide. Symptoms include malaise, muscle weakness, dizziness, sweating headache, salivation, nausea, vomiting, abdominal pain, diarrhea, central nervous system depression, and pulmonary edema. The ADI levels of thiodicarb are 0.03 mg/kg (Jones et al., 1989).

(8) Endosulfan:

It is an organochlorine pesticide of moderate mammalian toxicity which does not accumulate in the tissues of man or animals to any significant extent. Undiluted endosulfan is slowly and incompletely absorbed in the gastrointestinal tract of warm-blooded animals. Absorption is more rapid in the presence of alcohols, oils, and emulsifiers. These substances also accelerate the absorption of endosulfan through the skin. It is a central nervous system stimulant, producing convulsions. The ADI level of endosulfan is 0.006 mg/kg (Weber et al., 2010).

(9) Pyrethroids:

They were developed as a synthetic version of the naturally occurring pesticide pyrethrin, which is found in chrysanthemum.

They are mostly used these days because they are less toxic for mammals but significantly toxic to insects. They also inhibit cholinesterase. They have been developed based on natural pyrethroids (pyrethrin's I-IV) found in the chrysanthemum flower. They have been modified to increase their stability in the environment. The natural pyrethrins have an immediate knockdown effect but are less toxic and less persistent. Some synthetic pyrethroids are toxic to the nervous system. Synthetic pyrethroids have a more toxic and persistent effect. Examples of these are permethrin, bio-allethrin, resmethrin, cypermethrin, etc. Synthetic pyrethroids also have a half-life of 2-4 weeks. They are also general esterase inhibitors and have effects on other enzymes as well. Different groups of pesticides remained popular in different periods. In the early days, inorganic and plant extracts were popular, but in the '40s-50's organochlorine (OC) became popular, especially DDT was reported as a "Wonder drug" during the 2nd World War. For this great work of achievement, Muller was awarded the noble prize. In the '60s and 70's Organophosphates (OP) and Carbamates (CB) became popular, and OP is still being used. However, in the '80s synthetic pyrethroids (SP) dominated the sense, and still, the maximum import and use of pyrethroids are being done by government and private sectors because pyrethroids are comparatively safer and more effective as well. It is believed that in the next century, plant products will dominate due to their safe use and less polluting effect. Moreover, they also remain active physiologically by nature. At present, following pesticides are in major use: Cypermethrin, Permethrin, Bioallithrin, Fenvalerate, Methamidophos, Monocrotophos, Sumithion, Dimethoate, Endosulphan, Triazophos, Acephate, etc. (Ahamad and Kumar, 2023).

(10) Cypermethrin:

It is a composite pyrethroid; a broad spectrum, non-cumulative insecticide, and a fast-acting neurotoxin with good contact and stomach action. It has moderately high toxicity to mammals and is readily metabolized with immediate loss of activity. Cypermethrin is not a plant systemic, it is readily degraded on soil or plants but has good residual activity on inert surfaces. Cypermethrin is primarily absorbed from the gastrointestinal tract. It may also be absorbed by inhalation of spray mist and only minimally through the intact skin. The ADI level of cypermethrin is 0.05 mg/kg (Kumar et al., 2012).

(11) Imidacloprid:

Imidacloprid is an Acetylcholine esterase inhibitor which when compared other older synthetic pesticides, appeared as the only molecule moderately toxic to mammals, including humans. It is, however, highly toxic to other "non-target" and beneficial insect species. So, as always, care should be taken to avoid misapplication. The ADI level of imidacloprid is 0.06 mg/kg (Motuang, 2020).

2. Mode of Action of pesticides

Pesticides are poisons and therefore toxic to the living organism at a particular dose. They are inhibitors of enzymes and disturb the normal biochemical reactions necessary for metabolism. Some of them are neurotoxins while others are cytotoxins. They affect the action of enzymes in the body. However, the body can degrade and detoxify them with the help of various enzymes for example (Ortiz-Hernández et al., 2013):

(1) Organochlorines: Organochlorines (OC) are degraded by dehydrochlorinases.

(2) Organophosphates: Organophosphates (OP) are degraded by general esterases such as cholinesterases (ChEase), Phosphomonoesterases (ACP, AKP), Carboxylesterases, and Oxidases.

(3) Carbamates: Carbamates (CB) and synthetic pyrethroids (SP) are also degraded by the above enzymes. Most of them are cholinesterase inhibitors that disturb the nerve transmission system. However, the body has the power to synthesize more enzymes and degrade these poisons by increasing the enzyme levels such as the development of resistance in case of pests.

3. Pesticide Uses

Modern agricultural practices especially the use of pesticides and fertilizers have brought a green revolution in many countries and have provided global food security. While pesticide uses have improved the world food supply and have been responsible for better growth and yield, their irresponsible and indiscriminate uses have greatly increased environmental health problems. There are more than 1000 agrochemicals that are being manufactured and used for agriculture as well as public health purposes. Pesticides are an essential tool for increasing agricultural production. To produce a good crop, favorable conditions and suitable chemicals are required (Syafrudin et al., 2021).

Various insects and ticks are vectors that transmit pathogens among individuals of the same species or from an alternate host to people or domestic and wild animals. Important human diseases that are vectored by invertebrates (**Box 2**)

4. Pesticide Behavior in the Environment

When pesticides are applied to a target plant or disposed off, they have the potential to enter the environment. On entering the environment, pesticides can undergo processes such as transfer (or movement) and degradation (Scholtz and Bidleman, 2007; Liu et al., 2015). Pesticide degradation in the environment produces new chemicals (Marie et al., 2017). They relocate from the target site to other environmental media or non-target plants by transfer processes including adsorption, leaching, volatilization, spray drift, and runoff (Figure 1) (Robinson et al., 1999). The different types of chemicals indicate their differences in environmental behavior. For example, organochlorine compounds such as DDT have low acute toxicity but shows significant ability to accumulate in tissues and persist in causing long-term damage. They have been banned from sale in most countries, but their residues remain in the environment for a long time because of their nature. While organophosphate pesticides are of low persistence, they have appreciable acute toxicity in mammals (Kim et al., 2017; Damalas and Eleftherohorinos, 2011).

5. Pesticide Exposure:

Pesticide exposure occurs through different routes which are mentioned as:

(1) Dermal exposure: It occurs by not washing hands after handling pesticides or their containers. Splashing or spilling pesticide on the skin by wearing pesticide-contaminated clothing and applying pesticides in the windy weather. Touching treated plants or soil also leads to dermal exposure. Exposures occur by rubbing eyes or forehead with pesticides contaminated gloves or hands, splashing pesticides in eyes, application in windy weather, drift exposure, and mixing/loading of dry formulations without wearing goggles. Dermal assimilation may happen because of a sprinkle, spill, or spray drift, when mixing, stacking, arranging, and additionally cleaning pesticides (Salvatore et al., 2008). Absorption may likewise result from exposure to large quantities of residue. Pesticide makings change comprehensively in physicochemical properties and in their ability to be assimilated through the skin (Damalas and Koutroubas, 2016).

(2) Inhalational exposure: Exposed to drift during or after spraying, mixing/loading, dust, powders, or other dry formulations. Use of inadequate or poorly fitted respirators (Beard et al., 2014).

(3) Oral ingestion: The consumption of the chemical through the mouth into the digestive tract is called oral ingestion. This happens through occupational, intended, or in-intentional pesticide use when a very minor quantity of spray vapor enters the nose and mouth and is gulped during spraying. When a pesticide is introduced through oral contact, the most serious poisoning may result. Oral exposure to a pesticide typically rises by chance due to inattention or for intended reasons. The most common instances of unintentional oral exposure were accounted to happen when pesticides were exchanged from their unique marked container to an unlabeled bottle or food vessel. There are numerous cases in which individuals have been harmed by drinking pesticides kept in soda pop containers or after drinking water stored in pesticide-contaminated bottles (Tudi et al., 2022; Gilden et al., 2010).

(4) Respiratory exposure: Because of the presence of unstable constituents of pesticides, their potential for respiratory introduction is extraordinary. Inward breath of adequate amounts of pesticides may make genuine harm to the throat, nose, and lung tissues. Though, the danger of pesticide exposure is overall comparatively small when pesticides are sprayed in huge drops with traditional application equipment. In any case, if low-volume equipment is utilized to apply a concentrated material, the potential for respiratory exposure is greater because of the creation of minor drops (Amaral, 2014).

(5) Eye exposure: The potential for chemical damage is great for tissues of eyes. A few pesticides were accounted for to be captivated by the eyes in sufficient amounts to cause genuine or even lethal disorder (Tudi et al., 2022). Granular pesticides represent a specific danger to the eyes relying upon the mass and weight of individual particles (Jaga and Dharmini, 2006). If pesticides are applied through power equipment, the pellets may skip off vegetation or different surfaces at high speed to cause critical eye harm (Fareed et al., 2012). Eye safety is additionally required when estimating or mixing concentrated or very poisonous pesticides. Defensive face shields or goggles ought to be worn at whatever spraying pesticides or to avoid eye contact with dirt.

6. Pesticides Poisonings:

The agrochemical industry has offered thousands of compounds. The health of the pesticide handlers and farmers is at high risk due to the irrational use of pesticides. Pesticides cause acute and chronic health effects; organophosphate and carbamate groups are more important. These insecticides inhibit cholinesterase, an enzyme critical for the normal functioning of the nervous system.

6.1. Widespread presence of pesticides poisoning

In USA, more than 18,000 products are licensed for use and each year more than 2 billion pounds of pesticides are applied to crops, gardens, homes, etc. (Mcmahon and Chen, 2001). The major economic and environmental losses due to the application of pesticides in public health was 1.1 billion dollars per year in the USA (Pimentel, 2005). Such widespread use resulted in pervasive human exposure. Evidence continues to accumulate that pesticide exposure is associated with impaired health. Occupational exposure is known to result in an annual incidence of 18 cases of pesticide-related illness for every 100,000 workers in the U.S (Calvert et al., 2004). Pesticide poisoning is a major public health problem in many developing countries (Shou-zhen, 1987; Jeyaratnam, 1990). In the developing world, pesticide poisoning causes more deaths than infectious diseases. Pesticide poisoning among farmers and occupational workers in developing countries is alarming (McCauley et al., 2006). WHO estimated approximately 20,000 workers die from exposure every year, the majority in developing countries (Pimentel et al., 1992; Kishi et al., 1995). The number of intoxications with organophosphates is estimated at some 3000,000 per year and the number of deaths and casualties some 300,000 per year (Eyer, 2023). Ahmed and coworkers have reported that 64 percent of fatal cases of acute pesticide poisoning in Multan, Pakistan occurred due to OPs pesticide spraying (Rauf et al., 2002). However, another study revealed 21 percent of occupational pesticide poisoning in the hospitalized patient (Chowdhary et al., 2014).

6.2. Acute toxicity

Organophosphorus compounds exert acute systemic toxicity by inhibiting the enzymes AChE through phosphorylation. Pesticides binds to cholinesterase and block the hydrolysis of the acetylcholine and acetic acid at the post-synaptic junction (Chan et al., 1998; Mason, 2000). OPs-induced neuronal symptoms are a consequence of axonal death. Following OPs exposure inhibition of neuronal enzymes, called neuropathy target esterase, occurs and many of them are irreversible. Please see **Box 3.**

Oxidative stress

Recent studies have shown that oxidative stress could be an important component of the mechanism of Organophosphates toxicity. Several studies explained that oxidative stress is involved in OPs toxicity (Prakasam et al., 2001; Hsu et al., 2001). Repeated daily oral doses of pesticide in rats altered the biochemical parameters and antioxidant status (Manna et al., 2004). Several studies revealed that OPs may induce oxidative stress leading to the generation of free radicals and alteration of antioxidant status (Bagchi et al., 1995; Abdollahi et al., 2004). Toxic effects of pesticides on human beings especially by omitting radical production can be confirmed by the direct measurement of lipid peroxidation by-product malondialdehyde (MDA) (Muniz et al., 2008). The study revealed significant rise in Plasma malondialdehyde (MDA) levels in exposed farmers than in controls and the results were consistent with other studies suggesting that pesticides increase oxidative stress in humans (Singh et al., 2007). There is increasing evidence that OP and carbamate induced oxidative stress through the generation of free oxygen radicals, leading to lipid peroxidation and DNA damage (Hazarika et al., 2003; Vidyasager et al., 2004; Shadnia et al., 2005). Muniz and coworkers reported MDA levels 4.9 times and 24 times higher in farm workers and applicators respectively than in controls. Pesticides induce a wide array of human health effects through oxidative stress causing cytogenetic damage and carcinogenicity (Mansour, 2004).

Carcinogenesis

Epidemiological studies have implicated pesticides as a causative agent in human cancer (Zahm and Blair, 1992). Cancer and even death are more frequent among farmers rather than in the general population (Cabello et al., 2001). Cytogenetic studies showed an increase in DNA damage and higher chromosomal aberrations (CAs) in exposed farmers compared to the control subjects (Naravaneni and Jamil, 2007). A study documented significant genotoxic exposure to pesticides based on a significant decrease in the level of serum ChE among workers involved in the pesticide manufacturing industry (Bhalli et al., 2006). There was an increased risk of lung cancer reported in German agricultural workers, which also increased with the length of exposure (Barthel, 1981).

Chronic toxicity

Depending upon the toxicity of the compound, dosage, and exposure time, the adverse effects of pesticide poisoning range from headaches, vomiting, skin irritation, and respiratory problems to other neurological disorders (Jørs et al., 2006). Available evidence suggests that there is a possibility of adverse effects occurring below OP compound concentrations that are generally considered to be safe based on the measurement of AChE inhibition (Singh and Sharma, 2004; Salvi et al., 2003). A study in Sri Lanka has shown inhibition of the AChE enzyme and impairment of sensory and motor nerve conduction due to long-term, low-level exposure to Ops (Simit et al., 2003). Farm workers and greenhouse workers exposed to organophosphates reported more symptoms than unexposed workers (Strong et al., 2004). Pesticide poisoning is associated with increased symptom prevalence (Kamil and Hoppin, 2004). Diverse trends were seen regarding the disposal of pesticide residues. Due to a casual attitude towards the handling of pesticides, many farmers threw pesticide containers in the field or irrigate water which increases environmental pollution and health hazards in the community.

Nephrotoxic effects

Cholinesterase inhibitor poisoning has both short and long-term neuropsychological sequelae (Roldán et al., 2005). Recent studies have examined a link between pesticide exposure and neurological outcome (Kamil and Hoppin, 2004). OPs being inhibitors of esterases lead to the accumulation of acetylcholine at nerve endings leading to cholinergic crises, by initial stimulation and eventually exhaustion of cholinergic synapses. Clinical features reported as anxiety depression, irritability, psychotic symptoms, and erectile disorders were more significant in pesticide applicators than in controls (Amr et al., 1997). Chronic low-dose exposure leads to neuropsychiatric consequences among the tobacco agricultural workers in Brazil (Salvi et al., 2003). The intermediate syndrome is a major cause of morbidity and mortality in patients with acute OP poisoning (Yang and Deng, 2007).

Hepatic dysfunctions

Liver enzymes may be used to detect the effect of pesticides before adverse clinical health effects occur (El-Demerdash et al., 2001). Prolonged exposure to multiple pesticides, affected the liver and kidney (Azmi et al., 2006). There is also an increase in the prevalence of liver disorders among Ranch Hand workers in the high exposure category (Michalek et al., 2001). Statistically significant aspartate aminotransferase (AST) levels were found in agriculture workers continuously exposed to pesticides (Hernández et al., 2006). Higher levels of gamma-glutamyl transferase (GGT), (GOT), were found in the blood of occupational workers chronically exposed to pesticides (Misra et al., 1985). An increased risk of liver dysfunction was observed with elevated (AST), alanine aminotransferase (ALT), or lactate dehydrogenase (LDH) (El-Demerdash et al., 2001; Michalek et al., 2001). AST and ALT are involved in the breakdown of amino acids into α- keto acid, which are routed for complete metabolism through the Kreb's cycle and electron transport chain. Consequently, they are considered as a specific indicator of liver damage (Harper et al., 1979). The increased activity of serum AST and ALT indicates hepatocellular dysfunctions (Yousef et al., 2006). A positive correlation between pesticides with the liver enzymes has been reported by many researchers (Carvalho, 1991).

Conclusion

A major challenge for agriculture is to increase food production in order to meet the needs of the growing world population, without damaging the environment. In current agricultural practices, the control of pests is often accomplished by means of excessive use of synthetic chemical pesticides such as organochlorides, organophosphates, carbamates and pyrethroids, which causes severe health problems in human and animals as well. Despite the assessment of effectiveness, ease of availability and usage, economical and potential toxic effects of pesticides must be considered in order to gain pest sustainability on longer time frame. Due to these major problems, there is an urgent need to find out alternative ways and methods for controlling pests. Research should be carried out in development of effective pesticides or advancement of technologies being used. Measures must be undertaken to replace synthetic pesticides with herbal pesticides in the long run as they are found to be less polluting to environment and reduced danger of contamination of food. Integrated Pest Management system must be employed for better control of pests. Hence, plant-based pesticides (pyrethroids, essential oils, capsicum oleoresins, garlic, and neem-based products.) can offer a better alternative to synthetic pesticides and enabling safer control of pests.

Author Contributions

A.A. conceptualized the study design and wrote, J.A. wrote and revised, M.J.N. wrote, revised and edited the paper.

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Competing financial interests

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References

Abdollahi, M., Mostafalou, S., Pournourmohammadi, S., & Shadnia, S. (2004). Oxidative stress and cholinesterase inhibition in saliva and plasma of rats following subchronic exposure to malathion. Comparative Biochemistry and Physiology Part C: Toxicology & Pharmacology, 137(1), 29-34.

Abubakar, Y., Tijjani, H., Egbuna, C., Adetunji, C. O., Kala, S., Kryeziu, T. L., ... & Patrick-Iwuanyanwu, K. C. (2020). Pesticides, history, and classification. In Natural remedies for pest, disease and weed control (pp. 29-42). Academic Press.

Ahamad, A., & Kumar, J. (2023). Pyrethroid pesticides: An overview on classification, toxicological assessment and monitoring. Journal of Hazardous Materials Advances, 100284.

Aktar, M. W., Paramasivam, M., Sengupta, D., Purkait, S., Ganguly, M., & Banerjee, S. (2009). Impact assessment of pesticide residues in fish of Ganga river around Kolkata in West Bengal. Environmental monitoring and assessment, 157, 97-104.

Aktar, M. W., Sengupta, D., & Chowdhury, A. (2009). Impact of pesticides use in agriculture: their benefits and hazards. Interdisciplinary toxicology, 2(1), 1.

Alavanja, M. C., Sprince, N. L., Oliver, E., Whitten, P., Lynch, C. F., Gillette, P. P., ... & Zwerling, C. (2001). Nested case-control analysis of high pesticide exposure events from the Agricultural Health Study. American journal of industrial medicine, 39(6), 557-563.

Amaral, A. F. (2014). Pesticides and asthma: challenges for epidemiology. Frontiers in public health, 2, 6.

Amr, M. M., Halim, Z. S., & Moussa, S. S. (1997). Psychiatric disorders among Egyptian pesticide applicators and formulators. Environmental research, 73(1-2), 193-199.

Anees, M. A. (1974). Susceptibility of a Freshwater Teleost Channa Punctatus to Acute, Sublethal and Chronic Levels of Organophosphorus Insecticides. University of the Punjab (Pakistan).

Atwood, D., & Paisley-Jones, C. (2017). Pesticides industry sales and usage: 2008–2012 market estimates. US Environmental Protection Agency, Washington, DC, 20460, 2017-01.

Azmi, M. A., & Naqvi, S. N. H. (2011). Pesticide pollution, resistance and health hazards. Pesticides-The Impacts of Pesticides Exposure, 26.

Azmi, M. A., Naqvi, S. N. H., Azmi, M. A., & Aslam, M. (2006). Effect of pesticide residues on health and different enzyme levels in the blood of farm workers from Gadap (rural area) Karachi—Pakistan. Chemosphere, 64(10), 1739-1744.

Bagchi, D., Bagchi, M., Hassoun, E. A., & Stohs, S. J. (1995). In vitro and in vivo generation of reactive oxygen species, DNA damage and lactate dehydrogenase leakage by selected pesticides. Toxicology, 104(1-3), 129-140.

Barthel, E. (1981). Increased risk of lung cancer in pesticide-exposed male agricultural workers. Journal of Toxicology and Environmental Health, Part A Current Issues, 8(5-6), 1027-1040.

Beard, J. D., Umbach, D. M., Hoppin, J. A., Richards, M., Alavanja, M. C., Blair, A., ... & Kamel, F. (2014). Pesticide exposure and depression among male private pesticide applicators in the agricultural health study. Environmental health perspectives, 122(9), 984-991.

Bernardes, M. F. F., Pazin, M., Pereira, L. C., & Dorta, D. J. (2015). Impact of pesticides on environmental and human health. Toxicology studies-cells, drugs and environment, 195-233.

Bhalli, J. A., Khan, Q. M., Haq, M. A., Khalid, A. M., & Nasim, A. (2006). Cytogenetic analysis of Pakistani individuals occupationally exposed to pesticides in a pesticide production industry. Mutagenesis, 21(2), 143-148.

Bradberry, S. M., & Vale, J. A. (2017). Chlorophenoxy Herbicides 89.

Cabello, G., Valenzuela, M., Vilaxa, A., Durán, V., Rudolph, I., Hrepic, N., & Calaf, G. (2001). A rat mammary tumor model induced by the organophosphorous pesticides parathion and malathion, possibly through acetylcholinesterase inhibition. Environmental health perspectives, 109(5), 471-479.

Calvert, G. M., Plate, D. K., Das, R., Rosales, R., Shafey, O., Thomsen, C., ... & Lackovic, M. (2004). Acute occupational pesticide-related illness in the US, 1998–1999: surveillance findings from the SENSOR-pesticides program. American journal of industrial medicine, 45(1), 14-23.

Carvalho, F. P. (2017). Pesticides, environment, and food safety. Food and energy security, 6(2), 48-60.

Carvalho, W. A. (1991). Risk factors related with occupational and environmental exposure to organochlorine insecticides in the state of Bahia, Brazil, 1985. Boletin de la Oficina Sanitaria Panamericana. Pan American Sanitary Bureau, 111(6), 512-524.

Chan, T. Y. K., & Critchley, J. A. J. H. (1998). Insecticide poisoning with organophosphates and carbamates. HONG KONG PRACTITIONER, 20, 604-614.

Chowdhary, S., Bhattacharyya, R., & Banerjee, D. (2014). Acute organophosphorus poisoning. Clinica chimica acta, 431, 66-76.

Cooper, J., & Dobson, H. (2007). The benefits of pesticides to mankind and the environment. Crop Protection, 26(9), 1337-1348.

Damalas, C. A., & Eleftherohorinos, I. G. (2011). Pesticide exposure, safety issues, and risk assessment indicators. International journal of environmental research and public health, 8(5), 1402-1419.

Damalas, C. A., & Koutroubas, S. D. (2016). Farmers' exposure to pesticides: toxicity types and ways of prevention. Toxics, 4(1), 1.

Dhouib, I. B., Annabi, A., Jallouli, M., Marzouki, S., Gharbi, N., Elfazaa, S., & Lasram, M. M. (2016). Carbamates pesticides induced immunotoxicity and carcinogenicity in human: A review. Journal of Applied Biomedicine, 14(2), 85-90.

Di Blasio, A., Bertolini, S., Gili, M., Avolio, R., Leogrande, M., Ostorero, F., ... & Zoppi, S. (2020). Local context and environment as risk factors for acute poisoning in animals in northwest Italy. Science of the Total Environment, 709, 136016.

do Nascimento, C. P., Maretto, G. X., Marques, G. L. M., Passamani, L. M., Abdala, A. P., Schenberg, L. C., ... & Sampaio, K. N. (2017). Methamidophos, an organophosphorus insecticide, induces pro-aggressive behaviour in mice. Neurotoxicity research, 32, 398-408.

El-Demerdash, F. M., Yousef, M. I., & Elagamy, E. I. (2001). Influence of paraquat, glyphosate, and cadmium on the activity of some serum enzymes and protein electrophoretic behavior (in vitro). Journal of Environmental Science and Health, Part B, 36(1), 29-42.

Eyer, P. (2003). The role of oximes in the management of organophosphorus pesticide poisoning. Toxicological reviews, 22, 165-190.

Fareed, M., Kesavachandran, C. N., Pathak, M. K., Bihari, V., Kuddus, M., & Srivastava, A. K. (2012). Visual disturbances with cholinesterase depletion due to exposure of agricultural pesticides among farm workers. Toxicological & Environmental Chemistry, 94(8), 1601-1609.

Fenik, J., Tankiewicz, M., & Biziuk, M. (2011). Properties and determination of pesticides in fruits and vegetables. TrAC Trends in Analytical Chemistry, 30(6), 814-826.

Freeman, S., Kaufman-Shriqui, V., Berman, T., Varsano, R., Shahar, D. R., & Manor, O. (2016). Children's diets, pesticide uptake, and implications for risk assessment: An Israeli case study. Food and Chemical Toxicology, 87, 88-96.

Gilden, R. C., Huffling, K., & Sattler, B. (2010). Pesticides and health risks. Journal of Obstetric, Gynecologic & Neonatal Nursing, 39(1), 103-110.

Grilo, A., Moreira, A., Carrapiço, B., Belas, A., & São Braz, B. (2021). Epidemiological study of pesticide poisoning in domestic animals and wildlife in Portugal: 2014–2020. Frontiers in Veterinary Science, 7, 616293.

Harper, H. A., Rodwell, V. W., & Mayes, P. A. (1979). The fat-soluble vitamins. Vitamin A. Review of physiological chemistry. 17th edition., Lange. Medical Publication, Los Altos, California, 148.

Hazarika, A., Sarkar, S. N., Hajare, S., Kataria, M., & Malik, J. K. (2003). Influence of malathion pretreatment on the toxicity of anilofos in male rats: a biochemical interaction study. Toxicology, 185(1-2), 1-8.

Hernández, A. F., Gómez, M. A., Pérez, V., García-Lario, J. V., Pena, G., Gil, F., ... & Pla, A. (2006). Influence of exposure to pesticides on serum components and enzyme activities of cytotoxicity among intensive agriculture farmers. Environmental research, 102(1), 70-76.

Hsu, D. Z., Hsu, C. H., Huang, B. M., & Liu, M. Y. (2001). Abamectin effects on aspartate aminotransferase and nitric oxide in rats. Toxicology, 165(2-3), 189-193.

Isman, M. B. (2006). Botanical insecticides, deterrents, and repellents in modern agriculture and an increasingly regulated world. Annu. Rev. Entomol., 51, 45-66.

Jaga, K., & Dharmani, C. (2006). Ocular toxicity from pesticide exposure: A recent review. Environmental health and preventive medicine, 11, 102-107.

Jeyaratnam, J. (1990). Acute pesticide poisoning: a major global health problem. World health statistics quarterly 1990; 43 (3): 139-144.

Jones, R. L., Hunt, T. W., Norris, F. A., & Harden, C. F. (1989). Field research studies on the movement and degradation of thiodicarb and its metabolite methomyl. Journal of contaminant hydrology, 4(4), 359-371.

Jørs, E., Morant, R. C., Aguilar, G. C., Huici, O., Lander, F., Bælum, J., & Konradsen, F. (2006). Occupational pesticide intoxications among farmers in Bolivia: a cross-sectional study. Environmental Health, 5(1), 1-9.

Kamel, F., & Hoppin, J. A. (2004). Association of pesticide exposure with neurologic dysfunction and disease. Environmental health perspectives, 112(9), 950-958.

Kim, K. H., Kabir, E., & Jahan, S. A. (2017). Exposure to pesticides and the associated human health effects. Science of the total environment, 575, 525-535.

Kishi, M., Hirschhorn, N., Djajadisastra, M., Satterlee, L. N., Strowman, S., & Dilts, R. (1995). Relationship of pesticide spraying to signs and symptoms in Indonesian farmers. Scandinavian journal of work, environment & health, 124-133.

Kumar Singh, A., Nath Tiwari, M., Prakash, O., & Pratap Singh, M. (2012). A current review of cypermethrin-induced neurotoxicity and nigrostriatal dopaminergic neurodegeneration. Current neuropharmacology, 10(1), 64-71.

Liang, C. A., Chang, S. S., Chen, H. Y., Tsai, K. F., Lee, W. C., Wang, I. K., ... & Yen, T. H. (2023). Human Poisoning with Methomyl and Cypermethrin Pesticide Mixture. Toxics, 11(4), 372.

Liu, Y., Mo, R., Tang, F., Fu, Y., & Guo, Y. (2015). Influence of different formulations on chlorpyrifos behavior and risk assessment in bamboo forest of China. Environmental Science and Pollution Research, 22, 20245-20254.

Manna, S., Bhattacharyya, D., Mandal, T. K., & Das, S. (2004). Repeated dose toxicity of alfa-cypermethrin in rats. Journal of veterinary science, 5(3), 241-245.

Mansour, S. A. (2004). Pesticide exposure—Egyptian scene. Toxicology, 198(1-3), 91-115.

Marie, L., Sylvain, P., Benoit, G., Maurice, M., & Gwenaël, I. (2017). Degradation and transport of the chiral herbicide s-metolachlor at the catchment scale: Combining observation scales and analytical approaches. Environmental Science & Technology, 51(22), 13231-13240.

Mason, H. J. (2000). The recovery of plasma cholinesterase and erythrocyte acetylcholinesterase activity in workers after over-exposure to dichlorvos. Occupational Medicine, 50(5), 343-347.

McCauley, L. A., Anger, W. K., Keifer, M., Langley, R., Robson, M. G., & Rohlman, D. (2006). Studying health outcomes in farmworker populations exposed to pesticides. Environmental health perspectives, 114(6), 953-960.

Mcmahon TF, Chen J. US Environmental Protection Agency Office of Pesticide Programs 2001.

Michalek, J. E., Ketchum, N. S., & Longnecker, M. P. (2001). Serum dioxin and hepatic abnormalities in veterans of Operation Ranch Hand. Annals of epidemiology, 11(5), 304-311.

Misra, U. K., Nag, D., Bhushan, V., & Ray, P. K. (1985). Clinical and biochemical changes in chronically exposed organophosphate workers. Toxicology letters, 24(2-3), 187-193.

Motaung, T. E. (2020). Chloronicotinyl insecticide imidacloprid: Agricultural relevance, pitfalls and emerging opportunities. Crop Protection, 131, 105097.

Muniz, J. F., McCauley, L., Scherer, J., Lasarev, M., Koshy, M., Kow, Y. W., ... & Kisby, G. E. (2008). Biomarkers of oxidative stress and DNA damage in agricultural workers: a pilot study. Toxicology and applied pharmacology, 227(1), 97-107.

Muñoz-Quezada, M. T., Lucero, B., Iglesias, V., Levy, K., Muñoz, M. P., Achú, E., ... & Villalobos, M. (2017). Exposure to organophosphate (OP) pesticides and health conditions in agricultural and non-agricultural workers from Maule, Chile. International journal of environmental health research, 27(1), 82-93.

Naravaneni, R., & Jamil, K. (2007). Determination of AChE levels and genotoxic effects in farmers occupationally exposed to pesticides. Human & experimental toxicology, 26(9), 723-731.

Nielsen, E. G. (1987). The magnitude and costs of groundwater contamination from agricultural chemicals: A national perspective (No. 576). US Department of Agriculture, Economic Research Service.

Nougadère, A., Sirot, V., Cravedi, J. P., Vasseur, P., Feidt, C., Fussell, R. J., ... & Hulin, M. (2020). Dietary exposure to pesticide residues and associated health risks in infants and young children–results of the French infant total diet study. Environment international, 137, 105529.

Ortiz-Hernández, M. L., Sánchez-Salinas, E., Dantán-González, E., & Castrejón-Godínez, M. L. (2013). Pesticide biodegradation: mechanisms, genetics and strategies to enhance the process. Biodegradation-life of Science, 10, 251-287.

Pimentel, D. (2005). Environmental and economic costs of the application of pesticides primarily in the United States. Environment, development and sustainability, 7, 229-252.

Pimentel, D., Acquay, H., Biltonen, M., Rice, P., Silva, M., Nelson, J., ... & D'amore, M. (1992). Environmental and economic costs of pesticide use. BioScience, 42(10), 750-760.

Prakasam, A., Sethupathy, S., & Lalitha, S. (2001). Plasma and RBCs antioxidant status in occupational male pesticide sprayers. Clinica Chimica Acta, 310(2), 107-112.

Rauf, A., Karam, A., Rashid, I., & Ashiq, M. (2002). Acute poisoning due to commercial pesticides in Multan.

Repetto, R., & Baliga, S. S. (1996). Pesticides and the immune system: the public health risks (p. 100). Washington, DC: World Resources Institute.

Rivero, A., Vezilier, J., Weill, M., Read, A. F., & Gandon, S. (2010). Insecticide control of vector-borne diseases: when is insecticide resistance a problem?. PLoS pathogens, 6(8), e1001000.

Robinson, D. E., Mansingh, A., & Dasgupta, T. P. (1999). Fate and transport of ethoprophos in the Jamaican environment. Science of the total environment, 237, 373-378.

Roldán-Tapia, L., Leyva, A., Laynez, F., & Santed, F. S. (2005). Chronic neuropsychological sequelae of cholinesterase inhibitors in the absence of structural brain damage: two cases of acute poisoning. Environmental health perspectives, 113(6), 762-766.

Rusyniak, D. E., & Nañagas, K. A. (2004, June). Organophosphate poisoning. In Seminars in neurology (Vol. 24, No. 02, pp. 197-204). Copyright© 2004 by Thieme Medical Publishers, Inc., 333 Seventh Avenue, New York, NY 10001, USA.

Salvatore, A. L., Bradman, A., Castorina, R., Camacho, J., López, J., Barr, D. B., ... & Eskenazi, B. (2008). Occupational behaviors and farmworkers' pesticide exposure: findings from a study in Monterey County, California. American journal of industrial medicine, 51(10), 782-794.

Salvi, R. M., Lara, D. R., Ghisolfi, E. S., Portela, L. V., Dias, R. D., & Souza, D. O. (2003). Neuropsychiatric evaluation in subjects chronically exposed to organophosphate pesticides. Toxicological Sciences, 72(2), 267-271.

Scholtz, M. T., & Bidleman, T. F. (2007). Modelling of the long-term fate of pesticide residues in agricultural soils and their surface exchange with the atmosphere: Part II. Projected long-term fate of pesticide residues. Science of the total environment, 377(1), 61-80.

Shadnia, S., Azizi, E., Hosseini, R., Khoei, S., Fouladdel, S., Pajoumand, A., ... & Abdollahi, M. (2005). Evaluation of oxidative stress and genotoxicity in organophosphorus insecticide formulators. Human & experimental toxicology, 24(9), 439-445.

Shou-zhen, X. (1987). Health effects of pesticides: a review of epidemiologic research from the perspective of developing nations. American journal of industrial medicine, 12(3), 269-279.

Singh, S., & Sharma, N. (2000). Neurological syndromes following organophosphate poisoning. Neurology India, 48(4), 308.

Singh, V. K., Reddy, M. K., Kesavachandran, C., Rastogi, S. K., & Siddiqui, M. K. J. (2007). Biomonitoring of organochlorines, glutathione, lipid peroxidation and cholinesterase activity among pesticide sprayers in mango orchards. Clinica chimica acta, 377(1-2), 268-272.

Smit, L. A., van-Wendel-de-Joode, B. N., Heederik, D., Peiris-John, R. J., & van der Hoek, W. (2003). Neurological symptoms among Sri Lankan farmers occupationally exposed to acetylcholinesterase-inhibiting insecticides. American journal of industrial medicine, 44(3), 254-264.

Strong, L. L., Thompson, B., Coronado, G. D., Griffith, W. C., Vigoren, E. M., & Islas, I. (2004). Health symptoms and exposure to organophosphate pesticides in farmworkers. American journal of industrial medicine, 46(6), 599-606.

Syafrudin, M., Kristanti, R. A., Yuniarto, A., Hadibarata, T., Rhee, J., Al-Onazi, W. A., ... & Al-Mohaimeed, A. M. (2021). Pesticides in drinking water—a review. International journal of environmental research and public health, 18(2), 468.

Townson, H. (1992). Public health impact of pesticides used in agriculture: Geneva: World Health Organization, 1990. 128 pp. Price Sw. fr. 21.00. ISBN 92-4-156139-4.

Trautmann, N. M., Porter, K. S., & Wagenet, R. H. (1985). Pesticides: health effects in drinking water.

Tudi, M., Li, H., Li, H., Wang, L., Lyu, J., Yang, L., ... & Connell, D. (2022). Exposure routes and health risks associated with pesticide application. Toxics, 10(6), 335.

Vidyasagar, J., Karunakar, N., Reddy, M. S., Rajnarayana, K., Surender, T., & Krishna, D. R. (2004). Oxidative stress and antioxidant status in acute organophosphorous insecticide poisoning. Indian journal of pharmacology, 36(2), 76.

Wang, J., & Leung, D. (2009). Applications of ultra-performance liquid chromatography electrospray ionization quadrupole time-of-flight mass spectrometry on analysis of 138 pesticides in fruit-and vegetable-based infant foods. Journal of Agricultural and Food Chemistry, 57(6), 2162-2173.

Ward, M. H., Nuckols, J. R., Weigel, S. J., Maxwell, S. K., Cantor, K. P., & Miller, R. S. (2000). Identifying populations potentially exposed to agricultural pesticides using remote sensing and a Geographic Information System. Environmental health perspectives, 108(1), 5-12.

Weber, J., Halsall, C. J., Muir, D., Teixeira, C., Small, J., Solomon, K., ... & Bidleman, T. (2010). Endosulfan, a global pesticide: a review of its fate in the environment and occurrence in the Arctic. Science of the Total Environment, 408(15), 2966-2984.

WHO, G. (2010). The WHO recommended classification of pesticides by hazard and guidelines to classification 2009.

Yang, C. C., & Deng, J. F. (2007). Intermediate syndrome following organophosphate insecticide poisoning. Journal of the Chinese Medical Association, 70(11), 467-472.

Yousef, M. I., Awad, T. I., & Mohamed, E. H. (2006). Deltamethrin-induced oxidative damage and biochemical alterations in rat and its attenuation by Vitamin E. Toxicology, 227(3), 240-247.

Zahm, S. H., & Blair, A. (1992). Pesticides and non-Hodgkin's lymphoma. Cancer Research, 52(19_Supplement), 5485s-5488s.

Zanella, R., Prestes, O. D., Friggi, C. D. A., Martins, M. L., & Adaime, M. B. (2012). An overview about recent advances in sample preparation techniques for pesticide residues analysis in cereals and feedstuffs. Pesticides: Recent trends pesticide residue assay, 149-170.