Review Article

Use of Insecticides and their Impact on Viral Diseases in Humans, Animals and Environment

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Abstract | All ecosystems, including humans, animals, and insects, are secretly threatened by pesticides. They keep pests under control, contribute significantly to crop productivity, and shield humans from vector-borne and viral illnesses, yet they also seriously contaminate our environment. These hazardous materials can be found in plants, soil, water, air, food, and feed. Through the food chain, their residues build in humans and animals after entering plants and animal products. They destroy useful species in the ecosystem and put our lives and health in peril. This review highlights the current standing of the impact of insecticides on viral diseases in man and animals. We observed that in addition to their surroundings, people also consume these hazardous substances from the air, water, and agricultural goods. They result in mortality and a variety of illnesses, malignancies, and mutations. These substances deplete pollinator populations and damage honeybee hives. Furthermore, the extensive use of pesticides severely suppresses wildlife, birds, and soil organisms. They harm soil microbes including viruses, pollinators, animals, humans, and honeybees. In addition to having an adverse effect on human health, increased pesticide use reduces the population of helpful organisms like honey bees and pollinators. If these living things disappear, there will be a lack of food, the economy will collapse, and the need for food and feed will rise, endangering our life. Thus, fresh crises like starvation and illness undermine our affluence. To reduce vector-borne diseases in crops, it is critical to manage plant pathogen-carrying insects and mites. Pesticides are useful in controlling vector populations because they limit the number of people who can contract and spread a virus, which may reduce the prevalence of sickness. Aside from their deadly toxicity, certain pesticides have characteristics that alter feeding patterns or otherwise impede the spread of viruses.

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Introduction

The purpose of pesticides is to keep rodents, insects, flies, mosquitoes, and other pests away from us. Throughout the world, they are extensively utilized for domestic, medical, municipal, and agricultural applications. Throughout the world, they are extensively utilized for domestic, medical, weeds, and agricultural applications (Das DK, 2011). They are present in food, drink, air, soil, and even breast milk. Currently, agrochemical dangers, pesticide resistance, population expansion, food security, destruction of the environment, and climate change are some of the major global concerns that modern agriculture needs to address (Sarwar M, 2015). These substances guard crops and agricultural products from pests like insects, weeds, and illnesses. They are known as plant protection products because they improve the efficiency of agricultural production (Wahab *et al*., 2016). A crucial component of agricultural management, pesticides have a significant role in raising crop output and quality.Some insecticides are persistent and, when administered in larger quantities, could be disastrous for ecosystems because they go up the food chain. Over half of the world's population lives in areas where two or more of the major vector-borne diseases are present, and these diseases include malaria, dengue, lymphatic filariasis, schistosomiasis, chikungunya, onchocerciasis, Chagas disease, leishmaniasis, Zika virus disease, yellow fever, Japanese encephalitis, and tick-borne diseases. An estimated 17% of all infectious diseases are caused by vector-borne diseases (Kyu *et al*., 2017). Despite the wide range of pathogenic agents, their prevalence, severity, and therapeutic options, all vector-borne illnesses share the ability to be stopped by vector management, whether they are spread by tick, mosquito, blackfly, triatomine, sand fly, or snail vectors. In fact, the majority of vector-borne diseases have shown to be extremely important to manage and eradicate, proving the crucial necessity of vector control efforts.Insecticides are the only option to combat these viral diseases.

These substances are widely utilized around the world because they provide easier, more affordable, and more effective control over weeds, illnesses, and pests (Nicolopoulou-Stamati *et al*., 2016).Even though the use of pesticides has enhanced crop yields, the widespread, careless, overuse, and improper use of all these chemicals has severely harmed the ecosystem and exacerbated environmental pollution and toxicity (Qian *et al*., 2018).The principal elements that comprise the agro-ecosystem are plants, crops, water, and soil (Stanley *et al*., 2016). These elements interact dynamically with one another to keep the ecosystem vibrant and long-lasting. Toxicants have compromised several ecological components (Silva *et al*., 2019). Anthropogenic activities also pose a serious threat to global food security, ecological health, and public safety (Zhang *et al*., 2015). The decline in soil biodiversity and food safety are major global problems, as pesticide use contaminates these areas (Costa *et al*., 2008). Since pesticides are all substances that are active and have dangers and hazards, the authority department should pass and approve them (Mubushar *et al*., 2019). Contaminated soil is carried by the wind and water, which damages ecosystems and creates more exposure pathways that might affect the health of people and other non-target organisms. Soil, the atmosphere, water, and plants can all become contaminated by these pollutants (Wu *et al*., 2018). In addition to killing pests, they may also be poisonous to beneficial insects, birds, fish, non-target plants, humans, and other creatures (Khan *et al*., 2017). According to data from the US Geological Survey (USGS), pesticides were present in over 90% of fish and water samples taken from US streams.

Pesticides are useful in crop production and in controlling plant illnesses carried by vectors, but they also pose a risk to the health of a sizable portion of the human population (Solecki *et al*., 2019). Though not necessarily selective, some compounds have negative effects on species that are not their intended targets (Talib *et al*., 2018).

People are typically exposed to these hazardous chemicals at work and in the food chain, and those who are impacted experience both acute and long-term poisoning symptoms. There are 1500 different kinds of pesticides used worldwide; each has a unique composition and structure, and they can have detrimental effects on both the environment and human health (Herit *et al*., 2019).

Approximately 2 million tons of pesticides are used annually in agriculture, with the US and Europe accounting for 69% of this total. Pesticide residues build up in plants and the products they produce, which pollutes the environment. It is possible for developmental exposure to different kinds of environmental toxins and pesticides to cause harmful neurological ef-

fects on humans or animals (Miller *et al.*, 2017). Some health issues brought on by these toxicants include cancer, birth defects, endocrine (hormone) system disorders, and diseases of the central nervous system. It was discovered that the widespread use of pesticides causes both human cancer and ecotoxicological damage in birds (Ahmad *et al.*, 2018). For example Bemisia tabaci is the carrier of the global viral disease known as Cucurbit Yellow Stunting Disorder Virus (CYSDV), which affects cucurbit crops. Epidemics of CYSDV have plagued cantaloupe production in the southwestern United States since 2006, when it was first discovered in Arizona and California. CYSDV is a phloem-limited virus that is semi-persistently vectored by B. tabaci. Certain insecticide applications have the potential to reduce CYSDV transmission. Certain insecticides can dramatically lower the spread of CYSDV. However, in persistently high infestation locations like the southwestern USA, pesticide management of CYSDV incidence in cantaloupes has limitations and frequently simply delays the development of the illness rather than preventing it (Castle *et al.*, 2017).

Insecticides and their effects

A insecticide is a compound, or combination of substances, used to manage agricultural pests (weeds, insects, etc.) that pose a threat to people, pets, plants, and other living things, as well as the environment and public health (Carvalho *et al.*, 2017). In addition to being useful, pesticides pose a health risk to both people and animals because of their toxicity (Deadman., 2017). They cause harm to all living things and contaminate the environment. Broad-spectrum insecticides can be instantly harmful to both targeting and non-target species, and they effectively suppress a variety of Pest organisms. Pesticides with a narrow scope of action suppress certain pest organisms (Thomson, 2012). It is the most effective method of controlling certain pests and reducing the effects of natural enemies with narrow-spectrum pesticides. They can Onyett the pests that are wanted; yet many pesticides on the planet have a broad spectrum, which means that in addition to killing the intended pest, they also destroy non-target species that are present in the pest's surroundings (Adams, 2017).

Insecticides residues are present in a wide range of everyday foods and drinks, such as prepared meals, water, fruits and vegetables, juices, snacks, animal feed, and so forth. It is also claimed that chemical residues cannot be eliminated by washing and peeling (Britt J *et al.*, 2015).

Workers in the pesticide industry, home pest exterminators, and agriculture are frequently exposed to pesticides at work. A population that is ill or elderly, pregnant women, or children may be more vulnerable to the pesticide's effects than others (Raven *et al.*, 2011). Given that pesticide residues have been found in human breast milk, it is alarming that children may be negatively impacted by them. With detected levels of pesticides in freshwater supplies frequently exceeding established limits, the issue of pesticide contamination in animal feeds has grown significantly in importance and cost. Other sources of contamination include environmental pollution, insect and microbe activity, and animal activities (Manahan, 2013)

To improve the quality and competitiveness of animal products, endogenous toxins that are mostly caused by pesticide spraying against pests may also be present in animal feed. Animals are frequently given contaminated food and fodder, and these substances travel through their respiratory systems after feeding. In its broadest sense, the word "feed" usually refers to both forages and compound mixes of other substances.

Insecticides are categorized based on four factors: (1) target molecules; (2) mechanism of action; (3) chemical structure; and (4) potential health effects.

Insecticides categorized as (1) organochlorine pesticides, (2) organic phosphorus pesticides, (3) carbonates pesticides, (4) pyrethroid pesticides, (5) biorational Chemicals used for pest (6) microbiological pesticides, (7) growth regulators, and (8) neonicotinoids in the absence of the criteria. Insecticides have an adverse effect on both target and non-target organisms, but they will have a greater negative impact on targets than on other non-targets. The International Organization for Biological and Integrated Control (IOBC) uses the mortality rate to determine the risk of pesticides for beneficial organisms. When a chemical kills fewer than 25% of helpful species, it is considered innocuous; but, when it eliminates more than 75% of beneficial species, it is classified as dangerous. The impacts of pesticides are categorized; as no pesticide can destroy every type of creature, each pesticide has unique properties and effects on living things. Plants and weeds are killed by herbicides, insects are

killed by insecticides, and bacteria are destroyed by bactericides (Miller etal., 2016). In order to ensure crop yields and reduce post-harvest losses, the use of pesticides, such as insecticides, has evolved from ancient times to become a crucial and strictly necessary agricultural component. The task of achieving long-term development without causing environmental harm has never been greater, given the continuously growing population and worsening ecological circumstances (based on irrefutable and growing evidence of climate change coupled with increasing levels of pollution). Agriculture is a major problem for sustainable development in a world where food production needs to expand by 70–100% by 2050 to meet the food requirement of over 9 billion people.

Insecticide resistance management to combat viral diseases

The registration, acquisition, and effective use of pesticide products are affected by monitoring for signs of insecticide resistance and management to halt the development of insecticide resistance.Insecticide resistance was tracked by malaria programs in the chosen nations using the WHO susceptibility test on Anopheles spp. collected from beacon sites. Nepal was an exception, as there was no recent data available and no monitoring of pesticide susceptibility was done. The resistance to insecticide in malaria vectors was evidently managed at different phases in the chosen nations. In order to coordinate or realign the selection and application of pesticides across sectors, a number of nations were currently establishing plans for managing insecticide resistance in collaboration with the agriculture sector. Malathion and the majority of synthetic pyrethroids are not allowed to be used in agriculture in Sri Lanka and are only allowed to be used for mosquito control.

Insecticides effects on humans

Insecticides are ingested by humans from food, the air, water, soil, plants, and animals. When they are absorbed by the human body, the bloodstream distributes them throughout the entire body. The respiratory system, skin, gastrointestinal tract (GIT), and urine tract can all be used to expel them. The main entrance points for pesticides into the human body are the respiratory, oral, ocular, and skin (Saeed *et al.*, 2017). According to WHO estimates, at least one million people are hospitalized worldwide for pesticide poisoning each year, out of which over 4 million individuals (about twice the population of New Mexico) are affected. emerging nations due to their usage of harmful pesticides that are frequently outlawed and heavily limited by wealthy nations (WHO, 2020). According to estimates from the United Nations Environment Programme (UNEP), each year, pesticides poison at least 300,000 workers in the United States and as least 3 million agricultural workers in less developed nations.

According to the Academy of Sciences, between 4,000 and 20,000 incidences of cancer are reported to occur in the US each year because of pesticide residues in food. In comparison to the 1950s, the usage of synthetic pesticides has increased by more than 50 times, and their toxicity has increased for pests by 10-100 times. Some synthetic pesticides, such as carbamate, pyrethroids, neonicotinoids, organophosphates (such as parathion and malathion), dichlorodiphenyltrichloroethane or ethane (DDT), and organochlorine, are hazardous to beneficial species (Yuan *et al.*, 2019). When two or more chemicals interact and perhaps produce synergistic effects simultaneously, their efficacy is boosted. There are two kinds of chemicals in pesticides: inert and act. Inert substances let the active part function more efficiently while active elements destroy the bug (Gillois *et al.*, 2018). All living things are harmful to pesticides at specific dosages. When they reach the human body, they disrupt the regular bodily responses needed for metabolism and hinder enzyme function. Numerous detrimental health impacts associated with pesticides have been identified. The epidermis, gastrointestinal tract, brain, respiratory system, reproductive system, kidney system, and so on all exhibit similar pesticide side effects.

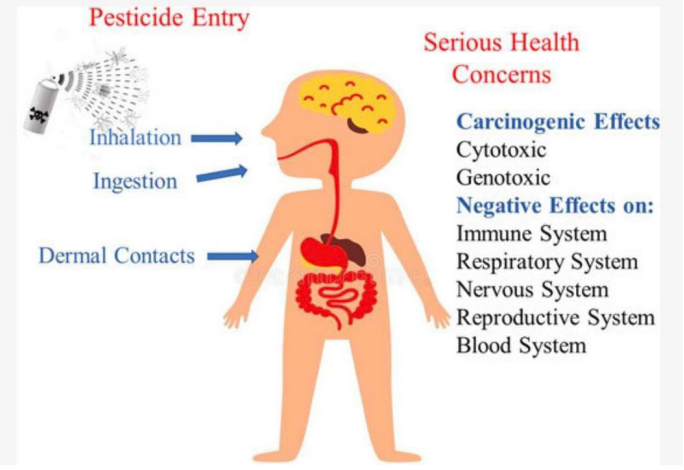


Figure 1: *Exposure routs and effects of pesticide exposure on human health (S et al., 2021).*

They have several harmful effects, including the potential to cause cancer, teratogenicity, mutagenicity, and endocrine-related problems (Groh *et al.*, 2017).

Furthermore, prolonged exposure to pesticides by work-related, unintentional, or purposeful means can cause severe intoxication, which can result in hospitalization or even death. Numerous clinical conditions, such as metabolic diseases, immunological disorders, neurotoxicity, endocrine disruption, reproductive problems, and malignancies, have been related to pesticide exposure (Lynch, 2012). About 100 trillion bacteria and equal numbers of human and microbial cells can be found in the human intestines. The microbiota in the gut absorbs fats, breaks down fiber, and facilitates the absorption of calcium, magnesium, and fatty acids. The growth and maturation of the gastrointestinal tract depend on the bacteria (López-Gálvez *et al.*, 2019). Therefore, it is their initial target because it is the GI tract's primary biological and physical barrier to drugs. These substances destroy intestinal cells and mucosa, suppress microbiota, and induce dysbiosis in the gut. They also affect metabolites (Wright, 2007). They are the source of noncommunicable illnesses, including autoimmune disorders, nonalcoholic fatty liver disorder, food allergies, and irritable bowel syndrome. Anorexia, dizziness, sweating, agitation, irritation of the epidermis, nose, throat, and eyes, weariness, restlessness, and insomnia are among the symptoms of mild pesticide poisoning (Gupta, 2018). In addition, a few more symptoms that are present in a moderate poisoning state are allergies, cramping in the abdomen, nausea, vomiting, headaches, lacrimation, excessive salivation, breathing difficulty, seizures, loss of consciousness, and rapid heartbeat. Severe poisoning symptoms include difficulty breathing, mucus or additional phlegm in the airways, skin burns, rapid breathing, adrenal hemorrhages, pancytopenia, pulmonary fibrosis, loss of reflexes, severe weakness, and even death. Organochlorine insecticides have been linked to hematological and hepatic alterations, carcinogenicity, detrimental effects on embryonic development, and lipid metabolism (Cimino *et al.*, 2017). Acute clinical symptoms include paresthesia (of the oral cavity, lips, and face), seizures, tremors, tonic clonic seizure disorders, and fever when exposed to these substances (Marshall, 2001). According to reports, pyrethroids induce deoxyribonucleic acid (DNA) damage in human sperm, and they may also have detrimental effects on the endocrine, central neurological, and reproductive systems and increase the risk of cancer. It may also result in seizures, incoordination, hyperexcitation, aggression, and whole-body tremors (Boutin *et al.*, 2014). Numerous illnesses and health impacts, including stroke, diabetes, hypertension, autism, kidney failure, Parkinson's disease, Alzheimer's disease, and cancer, are linked to organophosphate insecticides. Moreover, some organophosphate insecticides show potent mutagenic and teratogenic properties. Carbamate insecticides are linked to non-Hodgkin's lymphoma, dementia risk, and neurobehavioral problems (Isenring, 2010).

Neonicotinoid pesticides are implicated with Parkinson's disease, schizophrenia, and Alzheimer's disease, among other illnesses of the central nervous system. These substances cause sperm production and function to decrease in mammals, as well as pregnancy rates, embryo death rates, stillbirth and early delivery rates, and decreased child weight (Zimdahl, 2007).

Insecticides and human health

A medical risk assessment's main goal is to protect consumers from the harmful effects of toxicants in their food or water. Therefore, it is necessary to verify that the total amount of toxicants of interest in food or water samples does not surpass the daily recommended intake. Pesticide residues may have detrimental long-term effects on the health of people and animals and the ecosystem's stability (Pesiakova *et al.*, 2017). Pesticides have improved human health by slowing the spread of diseases carried by vectors. However, excessive and negligent use of it has had detrimental health impacts. Because pesticides are generic and poorly administered, people are more aware of the harm they inflict to infants and young children (Ruiz-Suárez *et al.*, 2015). The possibility of human exposure to pesticides has increased over the last few decades due to growing use of these chemicals. The World Health Organization reports that each year in poor nations, there are about 3,000,000 cases of pesticide poisoning and 220,000 fatalities. About 2.2 million people (about the population of New Mexico) are at increased risk of pesticide exposure; most of these people live in poor nations. Some, like carbamates and organophosphates, have a neurotoxic effect, while others may cause irritation to the skin or eyes. Certain pesticides may affect the hormone or endocrinology system of the body, but other pesticides may be carcinogenic (Martin, 2015). With an increasing global population and rising food prices, pesticide use is ris-

ing daily. Studies show that most pesticide residues are present in every agricultural product and in crops fed to animals. Almost all animal products, including meat, milk, dairy products, and eggs—foods that are seen as necessities by many—have pesticide residues found in them as well.

Influences of insecticides on livestock animals

Depending on how, where, and how long the substance is used, both domestic and wild animals may have negative health effects; however, these are typically unintentional (Chen Z *et al.*, 2019). These materials can be obtained by animals from tainted water and food. Consequently, milk and other fat-rich foods are the main contributors to the buildup of these poisons because of their lipophilic nature. Insecticides residues are widely dispersed throughout our environment, killing a large variety of nonhuman biota, including fish, birds, amphibians, bees, and small mammals (Rortais *et al.*, 2017). The populations of fish, fish-eating birds, marine mammals, and lions are among the creatures whose numbers are further reduced by the pesticides. It is believed that the buildup of dioxins, PCBs, and DDT—three types of persistent chlorinated hydrocarbons—in the food chain is what caused thousands of fatalities among Arctic seals. These substances build up fat and impair animals' immune systems. Similarly, the buildup of toxic pollutants is suspected to be the cause of the deaths of marine mammals in the Pacific Ocean, beluga whales in the Saint Lawrence Estuary, and striping dolphins in the Mediterranean.

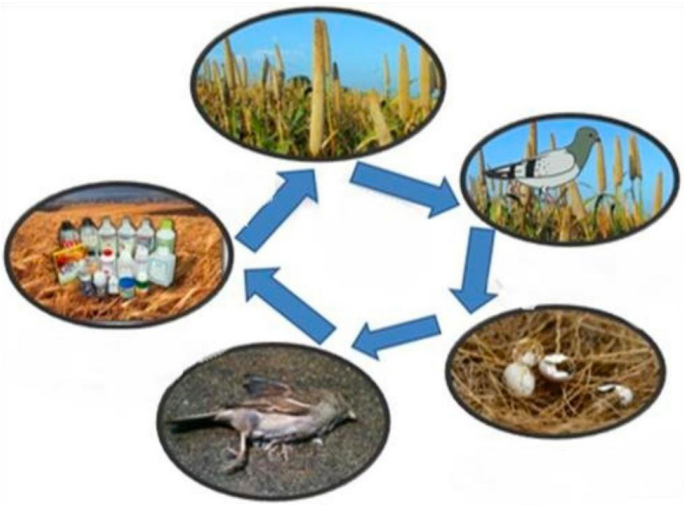


Figure 2: *Effects of insecticides on the life cycle and reproductive success of birds (Singh et al., 2022).*

Animal exposure to atrazine has been linked to reproductive damage and sexual maturation delays. In the 20th century, PCBs—organic chemicals that are incredibly toxic—were employed extensively in both industry and agriculture. It was prohibited worldwide in 2001. It has been discovered that fish, birds, and other migratory animals contain this poisonous chemical (Nicholls *et al.*, 2013). Furthermore, pesticides frequently cause intoxication in both domestic animals and people. According to reports, pesticide poisoning kills roughly 52.5% of birds and is the main cause of death for wild mammals. Numerous individuals employ toxic baits in unlawful, widespread, and non-selective ways, resulting in the extinction of numerous species. Poisoned baits were employed in Spain to eliminate wild animals that posed a threat to various industries, such as pigeon breeding, apiculture, and agriculture (Sanchez-Bayo and Goka, 2016). Their population has now been nearly wiped off (Law RJ, 2014). Environmental pesticides may be a significant factor in the underlying causes of infertility issues in dairy cattle. Pesticide exposure causes changes in females that include subfecundity, infertility, poor reproductive behaviors, growth retardation, intrauterine fetal death, and ovarian failure. Reproductive toxicants and endocrine disruptors are terms used to describe pesticide residues that negatively affect the reproductive system. These toxicants operate at multiple sites, such as the pituitary, hypothalamus, and reproductive organs, to modify or disrupt the reproductive hormone milieu (Jelani, 2013). Pesticide residues can harm sperm plasma membranes, which can be harmful to the male reproductive system.

Pathogenesis of diseases in animals due to Insecticides effects

Insecticides toxicity poses hazardous effects on plants, soil, humans, birds, and animals, causing poisonous physiological changes due to pollution of soil, air, and water. Pesticide toxicity can cause skin and eye irritation, nervous system issues, reproductive problems, and cancer by mimicking hormones' response. Most studies on lymphoma and leukemia showed positive associations with pesticide exposure (Miller GT, 2004).

Absorption and distribution

Pesticides enter the body through ingestion, inhalation or dermal absorption. Oral pesticides (ferbam, Ziram) or thiram combined with nickel increased metal levels

in rats' tissues, while nickel combined with ethylene- or propylene dithiocarbamates showed unchanged or reduced metal concentrations.

The pesticide might reach the CNS via peripheral nerves and nerve cord, may also inhibit cholinesterase enzyme.

Biochemical disruption

Many pesticides interfere with vital biochemical processes. Organophosphates and carbamates inhibit acetylcholinesterase, leading to an accumulation of acetylcholine and subsequent overstimulation of cholinergic receptors. This results in neuromuscular disturbances, respiratory failure, and potential death.

1. It has deleterious effects on the oxidative responses and hormonal levels of these snails.
2. It has genotoxic effects on DNA and RNA extracted from these snails (Amany *et al.*, 2017).

Oxidative stress

Oxygen's harmful effects are primarily due to reactive oxygen species, which are unstable and highly reactive molecules with various chemical structures, such as hydroxyl, superoxide, nitric oxide, and lipid peroxyl radicals (Halliwell, 1994).

Free radicals can damage cellular macromolecules, including proteins, carbohydrates, lipids, and nucleic acids, potentially leading to arteriosclerosis and DNA structure changes, potentially causing cancer (Rumley and Paterson, 1998).

Endocrine disruption

Chemicals with estrogenic or antiestrogenic effects disrupt thyroid function, while fewer chemicals affect other endocrine systems like androgens and adrenal steroids. Lead exposure in early development disrupts multiple endocrine systems, including gonadal steroids, adrenal steroids, and thyroid hormones. In utero exposure reduces hormone levels, puberty onset, and testosterone levels. Pesticides reduce luteinizing hormone levels, delay the onset of puberty and produce irregular estrous cycling in female animals, and reduce testosterone levels, sperm counts, and masculine sexual behavior in male animals (Ronis *et al.*, 1996).

Hepatotoxicity and Nephrotoxicity

Pesticides cause liver toxicity and kidney damage, hepatotoxic effects include enzyme inhibition, fatty liver, necrosis and fibrosis. Nephrotoxicity manifests glomerular damage,tubular necrosis and impaired renal function. AST and ALT were measured to assess liver injury; albumin was used to measure liver function (Abass *et al.*, 2010).

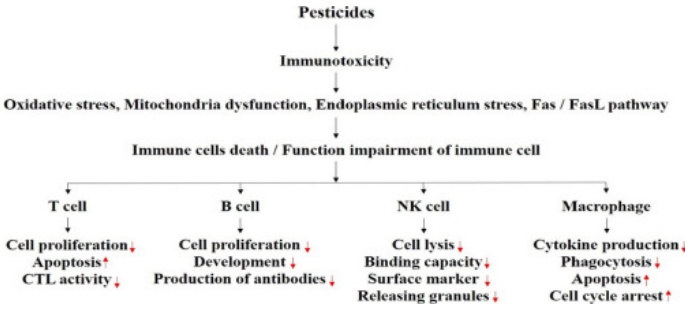
Chemical Basis	Examples	Site of toxicity	Major acute signs & symptoms
Chlorinated hydrocarbons	Methoxychlor, lindane, toxaphene, chlordane	Neurotoxin, CNS, kidney, liver	Apprehension, excitability, dizziness, headache, disorientation, weakness, paresthesia, convulsions
Organo-phosphates	Diazinon, malathion, parathion, chlorpyrifos, dichlorvos	Irreversible inhibition of red blood cell cholinesterase, acetylcholinesterase, plasma cholinesterase	**Mild:** fatigue, headache, blurred vision, dizziness, numbness of extremities, nausea, vomiting, excessive sweating and salivation, tightness in chest **Moderate:** weakness, difficulty talking, muscular fasciculations, miosis **Severe:** unconsciousness, flaccid paralysis, moist rales, respiratory difficulty, cardiac arrhythmias, and cyanosis
Carbamates	Aldicarb, carbaryl, carbofuran	Reversible inhibition of red blood cell acetylcholinesterase and plasma cholinesterase	Diarrhea, nausea, vomiting, abdominal, pain, excessive sweating and salivation, blurred vision, difficulty breathing, headache, muscular fasciculations
Phosphine fumigants	Aluminum or zinc phosphide	Lungs, CNS, liver, kidney	Dizziness, headache, nausea, vomiting, dyspnea, pulmonary edema
Chlorophenoxy derivatives	2,4-D and 2,4,5-T	Skin, eyes, respiratory and GI tracts	**Inhalation:** burning sensation in the nasopharynx and chest, dizziness **Ingestion:** vomiting, esophagitis, abdominal pain, diarrhea, muscle stiffness and twitching, metabolic acidosis
Dipyridyls	Diquat, paraquat	Injury to epithelium, cornea, liver, kidney, and linings of GI and respiratory tract	**Ingestion early:** nausea, vomiting, 48–72 hours **after exposure:** oliguria, jaundice, cough, dyspnea, tachypnea, and pulmonary edema, convulsions, coma

(Ellenhorn et al., 1997)

The levels of urea and creatinine in plasma measures kidney damage using the pirate method and procedure of jaffe (Jaffe E.R, 1972).

Immunosuppression

Pesticides suppress NK and cytotoxic T cell function, leading to immune suppression and allergic reactions. They induce mast cell degranulation, producing Th2 cytokines, promoting IgE binding to mast cells, and potentially initiating autoimmune diseases through disruption of the endocrine system.



(Corsini *et al.*, 2012)

Carcinogenesis

Carcinogenesis due to pesticides refers to the process by which exposure to pesticides leads to the development of cancer (linden,malathion). For instance, non-Hodgkin's lymphoma, Brain cancer, Breast cancer, Testicular cancer, Prostate cancer, Liver cancer, Lung cancer, Ovarian cancer.

Mechanisms

1. DNA damage and mutation
2. Oxidative stress and inflammation
3. Immune system suppression

Neurotoxicity

Harmful effects of pesticides on the nervous system, including the brain, spinal cord, and peripheral nerves. Organophosphates, organochlorines, pyrethroids, neonicotinoids, carbamates cause neurotoxicity (Balachandar *et al.*, 2022).

Example

1. Neurodegeneration (e.g., Parkinson's disease, Alzheimer's disease)
2. Neurodevelopmental disorders (e.g., ADHD, autism)
3. Neuropsychiatric symptoms (e.g., depression, anxiety)
4. Cognitive impairment (e.g., memory loss, reduced IQ)
5. Motor function deficits (e.g., tremors, weakness)
6. Sensory disturbances (e.g., numbness, tingling)
7. Seizures and epilepsy.

Reproductive and developmental toxicity

Pesticides can impact the male reproductive system at multiple sites, including testes, accessory sex glands, damage spermatozoa, alter Sertoli cell or Leydig cell function, and disrupt hormonal regulation.

These target female reproductive systems can cause sexual behavior changes, puberty onset, fertility, gestation time, pregnancy outcomes, lactation, and premature menopause, disrupting female reproduction.

The protective barrier of the placenta may not protect the developing embryo or fetus from harmful chemicals, such as insecticides, which can cause birth defects, impaired fertility, high abortion rates, and abnormal pregnancies due to their widespread use (Michal *et al.*, 1993).

Respiratory and gastrointestinal effects

Pesticide-induced asthma is influenced by pathogenetic mechanisms, with organophosphorus pesticides linked to increased asthma incidence,direct irritation, inflammation, and immunosuppression (Nicolopoulou-Stamati. *et al.*, 2016). Long-term occupational exposure to organophosphates, carbamate, has been linked to higher lung cancer mortality rates (Bonner *et al.*, 2005).

Pesticide residues in soil, water, and food can cause GUT dysbiosis. It also causes IBS, Crohn's disease and colon cancer. Ingestion of contaminated feed or water can lead to gastrointestinal irritation, ulceration, and disruptions in nutrient absorption (Conis E, 2022).

Insecticides Toxicity to Beneficial Microorganisms

To manage pests, pesticides are used by spraying on plants and soil; as a result, they mix with the soil and plant residue that is contributed to the soil (Sponsler *et al.*, 2019).

In the soil, the pesticides undergo physical, chemical, and biological transformations. Living things in the soil are extremely harmful to certain chemical compounds. According to several reports, pesticides negatively impact the microbiological characteristics of soil. They change an organism's enzymatic activity. For

example, invertase in soil is negatively impacted by buprofezin (Coulon *et al.*, 2018). After one addition, the digestive enzyme's activity is increased; however, after three further applications, the activity gradually decreases. However, pesticides play a crucial role in the breakdown of pesticides, including herbicides, insecticides, and fungicides, in soil and water. However, they are also negatively impacted by the toxicity of these substances (Crenna *et al.*, 2017).

With their lengthy half-lives, many pesticides can cause significant harm to the ecosystem when they are present. The growing use of harmful pesticides is the reason for soil contamination.

In addition to eliminating specific pests, these chemicals also restrict beneficial species that are not selective but are vital to the health of the soil and plants (Maddela and Venkateswarlu, 2018) . Agrochemicals that destroy helpful non-target microorganisms in the soil have a detrimental effect on the cycling and retention of nutrients, deplete the soil's supply of nutrients, and ultimately lower soil fertility. These substances are persistent and long-lasting in soil, which means they continuously have a detrimental effect on the soil's microbial flora. The fate of pesticides in soil is determined by four factors: (1) chemical qualities, (2) soil parameters, (3) application technique, and (4) site conditions.

Both macro and microbes are essential to the ecosystem's services and operations. Earthworms are among the essential soil organisms that contribute to the development of soil. They are the most significant microorganisms in the soil and are referred to as "engineers of the soil ecosystem". They assist in supplying plants with nutrients. They contribute to soil formation, improve soil fertility, and aid in the decomposition of organic materials, among other crucial roles in soil processes (El-Naas *et al.*, 2017). Their sensitivity to toxins found in soil is high. These substances raise the possibility of toxicity for microorganisms that live in the soil and earthworms. Since these substances build up in food, high absorption or ingestion of them can have an impact on microbes (Muturi *et al.*, 2017). Legumes can fix 100–200 kgN/hectare annually; however, the use of chemicals, particularly insecticides, slows down the rate of nitrogen fixation. Rhizobium meliloti and lucerne cannot communicate symbiotically when exposed to pollution and organochlorine herbicides. Pesticides decrease the efficiency of symbiotic nitrogen fixation, but they also have many other negative effects that are widespread and destroy many organisms, which brings disaster to nature by reducing beneficial insects, microbes, living things, fish, and so forth (Sandhu *et al.*, 2010). Ultimately, this results in a delay in symbiotic nitrogen fixation and a decline in crop yield. They induce birth deformities, kill organisms, stop them from growing, and cause a variety of diseases. These toxicants enter the human body through the mouth, skin, lungs, and eyes and affect living things. These substances have an impact on the gastrointestinal tract, cardiovascular system, kidneys, lungs, the epidermis liver, spleen, and neurological system (Johnsen *et al.*, 2001). Pesticides have been connected to cancer, genetic disorders, and a few other prevalent illnesses. Pesticide exposure, both acute and chronic, can cause a range of harmful effects (Pepper *et al.*, 2013). Various diseases pose a threat to human health. When agrochemicals are used cautiously and in accordance with guidelines, the harmful effects of pesticides on the surrounding environment are lessened (Lehman *et al.*, 2015). Furthermore, it is essential to abide by any pesticide regulations and proposals made by authorities to maintain a healthy environment. Effective insecticides that have fewer negative effects on people, animals, pollinators, and beneficial creatures are being developed by scientists (Smith *et al.*, 2015). It may contribute to non-target creatures' sustainability.

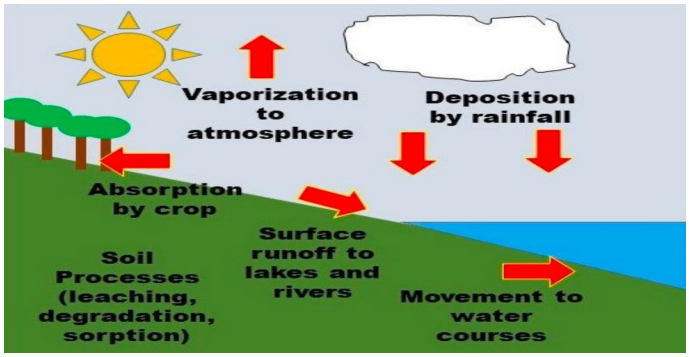


Figure 3: *Insecticides behaviors in the Natural Environment (Daniel et al., 2021).*

Insecticides and the environment

A significant portion of the Insecticides sprayed on crops are either absorbed by the plants and animals or broken down by chemical or microbiological processes (Anwar *et al.*, 2011). However, a sizable portion of the applied amount is lost to the environment through runoff, leaching, and air drift, ending up in soils, surface water, and groundwater. You can pollute turf, water, soil, and other vegetation with pesticides.

Pesticides can be poisonous to a wide range of other creatures, including fish, birds, and beneficial insects, in addition to harming insects and weeds (Hicks, 2013). Continual use results in a decline in biodiversity. Many pesticides are difficult to break down; they linger in the soil, seep into surface and groundwater, and contaminate a large area of the environment (Lam, 2011).

They can infiltrate an organism, bioaccumulate in food chains, and then affect the environment based on their chemical characteristics. The detection of pesticides in freshwater supplies has become a significant and costly issue, as levels frequently surpass the established limitations (in the EU: 0.1 μg l–1 for any single active ingredient, or 0.5 μg l–1 for all pesticides). In Switzerland, the regulatory limit for pesticide levels was exceeded in 70% of surface waters. These days, pesticides can be found in every habitat on the planet and are frequently found in animals, both marine and terrestrial (Bajwa and Sandhu, 2014).

Conclusion

Pesticides pose a serious risk to human and animal health and have grown in popularity for usage in domestic, commercial, and agricultural settings as well as in the care of livestock. The more effective and beneficial alternative to tackle the issues pertaining to pesticide residue. Setting up legal requirements and pesticide usage management procedures are alternate strategies for preventing pesticide residue's harmful effects on the environment. The use of pesticides in agriculture has boosted the number of agricultural products produced since they shield plants from pests. While their application is crucial for crop yield, overuse of them pollutes the environment as well. The extensive use of pesticides has contaminated our food, feed, water, air, soil, and other sources. Due to their widespread use in agriculture, the home, medicine, and the municipality, many individuals are working with them at work, and their residues spread from one living thing to another via the food chain.

Author's Contribution

Muhammad Wasif Gulzar: Devised and developed the study strategy, created the search query, conducted the literature search, gathered the data, proofread the files, uploaded them, and sent them.

Musharraf Manzoor and Hassaan Ahmad Bajwa: Before submitting the work, they screened the articles, authored, evaluated, prepared, and cleared the final draft.

Riffat Maqsood and Hussain Abbas: Researched data and shared her reviews about pathogenesis of diseases in humans and animals caused by pesticides and immunopathology.

Muhammad Zain and Ali Hamza: Shared his reviews about adverse effects on microorganisms.

Muhammad Suleman and ShaheYar: Made his findings about insecticides' negative effects on the environment.

Abdul Wadood and Noman Aslam: Makes a comprehensive review of the final draft of the article and analyzes the final data before submission.

Data availability

No data was used for the research described in this article, as it is a review article.

Competing interests

Authors have declared that no competing interests exist. As of right now, neither among the writers nor anywhere else, are there any conflicts of interest.

References

Abass, K., Reponen, P., Mattila, S., Pelknen, O., 2010. Metabolism of carbosulfan II. Human interindividual variability in its in vitro hepatic biotransformation and the identification of the cytochrome P450 isoforms involved. Chem. Biol. Interact

Adams S. The Designer's Dictionary of Color. Abrams. 2017;1-257.

Ali Beg MA. Classification of Pesticides. In Pesticides Toxicity Specificity & Politics. 2017;22-45.

Anwar, T., Ahmad, I., and Tahir, S. E. E. M. A., 2011. Determination of pesticide residues in fruits of Nawabshah District, Sindh, Pakistan. Pakistan J. Bot. 43, 1133-1139.

Ahmad KS. Exploring the potential of Juglans regia-derived activated carbon for the removal of adsorbed fungicide Ethaboxam from soils. Environmental Monitoring and Assessment. 2018;190(12): 737.

Amany M. Abd El-Ghany [a], Nesreen M. Abd El-Ghany Molluscicidal activity of *Bacillus thuringiensis* strains against *Biomphalaria alexandrina* snails Volume 6, Issue 4, December 2017,

Pages 391-393.

Balachandar Vellingiri, Mamatha Chandrasekhar, S Sri Sabari, Abilash Valsala Gopalakrishnan, Arul Narayanasamy, Dhivya Venkatesan, Mahalaxmi Iyer, Kavindra Kesari, Abhijit Dey Ecotoxicology and Environmental Safety, 2022.

Bajwa, U., and Sandhu, K.S., 2014. Effect of handling and processing on pesticide residues in food – a review. J Food Sci Technol. 51: 201-220. DOI: 10.1007/s13197-011-0499-5.

Bonner MR, Lee WJ, Sandler DP, Hoppin JA, Dosemeci M, Alavanja MC. Occupational exposure to carbofuran and the incidence of cancer in the agricultural health study. Environ Health Perspect. 2005.

Boutin C, Strandberg B, Carpenter D, Mathiassen SK, Thomas PJ. Herbicide impact on non-target plant reproduction: What are the toxicological and ecological implications? Environmental Pollution. 2014; 185:295-306.

Cimino AM, Boyles AL, Thayer KA, Perry MJ. Effects of neonicotinoid pesticide exposure on human health: A systematic review. Environmental Health Perspectives. 2017;125(2):155

Britt J. Properties and effects of pesticides. In Principles of Toxicology: Environmental and Industrial Applications. 2015;309-324.

Carvalho FP. Pesticides, environment and food safety. Food and Energy Security. 2017;6(2):48-60.

Castle S, Palumbo J, Merten P, Cowden C, Prabhaker N. Effects of foliar and systemic insecticides on whitefly transmission and incidence of Cucurbit yellow stunting disorder virus. Pest Manag Sci. 2017 Jul;73(7):1462-1472. doi: 10.1002/ps.4478. Epub 2017 Feb 7. PMID: 27862891.

Conis, E. (2022). How to sell a poison: the rise, fall, and toxic return of DDT. First edition. New York: Bold Type Books.

Corsini , E, M Sokooti, C L Galli, A Moretto, C Colosio Pesticide induced immunotoxicity in humans: a comprehensive review of the existing evidence, Epub 2012 Oct 29Deadman ML. Sources of pesticide residues in food: Toxicity, exposure, and risk associated with use at the farm level. In Pesticide residue in foods. Springer, Cham. 2017;7-35.

Costa LG. Toxic effects of pesticides. Casarett and Doull's toxicology: The basic science of poisons. 2008; 8:883-930.

Coulon M, Schurr F, Martel AC, Cougoule N, Bégaud A, Mangoni P, Dalmon A, Alaux C, LeConte Y, Thiéry R, Ribière-Chabert M. Metabolisation of thiamethoxam (a neonicotinoid pesticide) and interaction with the Chronic bee paralysis virus in honeybees. Pesticide biochemistry and physiology. 2018; 144:10-18.

Crenna E, Sala S, Polce C, Collina E. Pollinators in life cycle assessment: towards a framework for impact assessment. Journal of Cleaner Production. 2017; 140:525-536.

Das DK. Introductory soil science. Kalyani Publishers. 2011;591-592.

Ellenhorn MJ, Schonwald S, Ordog G, Wasserberger J: Ellenhorn's Medical Toxicology: Diagnosis and Treatment of Human Poisoning,Williams & Wilkins, Maryland, 1997; 1614–63.

Gillois K, Lévêque M, Théodorou V, Robert H, Mercier-Bonin M. Mucus: An underestimated gut target for environmental pollutants and food additives. Microorganisms. 2018;6(2):53.

Groh KJ, Geueke B, Muncke J. Food contact materials and gut health: Implications for toxicity assessment and relevance of high molecular weight migrants. Food and Chemical Toxicology. 2017; 109:1-18.

Gupta RC. Toxicity of Pesticides. In Lu's Basic Toxicology: Fundamentals, Target Organs, and Risk Assessment. (7th Edition). CRC Press Taylor & Francis Group. 2018;453-486.

Halliwell B: Free radicals, antioxidants and human disease: Curiosity, causes or consequence. Lancet, 1994; 344: 721–724.

Harit G. Organochlorine pesticides: A threat to aquatic ecosystems. In Handbook of Research on the Adverse Effects of Pesticide Pollution in Aquatic Ecosystems 2019;41-63. IGI Global.

Jaffe, E.R. Oxidative Hemolysis, or What Made the Red Cell Break? N. Engl. J. Med. 1972. [PubMed]World Health Organization. The WHO recommended classification of pesticides by hazard and guidelines to classification 2019. (. License: CC BY-NC-SA 3.0 IGO.). Geneva: World Health Organization. 2020; 1-92.

Khan MS, Rahman MS, editors. Pesticide Residue in Foods: Sources, Management, and Control. Springer; 2017.

Lynch JJ, editor. Lippincott's Manual of toxicology. Lippincott Williams & Wilkins; 2012;139-161.

López-Gálvez N, Wagoner R, QuirósAlcalá L, Ornelas Van Horne Y, Furlong M, Avila EG,

Beamer P. Systematic literature review of the take-home route of pesticide exposure via biomonitoring and environmental monitoring. Int. J. Environ. Res. public health.2019;16(12):2177.

Manahan S. Fundamentals of environmental and toxicological chemistry: Sustainable science. CRC press. 2013;75- 116.

Michal, F., Kenneth, M. G., Negro-Vilar A, and Skakkebæk M. Impact of the environment on reproductive health: executive summary. Environment Health Perspective 1993.

Miller GT (2004) Sustaining the Earth, VIth edition.Thompson learning, Inc. Pacific Grove, California. Ch.IXth.

Miller TP, Rebek EJ, Schnelle MA. Banker plants for control of greenhouse pests. Oklahoma Cooperative Extension Service. 2017; 7334:1-7.

Miller GT, Spoolman S. Environmental science. (15th edition). Cengage Learning. 2016; 171:232.

Mubushar M, Aldosari FO, Baig MB, Alotaibi BM, Khan AQ. Assessment of farmers on their knowledge regarding pesticide usage and biosafety. Saudi Journal of Biological Sciences. 2019;26(7): 1903-1910.

Marshall EJP. Biodiversity, herbicides and non-target plants. In Brighton Crop Protection Conference Weeds. 2001;2: 855-862.

Nicholls CI, Altieri MA. Plant biodiversity enhances bees and other insect pollinators in agroecosystems. A review. Agron. Sustain. Dev. 2013;33(2):257-274.

Nicolopoulou-Stamati P, Maipas S, Kotampasi C, Stamatis P, Hens L. Chemical pesticides and human health: The urgent need for a new concept in agriculture. Frontiers in Public Health.2016; 4:148.

Nicolopoulou-Stamati P, Maipas S, Kotampasi C, Stamatis P, Hens L.Chemical Pesticides and Human Health: The Urgent Need for a New Concept in Agriculture. Front Public Health. 2016.

Pesiakova AA, Gusakova EV, Trofimova AN, Sorokina TY. Migratory birds are the source of highly toxic organic pollutants for indigenous people in the Russian Arctic. In IOP Conference Series: Earth and Environmental Science. 2017; 107:1755-1315.

Qian J, Shi C, Wang S, Song Y, Fan B, Wu X. Cloud-based system for rational use of pesticide to guarantee the source safety of traceable vegetables. Food Control. 2018; 87:192-202.

Raven PH, Berg LR, Hassenzahl DM. Environment. (7th Edition). John Wiley & Sons Inc. 2011;535

Rumley AG, Paterson JR: Analytical aspects of antioxidants and free radical activity in clinical biochemistry. Ann Clin BioChem, 1998;35: 181–200

Saeed MF, Shaheen M, Ahmad I, Zakir A, Nadeem M, Chishti AA, Shahid M, Bakhsh K, Damalas CA. Pesticide exposure in the local community of Vehari District in Pakistan: An assessment of knowledge and residues in human blood. Science of The Total Environment. 2017; 587:137-144.

Sarwar M. The dangers of pesticides associated with public health and preventing the risks. International Journal of Bioinformatics and Biomedical Engineering. 2015;1(2):130-136.

Stanley J, Preetha G. Pesticide toxicity to non-target organisms. Berlin, Germany: Springer; 2016.

Silva V, Mol HG, Zomer P, Tienstra M, Ritsema CJ, Geissen V. Pesticide residues in European agricultural soils–A hidden reality unfolded. Science of the Total Environment. 2019; 653:1532-1545.

Solecki RA, Ritz V, Pesticides. In Toxicology and risk assessment: A comprehensive introduction. (2nd Edition). John Wiley & Sons Ltd. 2019;703-722.

Talib AH, Al-Rudainy AJ, Gathwan MA, Thakir BM, Abdulfattah RK. The acute toxicity of herbicide roundup ultra in mosquito fish Gambusia affinis. J. Bio. Env. Sci. 2018;13(1):9-15. 15.

Wahab A, Hod R, Ismail NH, Omar N. The effect of pesticide exposure on cardiovascular system: A systematic review. Int J Community Med Public Health. 2016;3(1):1-10

Zhang M, Zeiss MR, Geng S. Agricultural pesticide use and food safety: California's model. JIA. 2015;14(11):2340-57..

Wu YC, Kabadi SV, Neal-Kluever A. Developmental neurotoxicity considerations for food additive safety. in food toxicology: Current Advances and Future Challenges. Apple Academic Press Inc. 2018;93-149.Ronis MJJ, Badger TM, Shema SJ, Roberson PK, Shaikh F. Reproductive toxicity and growth effects in rats exposed to lead at different periods during development. Toxicol Appl Pharmacol 36:361–371 (1996).

Thomson L. Pesticide impacts beneficial species.

Grape and Wine Research and Development Corporation. 2012; 5:1-7..

Yuan X, Pan Z, Jin C, Ni Y, Fu Z, Jin Y. Gut microbiota: an underestimated and unintended recipient for pesticide-induced toxicity. Chemosphere. 2019; 227:425-434. S. Ali; M. I Ullah; A.Sajjad ; Q. Shakeel; A. Hussain, Environmental and Health Effects of Pesticide Residues, January 2021 https://www.researchgate.net/publication/348555390

Wright RT. Environmental science: Toward a sustainable future. Jones & Bartlett Publishers; 2007;316.

Isenring R. Pesticides and the loss of biodiversity: How intensive pesticide use affects wildlife populations and species diversity. PAN Europe, London; 2010.

Zimdahl RL. Fundamentals of Weed Science. (3rd Edition). Academic Press, Elsevier Inc. 2007;395-436.Ruiz-Suárez N, Boada LD, HenríquezHernández LA, González-Moreo F, Suárez-Pérez A, Camacho M, Zumbado M, Almeida-González M, del Mar TraviesoAja M, Luzardo OP. Continued implication of the banned pesticides carbofuran and aldicarb in the poisoning of domestic and wild animals of the Canary Islands (Spain). Science of the Total Environment. 2015; 505:1093-1099.

Martin C. A re-examination of the pollinator crisis. Elsevier Ltd. Current Biology. 2015; 25:811–815.

Chen Z, Yao X, Dong F, Duan H, Shao X, Chen X, Yang T, Wang G, Zheng Y. Ecological toxicity reduction of dinotefuran to honeybee: New perspective from an enantiomeric level. Environment International. 2019; 130:104854.

Rortais A, Arnold G, Dorne JL, More SJ, Sperandio G, Streissl F, Szentes C, Verdonck F. Risk assessment of pesticides and other stressors in bees: Principles, data gaps and perspectives from the European Food Safety Authority. Science of the Total Environment. 2017; 587:524- 537.

D.Singh; V.Delu ; K. Yodhu ; T. Dahiya; A. Kour, N. Punia, Role of birds in agroecosystem: A review on agricultural and economic ornithology, July 2022 https://www.researchgate.net/publication/362031408

Sanchez-Bayo F, Goka K. Impacts of pesticides on honeybees. Beekeeping and Bee Conservation-Advances in Research. 2016; 4:77-97.

Jilani S. Comparative assessment of growth and biodegradation potential of soil isolate in the presence of pesticides. Saudi journal of biological sciences. 2013; 20(3):257-264.

Sponsler DB, Grozinger CM, Hitaj C, Rundlöf M, Botías C, Code A, Lonsdorf EV, Melathopoulos AP, Smith DJ, Suryanarayanan S, Thogmartin WE. Pesticides and pollinators: A socioecological synthesis. Science of the Total Environment. 2019; 662:1012-1027.

Maddela NR, Venkateswarlu K. Insecticides– Soil Microbiota Interactions. Springer International Publishing; 2018.

El-Naas MH, Mousa HA, El Gamal M. Microbial degradation of chlorophenols. In Microbe-Induced degradation of pesticides. Springer, Cham. 2017;23-58.

Muturi EJ, Donthu RK, Fields CJ, Moise IK, Kim CH. Effect of pesticides on microbial communities in container aquatic habitats. Scientific Reports. 2017; 7:44565.

Sandhu HS, Gupta VV, Wratten SD. Evaluating the economic and social impact of soil microbes. In Soil Microbiology and Sustainable Crop Production. 2010;399- 417.

Johnsen K, Jacobsen CS, Torsvik V, Sørensen J. Pesticide effects on bacterial diversity in agricultural soils–A review. Biol Fertil Soils. 2001;33(6):443-453.

Pepper IL, Gerba CP. Aeromicrobiology. In Environmental Microbiology. 2015;89- 110).

Yousaf S, Khan S, Aslam MT. Effect of pesticides on the soil microbial activity. Pakistan J. Zool. 2013;45(4).

Lehman RM, Cambardella CA, Stott DE, Acosta-Martinez V, Manter DK, Buyer JS, Maul JE, Smith JL, Collins HP, Halvorson JJ, Kremer RJ. Understanding and enhancing soil biological health: the solution for reversing soil degradation. Sustainability. 2015;7(1):988-1027.

Law RJ. An overview of time trends in organic contaminant concentrations in marine mammals: Going up or down, Marine Pollution Bulletin. 2014; 82:7-10.

Hicks, B. 2013. Agricultural pesticides and human health. In: National Association of Geoscience Teachers. Available fromhttp://serc.carleton.edu/NAGTWorkshops/ health/case_studies/pesticides.html

Lam, K. 2011. Effects of pesticides on human health. In: Toxipedia. Available from http://www. toxipedia.org/display/toxipedia/Effects+of+Pes-

ticides +on+Human+Health. Accessed Jan 16, 2014.

Daniel Ruan, H.;Wang, L.; Lyu, J.; Sadler, R.; Connell,D.; Chu, C.; Phung, D.T. Agriculture Development, Pesticide Application and Its Impact on the Environment.Int. J. Environ. Res. Public Health 2021,18, 1112. https://doi.org/10.3390/ijerph18031112

Kyu HH, Abate D, Abate KH, Abay SM, Abbafati C, Abbasi N, *et al*. Global, regional, and national disability-adjusted life-years (DALYs) for 359 diseases and injuries and healthy life expectancy (HALE) for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet. 2018; 392(10159):1859–922. https://doi.org/10.1016/S0140-6736(18)32335-3 PMID: 30415748