



PHYSIOLOGICAL IMPACTS OF PESTICIDAL CONTAMINATION: CHALLENGE TO SUSTAINABLE AGRICULTURE AND BIODEGRADATION METHODS

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ABSTRACT

Pesticides are chemicals used to eliminate pests and increase crop yield, as well as to control parasites in livestock. Their widespread use over the past two eras has led to increased agricultural yields but has also caused environmental issues. These chemicals can reduce the quality of the environment, impact vital ecosystem functions by decreasing species diversity, altering food pathways, and affecting energy patterns and nutrient cycling. Pesticides affect living organisms in various ways. Long-term exposure can reduce growth, reproduction, and survival of fish and other aquatic populations. Amphibians, which have semi-permeable skin and lay eggs in water, are particularly susceptible to pesticides during breeding and foraging. Birds can also be affected by continuous pesticide use. Ponds with standing water may recover more slowly from pesticide exposure compared to flowing water bodies. Livestock can be exposed to pesticides through contaminated fodder or water, which can have detrimental effects. Heavy pesticide treatment of soil can reduce beneficial soil microorganisms and alter the chemical structure of plants. Pesticide poisoning causes approximately one million global deaths and chronic disorders in humans each year. The use of pesticides also harms insect pollinators directly and indirectly through the reduction of appropriate pollinator communities, leading to crop damage. To reduce environmental contamination, it is important to minimize the use of pesticides and explore alternative methods of pest control.

Keywords: bioaccumulation, drinking water, non-target organisms, pesticide exposure, toxicant

INTRODUCTION

Numerous environmental contaminants, including pesticides, have serious effects on organisms, including humans (Chang *et al.*, 2013; Özkara *et al.*, 2016). Pesticides are used to eliminate pests, increase crop yields, and control parasites in livestock, but their extensive use has led to ecological and public health issues (Tudi *et al.*, 2021; Poudel *et al.*, 2020). With the advancement and intensification of agricultural production, pesticides and other chemicals are commonly used, resulting in increased agricultural yields and contamination of surface water, groundwater, and soil (Khan *et*

al., 2018). Continuous release of various pesticides and compounds into the environment poses a significant threat to marine ecosystems. These chemicals have disrupted the stability of aquatic species, leading to population increases in blackflies, rotifers, and copepods (Kousar and Javed, 2014; Mahboob *et al.*, 2014).

Exposure of non-target organisms in aquatic environments to pesticides occurs at varying levels (Ranatunga *et al.*, 2023). The residues of these chemicals in water, crops, fish, and ecosystems can pose severe threats to organisms, predators, and humans (Ali *et al.*, 2014; Auon *et al.*, 2014; Wasoh *et al.*, 2014). High concentrations of pesticides can lead to major water contamination, affecting fish development, reproduction, and survival, and

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causing various visible effects on aquatic populations (Rani *et al.*, 2022). Organochlorines, for example, can contaminate the tissues of almost all living organisms on Earth (Malik *et al.*, 2020). The delicate balance between species is disrupted by these harmful compounds and their associated chemicals. Pesticides can cause changes in species living in freshwater by affecting the functions of several enzymes, leading to physiological and biochemical modifications (Agbohessi *et al.*, 2015). The number of endangered species is increasing in all taxonomic classes due to environmental degradation caused by pesticides and related chemicals (Mahmood *et al.*, 2016). This review has outlined the impacts of pesticides on all taxonomic groups, with possible effects described as steps towards reducing the use of pesticides to avoid environmental contamination.

Availability of data on pesticide use, environmental concentrations, and their effects on non-target organisms may be limited or inconsistent, making it challenging to draw comprehensive conclusions (Malhotra *et al.*, 2021). Whereas, many studies are based on observational data, which can make it difficult to establish causality between pesticide exposure and observed effects (Stehle *et al.*, 2019). Controlled experiments are often limited by practical constraints and may not fully replicate real-world conditions. Additionally, long-term effects of pesticide exposure on ecosystems and human health are challenging to assess due to the complexity of ecological systems and the potential for delayed or cumulative effects. Yet, organisms in natural environments are often exposed to multiple stressors, such as pollution from various sources, habitat loss, and climate change, making it difficult to isolate the specific effects of pesticides (Gao *et al.*, 2020). Despite these limitations, research on the impacts of pesticides continues to advance our understanding of their effects on the environment and human health, helping to inform policies and practices aimed at reducing their negative impacts.

History of pesticidal usage

The use of pesticides worldwide has increased significantly, reaching about two million tonnes annually, with a continuing upward trend. Pesticides were first introduced in Pakistan in 1954, with an initial formulation of 254 metric tonnes. Subsequently, large quantities were

imported from the United States between 1960 and 1970, while dichlorodiphenyl trichloroethane (DDT) and benzene hexachloride (BHC) were locally produced (Tariq *et al.*, 2007). Presently, an estimated 70,000 tons of pesticides are used each year in Pakistan, with an annual growth rate of 6% (Gao *et al.*, 2020). Cotton crops account for 75% of pesticide use, with the remaining 25% used on vegetables, fruits, maize, paddy rice, and tobacco. Only a small fraction (approximately 0.1%) of the pesticides applied reach their intended target organisms, while the rest (99.9%) is dispersed in the air, soil, and water, leading to environmental contamination and affecting human health and other living organisms. The environmental impact is further exacerbated by improper packaging, careless disposal of pesticides, and the use of outdated pesticides in Pakistan (Wasoh *et al.*, 2014). This is often due to a lack of awareness among farming communities about the harmful effects of pesticides. Consequently, pesticides continue to contaminate soil, groundwater, surface water, and even drinking water sources, including bottled mineral water (Zia *et al.*, 2008).

Case study of pesticidal contamination in areas of Pakistan

In Pakistan, there is a lack of data on pesticide pollution in drinking water, primarily due to insufficient laboratory facilities. Only one or two labs in the country have the capability to detect pesticide concentrations in parts per billion. For the first time in Pakistan, pesticides were found in drinking water for cattle in Karachi, including benzene hexachloride (BHC) isomers (Tudi *et al.*, 2021). These chlorinated pesticides were detected in 10 out of 79 samples, with contamination levels reaching up to 16.7 g/L. In the past, organochlorine pesticides like DDT were widely used in Pakistan, both on crops and in malaria elimination programs (Poudel *et al.*, 2020). In Pakistan, the use of most organochlorine pesticides is prohibited. However, their presence can still be observed in the atmosphere due to their high longevity. Factories manufacturing DDT and its metabolites in Pakistan have been abandoned since the use of these poisonous pesticides was prohibited. DDT has a long half-life, making it hazardous (Ahad *et al.*, 2006). Similar cases of abandoned factories and the presence of banned pesticides can be found in Table 1.

Table 1. Presence, type, and number of pesticides within different samples in various areas of Pakistan

Location	ample	Type of Pesticides	Amount of pesticide	References
Karachi, Pakistan	Drinking water for cattle	Benzene hexachloride BHC	These chlorinated pesticides were present in 10 of the 79 samples, causing contamination of up to 16.7 g/L. s	Poudel <i>et al.</i> , (2020).
Summandri region of Faisalabad	Because cotton crops use the most pesticides, so cotton-growing sites have more chance to pesticide pollution in the water.	Monocrotophos, Cyhalothrin and Endrine	40-60, 0.2, 0.1-0.2 g/L concentrations respectively	Ahad <i>et al.</i> , (2000); Tudi <i>et al.</i> , (2021).
Multan, Pakistan	Twelve samples of groundwater engaged by six separate locations of cotton-growing area	Azinophos methyle, Phosphamidon, Carbofuran, Cypermethrin, Dimethoate, Diazinon, Dichlorvos, Esfenvalerate, Fenitrothion, Lindane, Malathion, Deltamethrin, Methyl parathion, Endosulfan were found	Maximum residual limits are exceeded in 33% of samples (MRLs)	Ahad <i>et al.</i> , (2000); Kousar and Javed, (2014)
Districts in Punjab: Bahawalnagar, Muzaffargarh, DG Khan, and Rajanpur.	Pesticide residues in shallow groundwater were examined in four cotton-growing	Bifenthrin, Carbofuran, λ-Cyhalothrin, Endosulfan, Methyl parathion, Monocrotophos were detected in there,	Samples were not exceeding maximum residual limits	Tariq <i>et al.</i> , (2007); Mahboob <i>et al.</i> , (2014)
KPK province, Pakistan. Mardan division is a tobacco, sugarcane and maize yielding area on a large scale; twelve different area's groundwater shown a pesticide's contamination in all taken samples.	Considerable quantities of pesticides were used for tobacco, sugarcane and maize crops. In KPK, it is a common practice to use a high number of pesticides on tobacco fields. By personal observation, it is detected that more than ten sprays used for single yield of tobacco.	Chlorpyrifos, Dichlorvos, Dimethoate, Endosulfan, Fenitrothion, Methyl parathion, Mevinphos, Profenphos are used in there	Pesticides with exceeding the maximum residual limits were detected with (0.82, 0.50 and 0.64 g/l) concentrations at three sites: Amber Swabi, Lahor Shakh Swabi, and Madras Kalay.	Jan <i>et al.</i> , (2009); Stehle <i>et al.</i> , (2019).
Ground plus surface water samples of Punjab. Aman Gharh, Nowshera	Ground plus surface water	Organochlorine pesticides, DDT	DDT metabolites observed by varying amount of 0.017–1.06 ng/mL in various ground plus surface water samples of Punjab. However, in few instances, particularly in the cotton yielding sites, maximum admissible limit has exceeded. In Aman Gharh, Nowshera, previous DDT-producing factory exposed DDT metabolites i.e. p,p'-DDT pollution within different water samples in range of 70-400 µg/L But, their results are inconsistent with other studies. Water samples of the similar zone had amounts of different pesticides in range 0-15µg/L	Ahad <i>et al.</i> , (2006); Gao <i>et al.</i> , (2020)
Groundwater and surface water, Punjab, Pakistan	Lake water, pondwater and ground water	DDT, Azinophos-methyle, Fenitrothion, Parathion methyle, α-Cypermethrin	Highest amount's sample was found in rainwater pond rather from well-water or surface water. Similarly, different DDT isomers were found in groundwater and surface water, with 0.947g/L and 1.06g/L respectively. In June 2004, fishes found dead in lake due to presence of pesticides (Azinophos-methyle,	Ahad <i>et al.</i> , (2006); Malhotra <i>et al.</i> , (2021)

			Fenitrothion, Parathion methyle, α -Cypermethrin) in range of 30.4 μ g/L	
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Simly and Rawal Lake, Pakistan	Treatment of lake water cause reduction in amount by 81%, which was still unsafe	Alpha-HCH, Azinophos-methyl, Cyfluthrin, Cyfluthrin, Deltamethrin, Diazinon, Endosulfan, Esfenvalerate, Fenitrothion, Heptachlor, Lindane, Parathion-methyl, α -Cypermethrin	Exceeded standard of European Union given for drinking water	Iram <i>et al.</i> , (2009); Ali <i>et al.</i> , (2014)
Nearby sites of old pesticide stocks in Punjab, Sindh and KPK	Water samples	γ -BHC, β -HCH, Endrin, Dieldrin, Heptachlor exoepoxide and Heptachlor endoepoxide.	Exceeded standard of European Union given for drinking water	Ahad <i>et al.</i> , (2006); Ranatunga <i>et al.</i> , (2023).

Pesticidal contamination and influences over living beings

Pesticidal contamination refers to the presence of pesticides in the environment, which can have various impacts on living beings. These contaminants can enter ecosystems through agricultural runoff, aerial drift, or direct application, and they can affect organisms at different trophic levels (Figure 1) (Gao *et al.*, 2020). Pesticides can have direct toxic effects on organisms that come into contact with them. This can lead to acute poisoning or chronic health problems. Different pesticides have varying degrees of toxicity, and their effects can depend on factors such as the dose, duration of exposure, and the species of organism. Pesticides can also have indirect effects on organisms by disrupting food chains (Ranatunga *et al.*, 2023). For example, pesticides can reduce the populations of insects that serve as food for other animals, leading to cascading effects throughout the ecosystem. This can ultimately impact the abundance and diversity of species in an ecosystem. They can bioaccumulate in organisms, meaning that they build up in the tissues of living beings over time. This can be particularly problematic for organisms at the top of the food chain, as they may consume prey that have already accumulated pesticides (Malhotra *et al.*, 2021). This process, known as biomagnification, can result in high levels of pesticide exposure for top

predators. These are typically designed to target specific pests, but they can also harm non-target organisms. For example, insecticides can unintentionally kill beneficial insects such as pollinators or natural predators of pests. Herbicides can also affect non-target plants, leading to changes in plant communities (Tudi *et al.*, 2021). It can have long-term effects on ecosystems. They can persist in the environment for extended periods, leading to chronic exposure for organisms. Pesticides can also contribute to the development of pesticide-resistant pest populations, which can pose challenges for pest management. Overall, pesticidal contamination can have wide-ranging impacts on living beings and ecosystems, highlighting the importance of careful pesticide use and environmental monitoring.

Effect on ecosystem and its integrity disruption

Pesticides have a negative impact on the environment, reducing its quality and affecting vital ecosystem functions. They decrease species diversity, alter food pathways, disrupt energy patterns, and interfere with nutrient cycling, thereby reducing the quality and stability of the biotic components of ecosystems (Figure 2) (Mahmood *et al.*, 2016). Residues of pesticides in water are a significant problem, posing severe danger to biological populations, including humans. Pesticides often migrate from

one area to another through runoff caused by rainfall (Agbohessi *et al.*, 2015). Spray drift, volatilization, and aerial application of pesticides are the main pathways through which they enter the air. The amount of drift depends on the size of the droplets and wind speed, while the rate of volatilization is influenced by factors such as the time after spraying, surface characteristics, temperature, humidity, wind velocity, and vapor pressure (Stehle *et al.*, 2019). Similarly, the instability or semi-volatility of pesticide compounds poses a serious threat of air pollution in major cities (Malik *et al.*, 2020).

Effect on fish and aquatic life

Pesticides in high concentrations have been found to adversely affect fish growth, reproduction, and survival, among other impacts on aquatic populations (Hussain *et al.*, 2012). They are recognized as one of the most significant water pollutants with widespread effects on marine ecosystems globally (Häder *et al.*, 2020). Fish are particularly susceptible to the effects of pesticides, which can interfere with enzymes and hormones critical for their normal function. Even continuous exposure to lower amounts of pesticides can have significant impacts on fish health (Bashir *et al.*, 2020). Pesticides that do not directly cause death can still lead to abrupt changes in fish physiology and behaviour, posing risks to their survival. Blood analysis is often used as an indicator of toxic stress in fish, providing insights into their health and functional status. Biochemical changes induced by pesticides include disruptions in metabolism, enzyme inhibition, growth retardation, and decreased species survival (Lu *et al.*, 2018). Exposure to pesticides in fishes can manifest through various signs, including anxiety, increased body movement, rapid respiration, excessive mucous secretion, convulsions, changes in coloration, loss of balance, and behavioural alterations (Li *et al.*, 2022). Endocrine-disrupting chemicals (EDCs) can disrupt normal growth and lead to the production of female features in male fishes, often accompanied by decreased fertility. There is a correlation between the levels of pesticides in fish tissues and the suppression of hormone levels. Imbalances in hormone levels during development can result in skeletal abnormalities, bone deformities, and inhibited growth (Ghosh *et al.*, 2022). Furthermore, some pesticides can disrupt the food supply or alter the aquatic habitat of fishes, even at low concentrations.

Many pesticides have the potential to cause death in fishes within a short period of time (Palioura and Diamanti-Kandarakis, 2015).

A study was conducted to investigate the haematological and genotoxic effects of butachlor, a chloroacetanilide herbicide, in freshwater fish (*Labeo rohita*). Fish exposed to elevated levels of butachlor (0.75-1.00 mg/L) exhibited symptoms such as increased breathing rate, gasping at the water's surface, uneasiness, movement of the operculum, loss of equilibrium, and erratic swimming (Ghosh *et al.*, 2022). Hematological analysis revealed a reduction in erythrocyte count, haemoglobin concentration, haematocrit levels, and lymphocyte count, while total leukocyte count increased. Morphological and nuclear abnormalities observed included pear-shaped erythrocytes, microcytes, tear-shaped erythrocytes, micronuclei in erythrocytes, nuclei with lobes, blebs, notches, and cells with nuclear remnants (Ghaffar *et al.*, 2015a). Similarly, the effects of different levels of triazophos insecticide on freshwater fish (*Labeo rohita*) were investigated. Triazophos exposure led to reductions in total erythrocyte count, hemoglobin level, serum total protein levels, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC). The numbers of lymphocytes and monocytes decreased, while the number of leukocytes increased significantly. The micronucleus assay revealed a higher percentage of micronuclei, blebbed, lobed, notched, binucleated, and heteropicnotic nuclei in pear-shaped erythrocytes. Serum analysis showed a significant increase in the levels of various enzymes and lipid peroxidation products, indicating serious hemato-biochemical and DNA damage effects in aquatic organisms exposed to triazophos (Ghaffar *et al.*, 2015b).

Effect on amphibians

The global decline in amphibian species has raised concerns about the importance of using species as bioindicators of environmental pollution (Pérez-Iglesias *et al.*, 2021). Pesticides can adversely affect the health of amphibians, impacting their populations in various ways. Pesticides can cause subtle immune or neurological changes that can ultimately lead to the destruction of amphibians. Additionally, pesticides can interfere with the normal growth and development of adolescent amphibians,

affecting recruitment in amphibian communities (Zhelev *et al.*, 2018). Anticholinesterase pesticides, such as Lambda cyhalothrin and monocrotophos, can bind to the cholinesterase enzyme, disrupting the nervous system and causing respiratory failure and death in amphibian species (Pérez-Iglesias *et al.*, 2023). These pesticides have been observed to cause severe damage to the liver, heart, and brain of the amphibian species *Rana cyanophlyctis*. The normal growth and development of amphibian larvae depend on functional and uncontaminated aquatic systems (Zhang *et al.*, 2019). However, water bodies are especially susceptible to pesticide contamination due to the deposition and distribution of contaminating substances in river, lake, and pond sediments. Sources of endocrine-disrupting chemicals (EDCs) affecting water bodies include municipal wastewater (Suárez *et al.*, 2021) and agricultural runoff containing pesticides and herbicides. These EDCs can accumulate in water systems and adversely affect amphibian reproductive processes. Exposure to certain pesticides, such as dimethoate, carbofuran, and chlorpyrifos, can affect the vitamin A levels in amphibians (Osman *et al.*, 2022) and reduce melanogenesis. Carbaryl, which acts by inhibiting acetylcholinesterase, can serve as a model for neurotoxins. Sublethal concentrations of carbaryl can have a significant impact on amphibian populations by directly or indirectly influencing metamorphosis timing and scale, ultimately affecting survival (El-Nahhal *et al.*, 2021). Studies have shown that tadpoles of *Rana* spp. are particularly sensitive to herbicides, and organochlorine pesticides are highly toxic to tadpoles, with effects manifesting during metamorphosis (Rajak *et al.*, 2023).

Effect on reptiles

Organochlorine pesticides in reptiles can alter enzyme activity and concentrations of sex hormones. These chemicals act as weak androgen receptors (Kanda, 2019). PCBs, dioxins, furans, and organochlorine pesticides, commonly found in highly contaminated areas, can cause atypical growth, such as the occurrence of unhatched eggs or malformed animals. Additionally, polluted eggs have been linked to reduced developmental success. The phytopesticide biosal has been found to have anticholinesterase effects in the kidney and liver (Matthiessen *et al.*, 2018).

Effect on birds

Continuous use of pesticides leads to a decrease in bird populations, primarily through indirect effects on soil. Pesticides applied to soil are consumed by earthworms and accumulate in birds that ingest them, resulting in significant bird losses (Ali *et al.*, 2021). Some pesticides can harm both bird embryos and adults, causing death and reproductive damage. Harmful effects on embryos include death or reduced hatchability and teratological effects caused by estrogen hormone-mimicking pathways. In adults, pesticides can cause acute mortality, sub-lethal stress, decreased fertility, and defective incubation (Saroop and Tamchos, 2024). Pesticides can also lead to behavioral changes, habitat destruction, and a decline in bird populations. Seabird nests have been found to contain deposits of organochlorine pesticides, serving as useful indicators of environmental pollution (Zaller and Zaller, 2020). Fish-eating birds are more affected by pesticides than predatory terrestrial birds because they ingest more toxins early in the food chain (Boudh and Singh, 2019).

Effects on invertebrates

Invertebrates, with their high growth rates, are able to recover quickly compared to birds and mammals with slower growth rates. Aquatic environments with flowing water can also recover more quickly in terms of organization and function compared to ponds with standing water (Gao *et al.*, 2020). The use of pesticides can lead to the removal of species that are vulnerable to one or more pesticides, resulting in a loss of species diversity. For example, even a single application of DDT can significantly reduce the number of arthropods in a cereal crop (Mahmood *et al.*, 2016). Orchards, which are complex ecosystems, are particularly susceptible to disturbance from continuous pesticide use. Increased insect attacks have been reported in orchards following pesticide application, with pests such as leafrollers, aphids, scales, codling moth, and tetranychid mites being affected chain (Boudh and Singh, 2019). Pesticides can reduce the populations of natural enemies of these pests, particularly predatory mites, leading to increases in the numbers of Collembola and sometimes Acarina in the soil (Gunstone *et al.*, 2021). The consistency of honey can be affected when honeybees are exposed to pesticides for

prolonged periods, with direct effects on beehives (Rajak *et al.*, 2023).

Effect on mammals

The application of dimethoate on grasslands reduces the population of mice and voles by decreasing insect accessibility, as insects are a primary food source for rodents. Excessive pesticide use in cereal crops can lead to a reduction in the quantity of partridges, as there are fewer insects available for young chicks to feed on (Lu *et al.*, 2018). Continuous pesticide use in agriculture can result in severe health issues, as pesticides become part of the food chain. Organochlorines, in particular, are highly lipophilic and accumulate in fatty foods (Li *et al.*, 2022). Pesticides primarily enter cattle through fodder or polluted water sources (Zhang *et al.*, 2019).

Effect on soil microorganisms

Continuous exposure to pesticides for soil treatment can lead to a decline in beneficial soil microorganisms (Prashar and Shah, 2016). Herbicides such as triclopyr, glyphosate, and 2,4-D have specific effects on soil bacteria. Triclopyr prevents the transformation of ammonia to nitrite by soil bacteria, glyphosate reduces the growth of free-living nitrogen-fixing bacteria, and 2,4-D decreases the growth of nitrogen-fixing microbes within the roots of certain bean plants, as well as reduces the actions of nitrogen-fixing blue-green algae, thus halting the alteration of ammonia to nitrates through bacteria. Mycorrhizal fungi are also affected by herbicides like oryzalin, trifluralin, roundup, and triclopyr, while oxadiazon reduces the number of spores of mycorrhizal fungi (Gunstone *et al.*, 2021). Pesticides can also impact the rapidity and effectiveness of nutrient flow by affecting sensitive microbes. Herbicide EPTC, when applied at regular doses, has been found to weaken the breakdown of cellulose within the soil system (Meena *et al.*, 2020). This process is particularly vulnerable to pesticide intrusion, as only two nitrifying bacterial genera, Nitrosomonas and Nitrobacter, are known so far. Some herbicides have been reported to either obstruct or stimulate nitrification in the soil (Saroop and Tamchos, 2024).

Effect on decomposers

Pesticides can have significant effects on decomposers. For example, the use of fungicides in orchards to control apple scab can lead to increased outbreaks of the disease and

lower production rates (Winkelmann *et al.*, 2019). Additionally, these pesticides can be harmful to earthworms, which play a crucial role in regulating apple scab by consuming diseased leaves on the soil surface. This can result in a decrease in organic matter through the soil fauna and microorganisms. These organisms are essential for decomposing cellulose, integrating decomposed matter into the soil, and converting minerals into elements accessible for plant growth. The widespread use of pesticides can impact soil organisms directly or indirectly, mainly by altering their food supply (Rajak *et al.*, 2023). Insecticide use in agricultural or grassland ecosystems, forests, and desert ecosystems can reduce soil micro arthropod populations, leading to a decrease in the rate of decomposition and mineralization. Although these effects may be temporary, they can ultimately reduce soil fertility (Van Bruggen *et al.*, 2016). The impacts of pesticides on decomposers in aquatic ecosystems are less well-documented. However, the vulnerability of arthropods as major decomposers in water suggests that insecticides may slow down the decay of organic matter in aquatic systems (Köhl, 2019).

Effect on plants

The use of pesticides in agricultural fields, grasslands, and forests can initially increase primary production (Malone *et al.*, 2018). However, their repeated use does not always lead to increased crop and forest production. For example, the repeated use of certain insecticides in orchards and on cotton has resulted in the emergence of new insect and mite pests, leading to a reduction in productivity (Gunstone *et al.*, 2021). Pesticides can also alter the chemical composition of plants. For instance, some organochlorine insecticides can increase the levels of certain macro- and microelement components in corn and beans while reducing the quantity of others (Prashar and Shah, 2016). Additionally, pesticides like endrin, DDT, lindane, and aldrin can stimulate the synthesis of significant amino acids such as proline, arginine, histidine, lysine, leucine, and tyrosine in corn, but decrease the amount of tryptophan. Furthermore, the herbicide simazine has been shown to enhance the uptake of water and nitrogen in barley, rye, and oat seedlings, leading to increased plant weight and total protein content (Meena *et al.*, 2020). Changes in plant components due to pesticide application

can have significant effects on insects feeding on plants (Prashar and Shah, 2016). For example, when suggested doses of pesticides are applied and nitrogen content in plants increases, there can be a threefold rise in the numbers of corn leaf aphids. Similarly, corn plants become more vulnerable to attack by corn borers (Malhotra *et al.*, 2021). The increase in nitrogen and phosphorus levels in rice fields due to insecticides such as monocrotophos and phosphamidon has been observed to result in a revival in the population of rice blue leafhoppers (Rajak *et al.*, 2023).

Effect on human life

Pesticide poisoning causes approximately one million deaths globally each year, along with chronic disorders (Lu *et al.*, 2018). No population is entirely protected from pesticide exposure, and the potential health impacts are a significant concern for developing countries with high pesticide use (Li *et al.*, 2022). During production and preparation, the risk of exposure to pesticides may be higher as complex processes are not hazard-free. Workers in manufacturing settings are at a higher risk as they are directly involved with various toxicants like pesticides and raw ingredients (Prashar and Shah, 2016).

Pesticides are known to be endocrine disruptors, meaning they can imitate or antagonize natural hormones, leading to serious health impacts. Long-term, low-dose exposure to pesticides is believed to be gradually linked to human health impacts such as immune suppression, hormone disruption, cancer, and reproductive irregularities (Mahmood *et al.*, 2016). The neurological effects of pesticides are connected to the intensity and concentration of exposure (Winkelmann *et al.*, 2019). Workers involved in the manufacturing of powder and liquid pesticide preparations have shown symptoms such as headache, nausea, fatigue, eye and skin irritation, as well as mental, nervous, and gastrointestinal symptoms linked to low plasma cholinesterase activity (Gunstone *et al.*, 2021). Dioxin, a component of some pesticides, is carcinogenic for humans and can affect the cardiovascular system (Ali *et al.*, 2021). Farm workers, their families, and passersby near fields where pesticides are applied can be exposed to measurable amounts of pesticides. Residues of pesticides have been found in the plasma of farm workers, leading to neuromuscular abnormalities, drug stimulation,

and alterations in steroid (Mahmood *et al.*, 2016). Pesticides can also enter the body through diet, especially through consumption of fatty foods (Prashar and Shah, 2016). Pesticides like endosulfan persist in the environment for long periods and bioaccumulate in plants and animals, eventually entering the human body (Boudh and Singh, 2019). Endosulfan primarily targets the central nervous system, with acute inhalation toxicity compared to dermal toxicity. It is also highly absorbed through the gastrointestinal pathway (Zaller and Zaller, 2020). Organochlorines are known to increase the risk of hormone-related cancers, and exposure to dioxins can lead to significant learning disabilities in children (Zhang *et al.*, 2019). Abnormal thyroid hormone levels have been associated with the presence of dioxin-like organochlorines and hexachlorobenzene (HCB) in serum (Meena *et al.*, 2020). Persistent organic pollutants such as organochlorine pesticides are linked to type 2 diabetes (Li *et al.*, 2020) and can affect the complement system, leading to immune system activation in humans (Gao *et al.*, 2020).

Effect on pollinators

Some of the familiar pollinators include various species of bees, fruit flies, bumblebees (*Bombus* sp.), honey insects (*Apis* sp.), beetles, and birds such as colibris and sunbirds. Pollinators can serve as bioindicators of ecosystem processes, wherein physical, chemical (Figure 3) (Winkelmann *et al.*, 2019), and biological events connect organisms to their environment through various interactions influenced by ecological pressures like parasites, diseases, competitors, predators, pesticides, and habitat changes fungi (Gunstone *et al.*, 2021). The use of pesticides, however, can directly harm insect pollinators and inadvertently damage crops due to the lack of appropriate pollinator communities (Zhang *et al.*, 2019).

Pesticide application also affects multiple pollinator functions, including foraging behaviour, colony mortality, and pollen-gathering efficiency. Most of our understanding of the impacts of pesticides on pollinator behaviour comes from bee research, as bees constitute a significant proportion of the insect pollinator population content (Meena *et al.*, 2020). For example, numerous laboratory trials have demonstrated the lethal and sublethal effects of neonicotinoid insecticides on bees' foraging behaviour, learning, and memory (Boudh and

Singh, 2019). Female bees, deprived of their full reproductive capacity due to additional duties within the colony, experience higher mortality rates and reduced pollen-gathering efficiency, ultimately leading to colony collapse following pesticide exposure (neonicotinoid and pyrethroid) (Winkelman *et al.*, 2019).

Sublethal doses of imidacloprid have been found to affect the longevity and foraging behaviour of honeybees (*A. mellifera*). Microsporidial infections from imidacloprid-treated hives have significantly increased in the gut of bees. Communication between pathogens and imidacloprid is believed to be a major factor contributing to honeybee colony mortality worldwide, including Colony Collapse Disorder (Li *et al.*, 2020). Imidacloprid has also been reported to reduce clutch output due to decreased bumblebee fecundity (Lu *et al.*, 2018). Field studies conducted in agricultural areas have found a decline in the abundance of bumblebees and butterflies associated with pesticide application. Bees (insect pollinators) have been identified as being at greater risk from pesticide use (Boudh and Singh, 2019).

Pesticides resistance development with time and sustainable farming

Populations of insects and mites with significant resistance to pesticides have evolved worldwide in various ecosystems, with nearly 400 out of 2,000 pest species developing resistance to multiple pesticides (Winkelman *et al.*, 2019). Resistance increases of up to 25,000 times have been observed, and resistance to one pesticide can lead to cross-resistance to other unrelated pesticides. Species with high genetic variability tend to evolve a significant degree of resistance, allowing them to dominate in pesticide-stressed environments and alter their stability and dynamic equilibrium. Resistance has also been observed in animals other than insects. For example, house mice developed twice the tolerance to DDT over ten generations of exposure (Gunstone *et al.*, 2021). Plants can also develop resistance to herbicides (Lu *et al.*, 2018), and some plant pathogens have developed resistance to fungicides (Prashar and Shah, 2016). Resistance appears to evolve more rapidly in organisms with short life cycles under intense selective pressure from persistent pesticide residues. The delicate balance among species that characterizes an ecosystem is disrupted by insecticides. These chemicals are now regularly found in drinking water, food, and

air, exposing all of us to a global experiment in pesticide exposure. The precise risks of these exposures may not be fully understood (Prashar and Shah, 2016). Given the implications of increasing pesticide use, the most rational and precautionary approach is to phase out the use of the most hazardous pesticides, reduce reliance on toxic pest control substances, and promote environmentally friendly pest management practices. Integrated Pest Management (IPM), first implemented in 1959, is crucial in this regard (Winkelman *et al.*, 2019). It involves minimal use of mildly toxic pesticides, which are integrated with biological and cultural methods to minimize pest damage. Pesticides are only used when pest attack thresholds are reached content (Meena *et al.*, 2020). There is a growing movement towards sustainable farming practices aimed at reducing the use of pesticides and fertilizers through a systematic approach. There is increasing interest in promoting organic farming, which emphasizes techniques such as crop rotation, green manure, compost, and biological pest control methods to maintain soil productivity (Malone *et al.*, 2018). Organic farming strictly excludes the use of synthetic pesticides and fertilizers, crop growth regulators, animal antibiotics, food additives, and genetically modified organisms.

Organic foods derived from organic farming are considered to be pesticide-free and are therefore seen as a potential alternative source for high-quality food, ensuring a secure diet in the future (Boudh and Singh, 2019). By promoting the use of organic diets, it implies that farmers will be encouraged to adopt organic farming practices. Market incentives are a strong driver to encourage the organic development of farmers. Understanding the long-term ecological impacts of pesticides before their release into the environment is crucial. By combining existing knowledge in the field with current pesticides and applying important chemodynamic principles to newly developed compounds, it is possible to predict the fate of new chemicals with a certain degree of accuracy before they are used in the environment content (Meena *et al.*, 2020).

Biodegradation: Possible recommended solution

Bioremediation is an environmentally friendly and cost-effective technology that involves the use of living organisms to clean up polluted areas (Gunstone *et al.*, 2021).

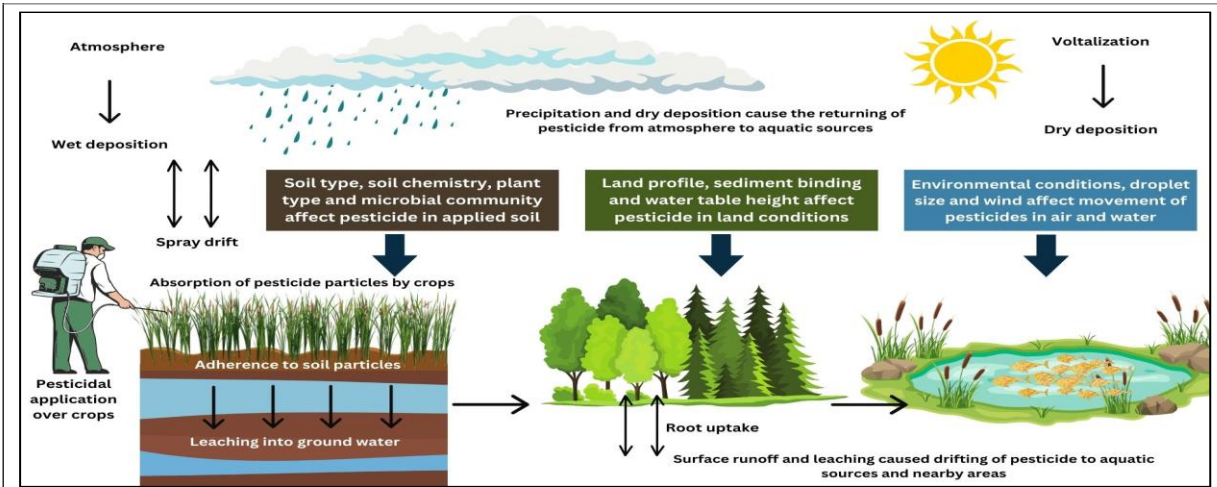


Figure 1. Sources of pesticidal contamination and its entry within non-point sources (Gao *et al.*, 2020).

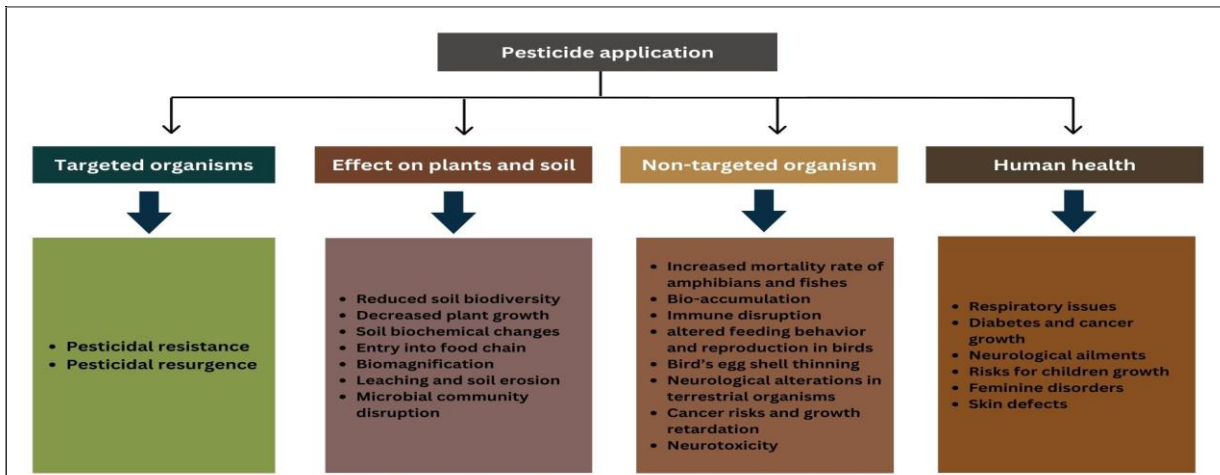


Figure 2. Summary of pesticidal physiological impacts over living beings and ecosystem disruption (Mahmood *et al.*, 2016).

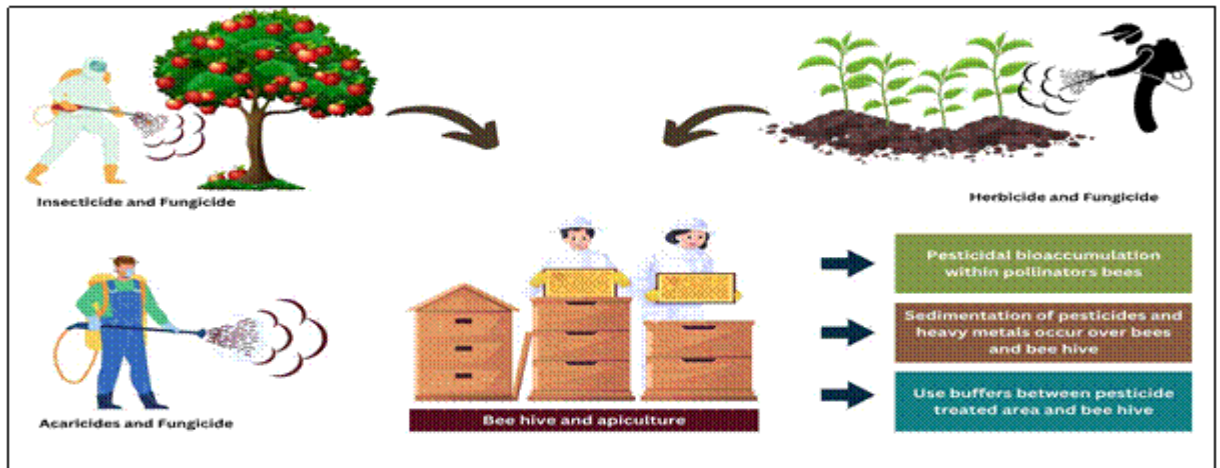


Figure 3. Impact of pesticidal contamination over pollinators, honeybees and apiculture (Winkelmann *et al.*, 2019)

It has gained significant acceptance and can be carried out on-site. There are several advantages of bioremediation that make it a preferable technology. The key biological agents involved in bioremediation are bacteria, yeast, or fungi (Malone *et al.*, 2018). In recent years, there has been a focus on isolating microorganisms capable of degrading or transforming pesticides in various ecosystems. Some bacterial strains and certain fungi have shown a high potential to degrade a wide range of pesticides (Zhang *et al.*, 2019). Ability of aquatic microorganisms to break down pesticides, with predominant genera such as *Pseudomonas* (41%) and *Aeromonas* (31%). Furthermore, studies evaluating water samples from Laguna Grande, an oligotrophic lake contaminated with nine pesticides, demonstrated the high pesticide removal capacity of isolates such as *Exiguobacter aurantiacum*, *Pseudomonas pseudoalcaligenes*, *Micrococcus luteus*, and *Bacillus sp.* (Prashar and Shah, 2016).

CONCLUSION AND FUTURE PROSPECTS

Inadequate storage and handling of pesticides increase the risk of contamination and exposure. In Pakistan, there has been insufficient planning at all levels for the proper management of pesticides (Gunstone *et al.*, 2021). The transfer of import and distribution of pesticides from the public to the private sector in the 1980s, along with the abolition of subsidies on pesticides and the withdrawal of aerial spraying policies, led to a situation where large quantities of pesticides, often banned ones, were under administrative control but lacked proper storage protocols. Many pesticide bags have deteriorated due to improper storage and lack of supervision, containers have been damaged, and metal drums have rusted, leading to pesticide leakage (Ahad *et al.*, 2009).

Estimates suggest significant amounts of outdated pesticides were stored: 3805 tons in Punjab, 2016 tons in Sindh, 179 tons in KPK, 128 tons in Balochistan, and 178 tons in the Federal Department of Plant Protection (Ahad *et al.*, 2006; (Boudh and Singh, 2019). Water contamination levels with pesticide residues vary across the country but often exceed standard limits. The situation is further exacerbated by the presence of high frequencies of pesticides in aquatic systems. Prolonged exposure to multiple pesticides can lead to cytotoxic changes and severely affect

the normal functioning of tissues such as the liver and kidneys, resulting in specific clinical consequences such as dyspnea and burning sensations in the urinary system. The International Agency for Research on Cancer has categorized these toxicants as cancer-causing agents for humans. Additionally endocrine-disrupting toxicants have adverse effects on the human endocrine system, leading to multiple hormonal dysfunctions.

The use of pesticides in today's agriculture cannot be entirely prevented because they are essential for controlling pests and achieving improved crop quality and quantity. However, these toxicants are known to have harmful impacts on human health and organisms in both aquatic and terrestrial environments. The only way to mitigate these harmful impacts is by properly managing their safe use. Agronomists and workers need to be aware of these harmful impacts of pesticides and related issues. It is essential to properly train agronomists and workers in the safe handling and use of pesticides to ensure sustainable progress while focusing on environmental and human safety.

In summary, negative ecological impacts from pesticides occur at all levels of biological organization. These impacts can be global or local, short-term or long-term, and acute or chronic. The most severe impacts include loss of biodiversity, alterations in growth, development, and behaviour, changes in community structure, alterations in ecological processes, and impacts on valuable species. These environmental impacts can have economic and social significance. Therefore, it is crucial to address environmental impacts in pesticide cause negative environmental impacts. The foundation for ecological risk assessment studies is to enhance understanding of how these tests and other data can be used to prevent environmental issues caused by pesticides.

AUTHOR'S CONTRIBUTION

R. Tahir: Literature review, Research analysis drafting, writing, reviewing.

F. Afzal: Literature review, Research analysis drafting, writing, reviewing.

H. Jamil: Writing, structural input.

M. Razzaq: Literature search, writing.

M. S. Khan: Literature search, writing

REFERENCES

- Agbohessi, P. T., I. I. Toko, V. Atchou, R. Tonato, S. N. M. Mandiki and P. Kestemont. 2015. Pesticides used in cotton production affect reproductive development, endocrine regulation, liver status and offspring fitness in African catfish *Clarias gariepinus* (Burchell, 1822). *Comparative Biochemistry and Physiology Part C: Toxicology and Pharmacology*, 167, pp.157-172.
- Ahad, K., T. Anwar, I. Ahmad, A. Mohammad, S. Tahir, S. Aziz and U. K. Baloch. 2000. Determination of insecticide residues in groundwater of Mardan Division, NWFP, Pakistan: a case study. *WATER SA-PRETORIA*, 26 (3): 409-412.
- Ahad, K., A. Mohammad, F. Mehboob, A. Sattar and I. Ahmad. 2006. Pesticide residues in rawal lake, Islamabad, Pakistan. *Bulletin of environmental contamination and toxicology*, 76 (3): 463-470.
- Ali, A., J. A. Khan, T. Khaliq, I. Javed, F. Muhammad, B. Aslam and M. Z. Khan. 2014. Hemato-biochemical disruptions by lambda-cyhalothrin in rats. *Pakistan Veterinary Journal*, 34 (1): 54-57.
- Ali, S., M. I. Ullah, A. Sajjad, Q. Shakeel and A. Hussain. 2021. Environmental and health effects of pesticide residues. *Sustainable Agriculture Reviews 48: Pesticide Occurrence, Analysis and Remediation*, 2 Analysis, pp. 311-336.
- Auon, M., F. Mahmood, A. Khan. and R. Hussain. 2014. Testicular and genotoxic effects induced by subchronic oral administration of chlorpyrifos in Japanese quail (*Coturnix japonica*). *Pakistan Journal of Agricultural Sciences*, 51 (4): 1005-1010.
- Bashir, I., Lone, F. A., R. A. Bhat, S. A. Mir, Z. A. Dar. and Dar, S.A., 2020. Concerns and threats of contamination on aquatic ecosystems. *Bioremediation and biotechnology: sustainable approaches to pollution degradation*, pp.1-26.
- Boudh, S. and J. S. Singh. 2019. Pesticide contamination: environmental problems and remediation strategies. *Emerging and eco-friendly approaches for waste management*, pp. 245-269.
- Chang, J., S. Liu, S. Zhou, M. Wang and G. Zhu. 2013. Effects of butachlor on reproduction and hormone levels in adult zebrafish (*Danio rerio*). *Experimental and toxicologic pathology*, 65 (1-2): 205-209.
- El-Nahhal, Y. and I. El-Nahhal. 2021. Cardiotoxicity of some pesticides and their amelioration. *Environmental Science and Pollution Research*, 28: 44726-44754.
- Gao, J., F. Wang, W. Jiang, J. Miao, P. Wang, Z. Zhou and D. Liu. 2020. A full evaluation of chiral phenylpyrazole pesticide flufiprole and the metabolites to non-target organism in paddy field. *Environmental Pollution*, 264: 114808.
- Ghaffar, A., R. Hussain, A. Khan and Z. A. Rao. 2015b. Hemato-biochemical and genetic damage caused by triazophos in fresh water fish, *Labeo rohita*. *International Journal of Agriculture and Biology*, 17 (3): 1-6.
- Ghaffar, A., R. Hussain, A. Khan, R. Z. Abbas and M. Asad. 2015a. Butachlor Induced Clinico-Hematological and Cellular Changes in Fresh Water Fish *Labeo rohita* (Rohu). *Pakistan veterinary journal*, 35 (2): 1-6.
- Ghosh, A., A. Tripathy and D. Ghosh. 2022, March. Impact of endocrine disrupting chemicals (EDCs) on reproductive health of human. In *Proceedings of the zoological society*, New Delhi: Springer India, 75 (1): 16-30.
- Gunstone, T., T. Cornelisse, K. Klein, A. Dubey. and N. Donley, 2021. Pesticides and soil invertebrates: A hazard assessment. *Frontiers in Environmental Science*, 9:122.
- Häder, D. P., A. T. Banaszak, V. E. Villafañe, M. A. Narvarte, R. A. González and E. W. Helbling. 2020. Anthropogenic pollution of aquatic ecosystems: Emerging problems with global implications. *Science of the Total environment*, 713: 136586.
- Hussain, R., F. Mahmood, A. Khan, M. T. Javed, S. Rehan and T. Mehdi. 2012. Cellular and biochemical effects induced by atrazine on blood of male Japanese quail (*Coturnix japonica*). *Pesticide Biochemistry and Physiology*, 103 (1): 38-42.
- Iram, S., Ahmad, I., K. A. R. A. M. Ahad, A. Muhammad and S. O. B. I. A. Anjum. 2009. Analysis of pesticides residues of Rawal and Simly lakes. *Pakistan Journal of Botany*, 41 (4): 1981-1987.
- Jan, M. R., J. Shah, M. A. Khawaja and K. Gul. 2009. DDT residue in soil and water in and around abandoned DDT manufacturing factory. *Environmental monitoring and assessment*, 155: 31-38.

- Kanda, R. 2019. Reproductive impact of environmental chemicals on animals. *Reproductive Sciences in Animal Conservation*, pp.41-70.
- Khan, M. N., M. Mobin, Z. K. Abbas and S. A. Alamri. 2018. Fertilizers and their contaminants in soils, surface and groundwater. *Encyclopedia of the Anthropocene*, 5: 225-240.
- Köhl, J. 2019. Use of biocontrol agents in fruit tree disease management. In *Integrated management of diseases and insect pests of tree fruit* Burleigh Dodds Science Publishing, pp. 311-336.
- Kousar, S. and M. Javed. 2014. Heavy metals toxicity and bioaccumulation patterns in the body organs of four fresh water fish species. *Pakistan Veterinary journal*, 34 (2): 161-164.
- Li, C., H. Wang, X. Liao, R. Xiao, K. Liu, J. Bai, B. Li and Q. He. 2022. Heavy metal pollution in coastal wetlands: A systematic review of studies globally over the past three decades. *Journal of Hazardous Materials*, 424: 127312.
- Lu, Y., J. Yuan, X. Lu, C. Su, Y. Zhang, C. Wang, X. Cao, Q. Li, J. Su, V. Ittekkot and R. A. Garbutt. 2018. Major threats of pollution and climate change to global coastal ecosystems and enhanced management for sustainability. *Environmental Pollution*, 239: 670-680.
- Mahboob, S., H. F. A. Al-Balwai, F. Al-Misned and Z. Ahmad. 2014. Investigation on the genotoxicity of mercuric chloride to freshwater *Clarias gariepinus*. *Pakistan Veterinary Journal*, 34 (1): 100-103.
- Mahmood, I., S. R. Imadi, K. Shazadi, A. Gul and K. R. Hakeem. 2016. Effects of pesticides on environment. *Plant, soil and microbes: volume 1: Implications in Crop Science*, pp. 253-269.
- Malhotra, N., K. H. C. Chen, J. C. Huang, H. T. Lai, B. Uapipatanakul, M. J. M. Roldan, A. P. G Macabeo, T. R. Ger and C. D. Hsiao. 2021. Physiological effects of neonicotinoid insecticides on non-target aquatic animals-an updated review. *International Journal of Molecular Sciences*, 22 (17): 9591.
- Malik, D. S., A. K. Sharma, A. K. Sharma, R. Thakur and M. Sharma. 2020. A review on impact of water pollution on freshwater fish species and their aquatic environment. *Advances in environmental pollution management: wastewater impacts and treatment technologies*, 1, pp.10-28.
- Malone, L. A., E. P. Burgess, E. L. Barraclough, J. Poulton and J. H. Todd. 2018. Invertebrate biodiversity in apple orchards: agrichemical sprays as explanatory variables for inter-orchard community differences. *Agricultural and Forest Entomology*, 20 (3): 380-389.
- Matthiessen, P., J. R. Wheeler and L. Weltje. 2018. A review of the evidence for endocrine disrupting effects of current-use chemicals on wildlife populations. *Critical Reviews in Toxicology*, 48 (3): 195-216.
- Meena, R. S., S. Kumar, R. Datta, R. Lal, V. Vijayakumar, M. Brtnicky, M. P. Sharma, G. S. M. K. Yadav, M. K. Jhariya, G. K. Jangir, and S. I. Pathan, 2020. Impact of agrochemicals on soil microbiota and management: A review. *Land*, 9 (2): 34.
- Osman, K. A., A. Ali, N. S. Ahmed and S. Ayman. 2022. Biochemical and genotoxic effects of some pesticides on the Egyptian Toads, *Sclerophrys regularis* (Reuss, 1833). *Watershed ecology and the environment*, 4: 25-134.
- Özkara, A., D. Akyıl and M. Konuk. 2016. Pesticides, environmental pollution, and health. In *Environmental health risk-hazardous factors to living species*. Intech Open.
- Palioura, E. and E. Diamanti-Kandarakis. 2015. Polycystic ovary syndrome (PCOS) and endocrine disrupting chemicals (EDCs). *Reviews in Endocrine and Metabolic Disorders*, 16 (4): 365-371.
- Pérez-Iglesias, J. M., L. Z. Fanali, L. Franco-Belussi, G. S. Natale, C. De Oliveira, J. C. Brodeur and M. L. Larramendy. 2021. Multiple level effects of imazethapyr on *Leptodactylus latinasus* (Anura) adult frogs. *Archives of Environmental Contamination and Toxicology*, 81 (3): 492-506.
- Pérez-Iglesias, J. M., G. S. Natale, J. C. Brodeur and M. L. Larramendy. 2023. Realistic scenarios of pesticide exposure alters multiple biomarkers in BOANA PULCHELLA (ANURA) Adult Frogs. *Ecotoxicology*, 32 (3): 309-320.
- Poudel, S., B. Poudel, B. Acharya and P. Poudel. 2020. Pesticide use and its impacts on human health and environment. *Environment Ecosystem Science*, 4 (1): 47-51.

- Prashar, P. and S. Shah, 2016. Impact of fertilizers and pesticides on soil microflora in agriculture. *Sustainable Agriculture Reviews*, 19: 331-361.
- Rajak, P., S. Roy, A. Ganguly, M. Mandi, A. Dutta, K. Das, S. Nanda, S. Ghanty and G. Biswas. 2023. Agricultural pesticides-friends or foes to biosphere?. *Journal of Hazardous Materials Advances*, 10: 100264.
- Ranatunga, M., C. Kellar and V. Pettigrove. 2023. Toxicological impacts of synthetic pyrethroids on non-target aquatic organisms: A review. *Environmental Advances*, pp.100388.
- Rani, R., P. Sharma, R. Kumar and Y. A. Hajam. 2022. Effects of heavy metals and pesticides on fish. In *Bacterial Fish Diseases*, Academic Press, pp. 59-86
- Saroop, S. and S. Tamchos. 2024. Impact of pesticide application: Positive and negative side. *Pesticides in a Changing Environment*, pp.155-178.
- Stehle, S., A. Blin, S. Bub, L. L. Petschick, J. Wolfram and R. Schulz. 2019. Aquatic pesticide exposure in the US as a result of non-agricultural uses. *Environment international*, 133: 105234.
- Suárez, R. P., A. P. Goijman, S. Cappelletti, L. M. Solari, D. Cristos, D. Rojas, P. Krug, K. J. Babbitt and G. I. Gavier-Pizarro. 2021. Combined effects of agrochemical contamination and forest loss on anuran diversity in agroecosystems of east-central Argentina. *Science of The Total Environment*, 759: 143435.
- Tariq, M. I., S. Afzal, I. Hussain and N. Sultana. 2007. Pesticides exposure in Pakistan: A review. *Environment International*, 33 (8): 1107-1122.
- Tudi, M., H. Daniel Ruan, L. Wang, J. Lyu, R. Sadler, D. Connell, C. Chu and D. T. Phung. 2021. Agriculture development, pesticide application and its impact on the environment. *International Journal of Environmental Research and Public Health*, 18 (3): 1112.
- Van Bruggen, A. H., A. Gamliel and M. R. Finckh. 2016. Plant disease management in organic farming systems. *Pest Management Science*, 72 (1): 30-44.
- Wasoh, H., M. Isa, W. Lutfi, W. Johari, A. Syahir, M. Yunus, A. Shukor, M. Azwady, N. A. Shaharuddin and M. Muskhazli. 2014. Development of a bacterial-based tetrazolium dye (MTT) assay for monitoring of heavy metals. *International Journal of Agriculture and Biology*, 16 (6); 1-6
- Winkelmann, T., K. Smalla, W. Amelung, G. Baab, G. Grunewaldt-Stöcker, X. Kanfra, R. Meyhöfer, S. Reim, M. Schmitz, D. Vetterlein and A. Wrede. 2019. Apple replant disease: causes and mitigation strategies. *Current issues in Molecular Biology*, 30 (1): 89-106.
- Zaller, J. G. and J. G. Zaller. 2020. Pesticide impacts on the environment and humans. *Daily poison: pesticides-an underestimated danger*, pp.127-221.
- Zhang, W., L. Chen, Y. Xu, Y. Deng, L. Zhang, Y. Qin, Z. Wang, R. Liu, Z. Zhou and J. Diao. 2019. Amphibian (*Rana nigromaculata*) exposed to cyproconazole: changes in growth index, behavioral endpoints, antioxidant biomarkers, thyroid and gonad development. *Aquatic Toxicology*, 208: 62-70.
- Zhelev, Z., S. Tsonev, K. Georgieva and D. Arnaudova. 2018. Health status of *Pelophylax ridibundus* (Amphibia: Ranidae) in a rice paddy ecosystem in Southern Bulgaria and its importance in assessing environmental state: haematological parameters. *Environmental Science and Pollution Research*, 25: 7884-7895.
- Zia, M. S., M. JamilQasim, A. Rahman and K. Usman. 2008. Natural resources pollution and degradation due to pesticide use in Pakistan 12th International conference on integrated diffuse pollution management (IWA DIPCON 2008). Khon Kaen University, Thailand, pp. 226-7.

(Received: October 15, 2021; Accepted: April 18, 2024)