Review Article

Induced-Toxicity of Pesticides on Edible Freshwater Fishes in Pakistan: A Review

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Abstract | Pesticides are extensively used throughout the world in industrial, health sector for agriculture and domestic purposes. Despite beneficial effect, these pesticides when released into the environment lead to induced toxicity in a large number of non-target organisms. Some of these are non-biodegradable and are persistently present in environment leading to environmental pollution. These chemicals eventually reach aquatic bodies and cause various histopathological, hematological, bio-chemical and enzymatic alterations in the bodies of aquatic organisms, especially fish, leading to huge economic loss. Consumption of the affected fishes also poses a serious health threat to humans. Pakistan being an agricultural country uses a variety of pesticides to protect its crops. The use of pesticides has substantially increased in Pakistan over the last decades, which when reach the water bodies, adversely affect the rich biodiversity found in aquatic systems of Pakistan. This review discusses research over past decades regarding toxic effects of pesticides induced in edible freshwater fishes of Pakistan and future considerations.

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Introduction

Industrial advancements and development of novel technologies are essential to achieve success and comfort in ongoing era, but these are causing deterioration of precious natural water resources on earth (Tahir *et al*., 2021). Increasing number of industries, modernization and urbanization eventually steered us to the contamination of our environment and left us to face the problem of environmental pollution. These pollutants include domestic wastes, industrial effluents, agro-chemicals, etc. that include different organic and inorganic substances, heavy metals such as cadmium, arsenic, and pesticides. An after effect of urbanization and industrialization is that the pollutants released from industries eventually reach the aquatic bodies where they get dissolved and cause water pollution (Ullah *et al*., 2014). Environmental pollution is an elaborate phenomenon having multiple aspects with partial or unidentifiable origins (Ullah *et al*., 2014). International Agencies reported that such chemical substances have high potential and a constant threat to aquatic life including fish and bioaccumulation of these pollutants eventually entre into human food chain and is the main cause of human health hazard (Ullah and Zorriehzahra, 2015).

In view of its consumption by human, industrial production, industrial irrigation and stabilization of biodiversity, fresh water is extremely valuable in terms of preserving life. However, these ecosystems are at risk of suffering biodiversity losses due to being vulnerable to environmental pollutants including pesticides (Geist, 2011; Pisa *et al*., 2015; El-Murr *et al*., 2015; Javed and Usmani, 2015).

Pesticides are chemical compounds that are used to get rid of pests including insects, rodents, fungi and unwanted plants, herbs, weeds etc. (Akashe *et al*., 2018). These chemical compounds are grouped into different classes such as insecticides, herbicides, rodenticides, fungicides etc. According to the chemical nature of pesticides; it is further divided into groups like carbamates, organochlorine, organophosphate, pyrethroids (widely used), and aliphatic fungicides, inorganic rodenticides, amide fungicides, ammonium herbicides. Pesticides are a big source of potential environmental hazards to birds, fish, and other animals as well as humans when they infiltrate food chain (Khan *et al*., 2012). An increased burden of chemicals can arise in environment due to non-biodegradability of some of these classes of pesticide chemicals (Mahboob *et al*., 2011). Effluents with pesticides resulted in a marked rise in the mortality rate, growth retardation and tissue damage in fish (Rana *et al*., 2011). Susceptibility of different fish species to these pesticides is different at different concentration. The changes in different body parts and systems of fish have been observed to be different than each other as well as in response to different pesticides (Ullah and Zorriehzahra, 2015).

Pakistan is an agricultural country with most of its agricultural land irrigated by canal systems from rivers and their tributaries. Main rivers are Indus, Kabul, Chenab, and Ravi. Freshwater ecosystems of Pakistan have rich biodiversity including a large number of edible fish species such as *Labeo rohita, Cirrhinus mrigala, Cyprinus carpio, Catla catla.* Agriculture run-off, sewage wastes, fall into the rivers causing aquatic pollution and adversely affect fish life, leading to various hematological, biochemical, histopathological changes in fish body which when consumed by human's results in different types of disorders in body. This review discusses research over past decade regarding toxic effects of pesticides induced in edible freshwater fishes of Pakistan and some future considerations.

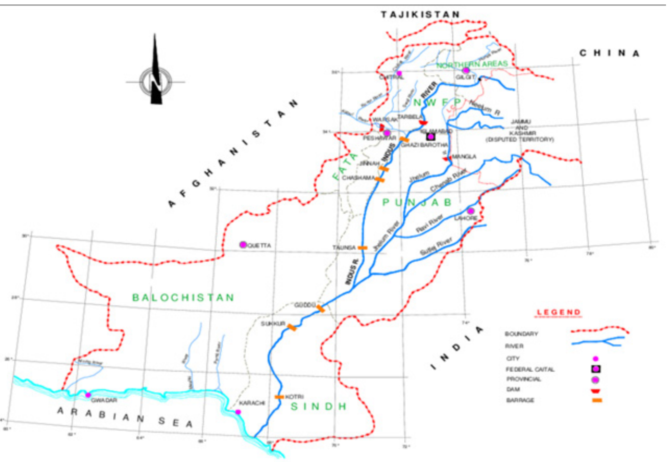

Figure 1: *Rivers of Pakistan (Majeed et al., 2008).*

General introduction of commonly-used pesticides (Modified from Yadav and Devi, 2017).

Organochlorine pesticides (OCPs)
Organochlorines pesticides are organic compound attached with five or more chlorine atoms. Organochlorines (OC) are widely used in health sector and agriculture as insecticides and these are non-biodegradable. These pesticides have a negative effect on insects' nervous system which cause disruption of the insect nervous system causing convulsions, then paralysis and eventually cause death, slowly and gradually. Most common examples of these pesticides includes: DDT, endosulfan, aldrin, lindane, dieldrin and chlordane. Production of DDT is now prohibited throughout the globe.

Organophosphate pesticides (OPPs)
Organophosphate pesticides are multi-purpose broad spectrum pesticides, which are derivatives of

phosphoric acid used to get rid of different types of pests and act when inhaled, ingested, or penetrate in skin, leading to stomach abnormalities, nervous system impairments in affected organisms. These are biodegradable pesticides, causing little environmental pollution and show delayed pest resistance. They are more toxic to animals as they have cholinesterase-inhibiting properties leads to excess accumulation of acetylcholine neurotransmitter across a synapse. This results in failure of nerve impulses to move across the synapse causing muscular cramps, paralysis and eventually death. Most common OPPs include malathion, diazinon, glyphosate, and parathion.

Carbamates (Carb)

The carbamates share similar structural makeup with organophosphates(OP), but carbamates are distinct in that they originate from carbamic acid. Carbamates work by interfering with transmission of nerve signals resulting in the death of the pest by poisoning. Under natural conditions, they are easily degraded with little environmental pollution. They are occasionally used as fumigants, contact poisons, and poisons for the stomach. Insecticides that contain carbamates include carbaryl, carbofuran, propoxur, and aminocarb.

Pyrethroids (PYR)

Synthetic pyrethroid insecticides are produced from natural pyrethrins. Compared to pyrethrins, they are more stable and have a longer residual impact in environment. These insecticides are only mildly hazardous to mammals and birds, but they are extremely toxic to fish and insects. Majority of synthetic pesticides are non-persistent and quickly break down when exposed to light. Pyrethroids are considered safe to use in food. Cypermethrin and Permethrin are examples of popular synthetic pyrethroid pesticides.

Pesticide-induced toxic effects on fish

Behavior: Different studies on pesticides over past decade have shown alterations in behavior of various fish species such as sluggish swimming movements, lethargy, faintness, and disruption in swimming ability which renders the fish more prone to predators, affect their feeding, orientation, and territory defense (Prashanth *et al*., 2011). Interruption in behavior of fish by pesticides makes the fish stressed and immunocompromised, making them susceptible to different kinds of pathogens and infections (Nwani *et al*., 2013). In freshwater fish *Labeo rohita* commonly known as Rohu , imidacloprid induced morphological and behavioral changes such as avoidance mechanisms, abrupt and sluggish swimming movement in all directions, occasional jumping and hitting on the walls of tank, rapid scale loss, mucous secretion, change in body color (Qadir and Iqbal, 2016), while organophosphates (profenofos, trizaophos) and carbamates (carbofuran, carbaryl) caused suffocation, lethargy, descending movement, irregular swimming, gulping before death (Mustafa *et al*., 2014) in the same fish. Also, fipronil resulted in shakings, twitching, dizziness, increased operculum movement, body curving, breathing troubles in *Cyprinus* carpio (common carp) (Ghaffar *et al*., 2018). There are many different studies confirming the effects of different pesticides on behavior of different freshwater fishes of Pakistan (Mahboob *et al*., 2015a; Ghaffar *et al*., 2020, 2021; Usman *et al*., 2020; Zulfiqar, 2020; Akram *et al*., 2022; Wang *et al*., 2022) mentioned in Table 2.

Hematology: Blood parameters were assessed as physiological indicators of animals exposed to stressful conditions such as the presence of toxic substances, because blood acts as a patho-physiological reflector of the whole body (Velisek *et al*., 2012). Various pesticides have been extensively studied to trace for hematological changes such as changes in number of RBCs and WBCs, thrombocytes, neutrophils, hemoglobin content, hematocrit values in different freshwater fish species of Pakistan such as in *Cirrhinus mrigala* (Indian carp) due to diazinon (Rauf and Arain, 2013; Haider and Rauf, 2014), Chlorfenapyr, dimethoate, and acetamiprid (Ghayyur *et al*., 2021), *Labeo rohita* (Rohu) exposed to acetamiprid (Alam *et al*., 2014), triazophos (Ghaffar *et al*., 2015a), butachlor, a chloroacetanilide herbicide (Ghaffar *et al*., 2015b), Chlorpyrifos (Ismail *et al*., 2018), Diafenthiuron (Riaz-ul-Haq *et al*., 2018), thiamethoxam (Ghaffar *et al*., 2020; Hussain *et al*., 2020), fipronil (Ghaffar *et al*., 2021), pyriproxifen (Naseem *et al*., 2022; Li *et al*., 2022), *Ctenopharyngodon idella* (Grass carp) to endosulfan (Ullah *et al*., 2017), *Cyprinus carpio* (Common carp) in response to fipronil and buprofezin (Qureshi *et al*., 2016), fipronil (Ghaffar *et al*., 2018), *Oreochromis mossambicus* (Mozambique tilapia) to Chlorpyrifos (Ghayyur *et al*., 2019), *Tor putitora* (Mahaseer) to cypermethrin (Bibi *et al*., 2014), *Oncorhynchus mykiss* (Rainbow Trout) to Chlorpyrifos (Ali *et al*., 2020), *Aristichthys nobilis* (Bighead Carp) to acetochlor (Mahmood *et al*., 2022), triclosan (Akram *et al*., 2022), *Hypophthalmichthys nobilis* (Bighead carp) to pendimethalin (Wang *et al*., 2022).

Histopathology: Histopathological changes have been traced in different organs such as brain, gills, liver, kidneys, intestines, blood and muscles of different edible freshwater fish species of Pakistan. Pesticides-induced changes in histopathology of fish include lamellar disorder, lesions, hyperplasia, congestion, epithelial stimulating, micro gliosis, hemorrhages, necrosis, discoloration, neuronal degeneration, karyorrhexis, hepatocellular hypertrophy, and accumulation of pesticides residues in muscles (Khan *et al*., 2018). The pesticide damage tissue, effect function of Kidney, centers in spleen, edema, and disruption of cardiac myofibers in heart have been reported over past decade from various freshwater fishes. Some of the lethal pesticides are cypermethrin (Khan *et al*., 2018), mixture of endosulfan and chlorpyrifos (Naz *et al*., 2019), thiamethoxam (Ghaffar *et al*., 2020), profenofos and carbofuran to *Labeo rohita* (Mahboob *et al*., 2014a), cypermethrin to *Tor putitora* (Ullah *et al*., 2015), fipronil plus buprofezin to *Cyprinus carpio* (Qureshi *et al*., 2016), DDT and HCHs to *Cyprinus carpio, Tor putitora, Glyptothorax punjabensis, Orienus plagiostomus* (Aamir *et al*., 2016), Chlorpyrifos to *Oncorhynchus mykiss* (Ali *et al*., 2020), acetachlor to *Aristichthys nobilis* (Mahmood *et al*., 2022), pendimethalin to *Hypophthalmichthys nobilis* (Wang *et al*., 2022), Lambda-cyhalothrin to *Ctenopharyngodon idella* (Niaz *et al*., 2022). Some other researchers have also reported the histopathological changes in edible freshwater fishes of Pakistan (Rana *et al*., 2011; Nasir *et al*., 2012; Eqani *et al*., 2013; Bibi *et al*., 2014; Mahboob *et al*., 2015; Jabeen *et al*., 2015; Ullah *et al*., 2017; Qadir and Iqbal, 2016; Robinson *et al*., 2016; Karim *et al*., 2016a, 2016b; Riaz *et al*., 2018; Hussain *et al*., 2020; Ghaffar *et al*., 2021; Naseem *et al*., 2022; Li *et al*., 2022) (Table 2).

Biochemical (Oxidative stress) variation

Exposure to pesticides induces various biochemical changes in fish body. Chlorpyrifos cause increased activity of antioxidant enzymes in freshwater fish *Oncorhynchus mykiss* (Ali *et al*., 2020). Activity of anti-oxidant enzymes such as superoxide dismutase, peroxidase, and glutathione S-transferase increases in liver, gills, kidneys, brain, muscles, and heart of *Labeo rohita* when treated with mixture of endosulfan and chlorpyrifos (Naz *et al*., 2019). Rise in quantity of oxidative stress biomarkers and decline in concentration of antioxidant enzymes occur when *Labeo rohita* is exposed to pyriproxifen (Li *et al*., 2022), *Aristichthys nobilis* to acetochlor (Mahmood *et al*., 2022), *Hypophthalmichthys nobilis* to pendimethalin (Wang *et al*., 2022).

Total protein content (TPC)

Various studies showed the changes in protein content in various tissues such as liver, gills, intestines, blood, and muscles of different edible freshwater fishes of Pakistan when exposed to different pesticides. Total protein content declined in *Cyprinus carpio* when exposed to Karate i.e. λ-Cyhalothrin, protein value recorded in different tissues, Muscles 20.77±1.21[a], Brain 26.01±2.06[a] and Liver 27.84±1.46[a] (Bibi *et al*., 2014), and fipronil and buprofezin (Qureshi *et al*., 2016). Exposure of *Labeo rohita* to Diafenthiuron, total serum protein (P = 0.004), cholesterol (P = 0.033) and creatinine (P = 0.002) were significantly reduced (Riaz-ul-Haq *et al*., 2018). *Catla catla* (Major Carp) recorded heights protein content range, 18.59±0.04 then used 0.038mg/L profenofos, reduce protein level 12.76±0.04, *Labeo rohita* (Rohu) protein content 19.18±0.02, used 0.06mg/L profenofos, decreased protein level 12.71±0.04. *Cirrhinus mrigala* (Mrigal carp) 14.62±0.02 protein value in healthy fish, used 0.041mg/L profenofos, reduced total protein level 8.70±0.01. showed decline in total protein when exposed to profenofos, (Ghazala *et al*., 2019). *Oreochrmois mossambicus* (Mozambique tilapia), also showed a decline in total protein content when treated with organophosphates, pyrethroids, and herbicide (Naqvi *et al*., 2017), and Chlorpyrifos (Ghayyur *et al*., 2019). *Oreochromis niloticus* (Nile Tilapia) also show a significant decrease in total protein content when exposed to malathion, Chlorpyrifos, and λ-Cyhalothrin, significant decrease total protein level in different tissue such as in brain (19.33±0.58) and muscle tissues (27.02±0.57) (Amin *et al*., 2021) and malathion (Zulfiqar, 2020). Exposure of *Ctenopharyngodon idella* (Grass Carp) to mixture of endosulfan+chlorpyrifos and endosulfan+bifenthrin decrease protein content interval of time reported in different tissues such as Hepatic, control group protein content 3.95±0.56B[a], lowest total protein recorded 1.98±0.21B[c], Muscle highest protein 1.04±0.17B[a] and lowest 0.18±0.01B[c], Gills highest protein 2.86±0.33B[a] and lowest 1.46±0.15B[c], Cardiac highest protein 0.86±0.12Ba and lowest 0.03±0.01Bc etc. (Usman *et al*., 2020), Lambda-cyhalothrin (Niaz *et al*., 2022) and *Aristichthys nobilis* (Bighead carp), to acetochlor (Mahmood *et al*., 2022) lead to decline in total protein content in investigated fish tissues followed by different standard procedure for determination of protein contents in different tissues of the different fresh water species.

Acute toxicity- LC50

Acute toxicity may be measured as oral, dermal and inhalational acute toxicity. LC50 is the measure of acute inhalation toxicity. Acute toxicity is expressed by various changes in behavior and physical activities, even death. However, different pesticides have distinct LC50 values in different organisms, determine by using Probit analysis and comparison was done by the APHA method (Mahboob *et al*., 2015). A list of common pesticides together with their lethal concentrations for different fish species have been listed in Table 1. For further information, "handbook of acute toxicity of chemicals to fish and other aquatic vertebrates" is also helpful (Johnson and Finley, 1980).

Inhibition of acetylcholinesterase (AChE)

Organophosphates and carbamates apparently share the common mechanism of acetylcholinesterase inhibition at nerve endings that results in excess acetylcholine accumulation in the nerve ending overstimulating the effector organ. Studies have shown that acetylcholinesterase inhibition in fish has been associated with exposure of fish to different pesticide. In a study conducted by (Haider and Rauf, 2014), acetylcholinesterase activity was inhibited in *Cirrhinus mrigala* exposed to diazinon. *Oncorhynchus mykiss* also showed a decline in AChE activity when exposed to Chlorpyrifos (Ali *et al*., 2020). Inhibition of AChE activity occurred in *Labeo rohita* when exposed to profenofos and carbofuran (Mahboob *et al*., 2014), and *Cyprinus carpio* when treated with λ-Cyhalothrin (Bibi *et al*., 2014).

Genotoxicity

Genotoxicity is a property possessed by some substances that makes them harmful to the genetic information contained in organisms. Heavy metal ions and polycyclic hydrocarbons are the most influencing genotoxicants for fishes. Pesticides-induced genotoxicity has been reported in various freshwater fishes of Pakistan. Genotoxic threats and increased DNA damage have been noticed in *Labeo rohita* when exposed to triazophos, used standard blood test, staining method, serum enzyme such asALT, AST, ALP and measured by spectrophotometrically (Ghaffar *et al*., 2015a),endosulfan (Ullah *et al*., 2017), thiamethoxam (Hussain *et al*., 2020), and pyriproxifen (Li *et al*., 2022), *Aristichthys nobilis* when treated with acetachlor (Mahmood *et al*., 2022), and triclosan (Akram *et al*., 2022) and *Hypophthalmichthys nobilis* to pendimethalin (Wang *et al*., 2022).

Table 1: *List of common pesticides along with their lethal concentrations for different fish species.*

Pesticide	Experimental fish	LC50 value	Exposure time	Reference
Diazinon	*Cirrhinus mrigala*	8.15 mg L-1	96 hr	Rauf and Arain, 2013
Triazophos	*Labeo rohita*	6.64 mg L-1	96 hr	Mustafa *et al*., 2014
Profenophos	*Labeo rohita*	0.32 mg L-1	96 hr	Mustafa *et al*., 2014
Carbofuran	*Labeo rohita*	1.4 mg L-1	96 hr	Mustafa *et al*., 2014
Carbaryl	*Labeo rohita*	8.24 mg L-1	96 hr	Mustafa *et al*., 2014
Profenofos	*Labeo rohita*	0.31 mg L-1	96 hr	Mahboob *et al*., 2014
Carbofuran	*Labeo rohita*	1.39 mg L-1	96 hr	Mahboob *et al*., 2014
Karate (λ-Cyhalothrin)	*Cyprinus carpio*	0.16 µL L-1	96 hr	Bibi *et al*., 2014
Imidacloprid	*Labeo rohita*	550 mg L-1	96 hr	Qadir *et al*., 2015
Cypermethrin	*Tor putitora*	63 µL L-1	96 hr	Ullah *et al*., 2015
Triazophos	*Cirrhinus mrigala*	1.05 mg L-1	96 hr	Mahboob *et al*., 2015
Profenophos	*Cirrhinus mrigala*	0.21 mg L-1	96 hr	Mahboob *et al*., 2015
Carbofuran	*Cirrhinus mrigala*	0.49 mg L-1	96 hr	Mahboob *et al*., 2015
Carbaryl	*Cirrhinus mrigala*	4.75 mg L-1	96 hr	Mahboob *et al*., 2015
Fipronil	*Cyprinus carpio*	0.665 mg L-1	96 hr	Qureshi *et al*., 2016
Chlorpyrifos	*Labeo rohita*	442.8 µg L-1	96 hr	Ismail *et al*., 2014; Ismail *et al*., 2018
Endosulfan+chlorpyrifos	*Oreochromis niloticus*	5.64 µg L-1	96 hr	Ambreen and Javed, 2018
Endosulfan+chlorpyrifos	*Labeo rohita*	1.95 µgL-1	96 hr	Naz *et al*., 2019
Endosulfan+bifenthrin	*Ctenopharyngodon idella*	4.23 µg L-1	96 hr	Ambreen and Javed, 2015
Endosulfan+chlorpyrifos	*Ctenopharyngodon idella*	4.60 µg L-1	96 hr	Ambreen and Javed, 2015

Table 2: *Effects of pesticide induced toxicity in different edible freshwater fishes of Pakistan studies over past decade.*

S. No	Fish	Common name	Name of pesticide	Sample	Changes noticed	Reference
1	*Labeo rohita*	Rohu	Organochlorine and nitrogen-containing pesticides (endosulphan. DDE, parathion methyl, isoproturon, atrizine, carbofuran, carbaryl, deltamethrin)	Fish muscles	Accumulation of pesticides residues in fish muscles	(Rana *et al*., 2011)
2	*Labeo rohita*	Rohu	Imidacloprid	Live fish	Avoidance Mechanisms, sluggish and abrupt swimming movements in all directions, occasional jumping, hitting on the tank walls, rapid scale loss, mucous secretion, body color changed to light brown. 96 hrs LC50 value is 550 mg L-1	(Qadir *et al*., 2016)
3	*Otolithes ruber*	Tiger-toothed croaker	Organochlorines (HCH, DDT, dieldrin, eldrin)	Fish tissue	Bioaccumulation of Heptachlor exo-epoxide and Methoxychlor in Fishes	(Nasir *et al*., 2012)
4	*Cirrhinus mrigala*	Mrigal carp	Diazinon	Blood	Hematological alterations, Decrease in total RBCs, WBCs, Hb, and Hct values, LC50 value is 8.15mg/L, Increase in death rate with increase in diazinon concentration and exposure.	(Rauf and Arain, 2013)
5	*Cyprinus carpio, Cirrhinus mrigala, Catla catla, Cirrhinus reba, Labeo calbasu,*	Common Carp, Mrigal carp, Major Carp, Reba Carp, Orange fin labeo	Organochlorine Pesticides (OCPs) and Polychlorinated Biphenyls (PCBs)	Fish muscles	Intake of fish pose health hazard to humans	(Eqani *et al*., 2013)
6	*Cirrhinus mrigala*	Mrigal carp,	Diazinon	Blood	Decline in RBCs, WBCs, Hb, Hct, mean corpuscular	(Haider and Rauf, 2014)
7	*Labeo rohita*	Rohu	Profenofos, Carbofuran	Brain, gills, muscles, kidneys, liver, blood	Disturbed metabolism and neurotransmission, Profenfos toxicity is high compared to carbofuran in context of Acetylcholinesterase and Butyrylcholinesterase inhibition in all tested organs	(Mahboob *et al*., 2014a)
8	*Catla catla*	Major Carp	Triazophos, Profenofos, Carbofuran, Carbaryl	Live fingerlings	Acute toxics stress, 100% mortality at 2.8 mg L-1 carbofuran dose for 96 hrs, Behavior: suffocation, movement towards bottom, erratic swimming, lethargy, gulping before mortality	(Mahboob *et al*., 2014b)
9	*Catla catla*	Major Carp	DDT, DDE, Endosulphan, Endosulfan sulphate, Cartap, Carbofuran	Flesh	Accumulation of pesticide in fish muscles	(Akhtar *et al*., 2014)
10	*Cyprinus carpio*	Common Carp	Karate (λ-Cyhalothrin)	Brain, liver, muscle tissue	Decrease in total protein content, Reduction of Acetylcholinesterase activity	(Bibi *et al*., 2014)
11	*Labeo rohita*	Rohu	Acetamiprid	Blood	Decrease in serum calcium, phosphate, and albumin, Increase in urea	(Alam *et al*., 2014)
12	*Labeo rohita*	Rohu	Organophosphates (Profenofos, Trizaophos) and Carbamates (Carbofuran, Carbaryl)	Live fish	Acute toxic stress, Behavioral stress exhibited by fish, suffocation, lethargy, fish rest at the bottom, irregular swimming, movement towards bottom, gulping before mortality.	(Mustafa *et al*., 2014)

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S. No	Fish	Common name	Name of pesticide	Sample	Changes noticed	Reference
13	*Labeo rohita*	Rohu	Triazophos	Blood	Microcytic hypochromic anemia, Decrease in lymphocyte and monocyte values, Increase in leukocyte count, DNA damage	(Ghaffar *et al*., 2015a)
14	*Ctenopharyngodon Idella*	Grass Carp	Endosulfan	Blood,liver, intestines, gills,	Blood: decline in total RBCs, WBCs, platelets, Hb, and PCV, Liver: degenerative changes, vacuolation, pyknosis etc. Gills: fusion and disruption, Intestines: atrophy of villi, increased goblet cells count	(Ullah *et al*., 2017)
15	*Tor putitora*	Mahseer	Cypermethrin	Blood, liver, gills, brain	Blood cells: decrease in RBSs count, Increase in WBCs count, Liver: glycogen vacuolization, hemorrhage vacuolization, congestion, fatty infilteration, hepatic necrosis, Gills : cellular infilteration, congestion, swollen tip of gill filament, hetropilic infilteration, damaged gill, Brain : discoloration, neuronal degeneration, Infilteration, severe spongiosis,	(Ullah *et al*., 2015)
16	*Cirrhinus mrigala*	Indian Carp	Triazophos, carbofuran, carbaryl, profenofos	Live fingerlings	Suffocation, Restlessness, Erratic swimming, Loss of equilibrium, Jerky movement, Mouth opened with rapid operculum movement, Lethargy, Gulping before death, 100% mortality at 1.6 mg L-1 of carbofuran for 96 hrs.	(Mahboob *et al*., 2015a)
17	*Catla catla*	Major Carp	Endosulfan, carbofuran, cypermethrin, profenophos, triazophos, deltamethrin	Fish muscles	Accumulation of endosulfan and profenofos in fish tissues, Higher concentrations of endosulfan, carbofuran and deltamethrin than permissible limits for fish set by International agencies, Health hazard to human and aquatic organisms	(Mahboob *et al*., 2015b)
18	*Tor putitora*	Mahseer	Cypermethrin	Liver, brain, gills	Liver: glycogen vacuolization, hemorrhage vacuolization, congestion, fatty infiltration, necrosis, Brain: discoloration, neuronal degeneration, infiltration and severe spongiosis, Gills: congestion, swollen tip of gill filament, cellular and hetrophilic infiltration, gill damage	(Ullah *et al*., 2015)
19	*Labeo rohita, Channa marulius, Cyprinus carpio*	Rohu, Great Snakehead, Common Carp	Pyrethroids, carbamates, neonicotenoids	Fish Muscles	Carbofuran detected in *Labeo rohita*, and *Cirrhinus marulius,* Cypermethrin detected in *Cirrhinus marulius*, Deltamethrin detected in *Cyprinus carpio*, and *Cirrhinus marulius.*	(Jabeen *et al*.,2015)
20	*Labeo rohita*	Rohu	Butachlor (Chloroacetanilide herbicide)	Blood	Decrease in RBCs, Hb, Hct, and lymphocyte value, Increase in total WBCs count, Morphological and nuclear abnormalities, mutagenic effects	Ghaffar *et al*., 2015b)
21	*Hypophthalmichthys molitrix*	Silver Carp	Deltamethrin	Liver, blood	Liver: necrosis, nuclear pyknosis, hypertrophy of cells, vacuolization, congestion of blood vessels, nuclear atrophy, Blood: Increased level of hepatic enzymes AST and ALT	(Karim *et al*., 2016a)

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S. No	Fish	Common name	Name of pesticide	Sample	Changes noticed	Reference
22	*Hypophthalmichthys ii. Molitrix*	Silver carp	Deltamethrin	Spleen, Kidneys	Kidneys: tissue damage, renal tubules degeneration, Dilation, lyses and degeneration of glomerular capillaries, narrowing of the tubular lumen, atrophy, Spleen: tissue damage, necrosis, alterations in number of melano-macrophage centres	(Karim *et al*., 2016b)
23	*Cyprinus carpio*	Common carp	Fipronil, buprofezin	Blood, Fish tissue	Decrease in total proteins content, globulin, RBCs, Thrombocytes, Hb, HCT, blood DNA content, Increase in WBCs and glucose concentrations, albumin unaltered, RBCs: necrosis, micro-nuclear formation and hyper-chromatosis, Gills: epithelial uplifting, lamellar necrosis, disorganization, fusion and atrophy, disruption of cartilaginous core, telangiectasia, Liver: hypertrophy of hepatocytes and nuclei, karyorrhexis, melano-macrophage aggregations, contractions of central vein, Kidneys: glomerular deterioration, Bowman's space and renal tubules dilation, altered tubular lumen and thyroidization of tubules, , hypertrophy of nucleus, cellular necrosis and atrophy	(Qureshi *et al*., 2016)
24	*Labeo rohita*	Rohu	Imidacloprid	Heart, liver, kidney	No histopathological changes observed in heart, Liver : Wrinkling of hepatocytes membrane, hepatocyte degeneration and necrosis, dilation of blood sinusoid, nuclear degeneration, hepatic nuclei' pyknosis, Kidneys : wide Bowman's space, cell necrosis and inflammation, enlargement of renal tubular lumen	(Qadir *et al*., 2016)
25	*Carnivorous species (Chitala chitala, Channa striata, Clupisoma gaura, Wallago attu, Rita rita, Sperata seenghala,), Herbivorous species (Catla catla, Cirrhinus mrigala, Labeo rohita, Cyprinus carpio, Cirrhinus reba, Labeo dyocheilus)*	Indian featherback or Indian knifefish, Chitol, Striped Snakehead, River Catfish, Wallago, Rita, Giant River-Catfish, Herbivorous species Major Carp, Mrigal carp, Rohu, Common Carp, Reba Carp, Brahmaputra Labeo, Kali	Organochlorine Pesticides (OCPs) and Polychlorinated Biphenyls (PCBs)	Muscles	OCPs and PCBs detected in edible fish species with highest concentrations recorded in carnivorous species, Health risk to consumers	(Robinson *et al*., 2016)
26	*Cyprinus carpio, Tor putitora, Glyptothorax punjabensis, Orienus plagiostomus*	Common carp, Mahseer, Sisorid catfish, Sattar snow trout	DDT (Dicholorodiphenyltricholoroethane), HCHs (Hexachlorocyclohexane)	Muscles, gills, stomach, liver tissues	Bioaccumulation of HCHs and DDT in fish especially in *G. punjabensis* and *C. carpio,* DDT intake with life time consumption of mentioned fish species pose cancer risk to local people.	(Aamir *et al*., 2016)

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S. No	Fish	Common name	Name of pesticide	Sample	Changes noticed	Reference
27	*Ctenopharyngodon idella*	Grass Carp	Atrazine (Herbicide)	Blood	Decrease in synthesis and activity of enzymes serum glutamic-pyruvic transaminase (SGPT), creatinine phosphokinases (CPK), lactate dehydrogenase (LDH), and alkaline phosphatase, resulting in enzyme accumulation in cells due to reduced permeability for mentioned enzymes.	(Khan *et al*., 2016)
28	*Oreochromis mossambicus*	Mozambique tilapia	Organophosphates (Chlorpyrifos, malathion), Pyrethroids (Cypermethrin, λ-Cyhalothrin), Insecticide	Blood	Increase in MN (Micronucleus) frequencies; Carcinogenic effect)	(Naqvi *et al*., 2016)
29	*Oreochromis mossambicus*	Mozambique tilapia	Organophosphates (Chlorpyrifos, malathion), Pyrethroids (Cypermethrin, λ-Cyhalothrin), Herbicide (Buctril)	Fish tissue	Decrease in protein content and metabolic dysfunction in investigated fishes	(Naqvi *et al*., 2017)
30	*Labeo rohita*	Rohu	Chlorpyrifos	Blood	Decline in total RBCs count, Hb, packed cell volume, Increase in total leucocyte count, Increase in MN (Micronucleus) induction	(Ismail *et al*., 2018)
31	*Labeo rohita*	Rohu	Endosulfan	Blood	DNA damage, genotoxic effects	(Ullah *et al*., 2017)
32	*Channa marulius, Channa punctatus, Labeo boga*	Great Snakehead, Spotted Snakehead, Boga, Boga Labeo	Organochlorine pesticides (DDT, endosulfan, andrin)	Fish tissue	Bioaccumulation of pesticide residues in fish tissues, Carcinogenic risk	(Riaz *et al*., 2018)
33	*Cyprinus carpio*	Common Carp	Fipronil	Blood	Convulsions, dizziness, fainting, Increased movement of operculum, jerking, body curvature, Breathing difficulties, Decrease in RBCs, Hb, Hct and albumin, Increase in leukocyte count, mean corpuscle volume, neutrophils, monocytes, lymphocytes, urea, creatinine, cholesterol, triglycerides, glucose, nuclear and cellular abnormalities.	(Ghaffar *et al*., 2018)
34	*Labeo rohita*	Rohu	Diafenthiuron	Blood	Increase in WBCs, RBCs, lymphocyte, Hb, Hct, MCV, Decrease in platelets count, plateletcrit, platelet distribution width, Disturbed concentration of total proteins, cholesterol, triglycerides, albumin, globulin, AST, calcium, potassium, and cadmium	(Riaz-ul-Haq *et al*., 2018)

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S. No	Fish	Common name	Name of pesticide	Sample	Changes noticed	Reference
35	*Labeo rohita*	Rohu	Cypermethrin	Blood, gills, liver, intestine	Blood: Rise in WBCs, platelets, blood glucose level, Decline in RBCs count, Hct, Hb, MCV, MCH, MCHC, Gills: lamellar disorder, cartilaginous core disruption, epithelial lifting, blood mobbing, fusion, twisting and shortening of secondary lamellae and degeneration and atrophy, Intestines: hemorrhages, intestinal necrosis, goblet cells' overproduction in villi, disintegration, shortening and fusion of villi, Liver: cell membrane dissolution, pyknosis, hyperplasia, congestion of blood, cellular necrosis, and vacuolization	(Khan *et al*., 2018)
36	*Oreochromis niloticus*	Nile Tilapia	Mixture of endosulfan and chlorpyrifos	Blood	Genotoxic threats, DNA damage	(Ambreen and Javed, 2018)
37	*Labeo rohita*	Rohu	Mixture of endosulfan and chlorpyrifos	Liver, gills, kidneys, brain, heart, muscles	Antioxidant enzymes i.e. Peroxidase, Superoxide dismutase, and Glutathione S-transferase activity increase in all investigated tissues, while catalase activity increased in liver, gills and kidneys, and decreased in brain, heart, and muscles	(Naz *et al*., 2019)
38	*Catla catla*, *Labeo rohita*, *Cirrhinus mrigala*	Major Carp, Rohu, Indian Carp	Profenofos	Muscles	Rapid increase in moisture content, decrease in proteins, fats, and carbohydrate content	(Ghazala *et al*., 2019)
39	*Orechromus mossambicus*	Mozambique tilapia	Chlorpyrifos	Blood	Biochemical parameters: Decrease in RBCs, Hb, and HCT, Anemic condition, Increase in WBCs and platelets count, Serological parameters: Increase in blood glucose level, cholesterol, cortisol, Decrease in total protein content, triglycerides	(Ghayyur *et al*., 2019)
40	*Ctenopharyngodon idella*	Grass Carp	Mixture of endosulfan+chlorpyrifos and endosulfan+bifenthrin	Live fish (behavior) Fish tissues	Behavior: abnormal behavior, fish try to escape, come to surface, gulp air, increased operculum movements, erratic movement, fast swimming, hyperactivity, Catalase activity and Total Protein Content decreases in liver, kidney, brain, heart, muscle, and gills	(Usman *et al*., 2020)
41	*Labeo rohita*	Rohu	Thiamethoxam	Live fish (behavior), blood	Behavior: bouncing movement, rapid operculum movement, erratic swimming, mucus secretion, fin tremors and darkening, isolated swimming on just one side, surface breathing, Hemato-biochemical parameters: Decrease in total RBCs count, Hb, packed cell volume, Increase in WBCs and neutrophils count, Morphological changes: stomatocytes, leptocytes, tear-shaped and dividing RBCs, Nuclear changes: micronuclei, RBCs with condensed nuclei and/or without nucleus, nuclear remnant in RBCs, Histopathology of gills: secondary lamellar atrophy, pyknosis of epithelial pillar cells in lamellae, lamellar degeneration, aneurysm, curling and congestion.	(Ghaffar *et al*., 2020)

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S. No	Fish	Common name	Name of pesticide	Sample	Changes noticed	Reference
42	*Labeo rohita*	Rohu	Thiamethoxam	Blood, Liver, Kidneys	Increased concentration of urea, creatinine, lipid peroxidation product, liver and cardiac function tests, blood DNA content, DNA damage in kidneys, liver, and blood cells, Liver: congestion, bile duct degeneration and disruption, condensation, abnormal sinusoids, eccentric nuclei fragmentation in nucleus, fatty infiltration, Kidneys: necrosis, congestion, edema, detachment of tubular epithelium, degeneration of renal tubules and glomerulus	(Hussain *et al*., 2020)
43	*Oncorhynchus mykiss*	Rainbow Trout	Chlorpyrifos	Blood, liver, gills	Blood: decline in RBCs, Hb, Hct, and Acetylcholinesterase activity, Rise in WBCs, Increased activity of antioxidant enzymes, Liver: hepatic degeneration, hyperaemia, abnormal sinusoids, dilation of central veins, Gills: fusion and curling of secondary lamella, cellular degeneration, necrosis, edema, hyperplasia, sloughing, narrowed water channels	(Ali *et al*., 2020; Yaseen *et al*., 2016)
44	*Oreochromis niloticus*	Nile Tilapia	Malathion	Live fish, Blood	Enhanced concentrations of urea and creatinine, kidney damage, serological alterations, Behavior: hyper-excitability, erratic movements, active swimming, Morphological changes: bulging of the eyes, over secretion of mucus, hemorrhage of eyes and body, tail rotting, scale erosion, and mortality	(Zulfiqar, 2020)
45	*Oreochromis niloticus*	Nile Tilapia	Malathion, Chlorpyrifos, λ-Cyhalothrin	Brain, gills, muscles, kidneys, liver, blood	Decrease in total protein content	(Amin *et al*., 2021)
46	*Labeo rohita*	Rohu	Fipronil	Liv e fish, blood, visceral organs	Behavior: loss of coordination, increased operculum movement, fin tremors, Blood: RBCs, monocytes, lymphocytes decreased, WBCs, neutrophils increased, nuclear abnormalities in RBCs, Histopathology: severe lesions in gills and liver, Increased levels of ALP, AST, ALT and LDH	(Ghaffar *et al*., 2021)
47	*Cirrhinus mrigala*	Mrigal carp	Chlorfenapyr, Dimethoate, Acetamiprid	Tissues, blood	Decrease in RBCs, Hb, PCV, MCHC, T3 and T4, Increase in WBCs and Platelet count, TSH, corticol, ALP, AST, ALT. LDH levels, Histopathological alterations in gills and liver	(Ghayyur *et al*., 2021)
48	*Labeo rohita*	Rohu	Pyriproxifen (PPF)	Visceral organs, blood	Decline in RBCs, HCT, Hb, Increase in WBCs, neutrophils, and biomarker values of liver, kidneys and heart, Liver: necrosis, inflammatory exudate, edema, Kidneys: tubular necrosis, widening of Bowman's space, edema, Brain: micro-gliosis, degeneration, hemorrhages, neural pyknosis, Heart: edema, neutrophilic myocarditis, cardiac myofibers disruption	(Naseem *et al*., 2022)

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S. No	Fish	Common name	Name of pesticide	Sample	Changes noticed	Reference
49	*Labeo rohita*	Rohu	Pyriproxifen (PPF)	Visceral organs, blood	Nuclear and morphological alterations in RBCs, Increase in miconucleus, pear-shaped RBCs, nuclear remnants, RBCs with a blebbed nucleus, and spherocytes, Increased DNA damage, Rise in quantity of oxidative stress biomarkers, Decline in antioxidant enzymes' concentration	(Li *et al.*, 2022)
50	*Aristichthys nobilis*	Bighead Carp	Acetochlor	Visceral organs, blood	Isolated cells of kidneys, brain, gills, and liver showed increased DNA damage and low cellular proteins, Increased morphological and nuclear changes, Rise in quantity of biomarkers of oxidative stress	(Mahmood *et al.*, 2022)
51	*Aristichthys nobilis*	Bighead Carp	Triclosan	Blood, Visceral organs	Behavior: jerking movement, erratic and irregular swimming, mucus secretion from the mouth, Decline in RBCs, Hb, and Hct values, Rise in WBCs, neutrophils, AST, ALT, urea, creatinine, and cardiac biomarkers, increased DNA damage, nuclear and morphological variations in RBCs, Gills: lamellar uplifting and disorganization, twisting of secondary lamellae, and epithelial cell necrosis in lamellae, Liver: congestion, necrosis, fatty infilteration, Kidneys: increased urinary spaces, tubular necrosis, Brain: necrosis, atrophy of neurons,	(Akram *et al.* 2022)
52	*Hypoph-thalmichthys nobilis*	Bighead Carp	Pendimethalin	Visceral organs, blood	Behavior: overproduction of mucus, loss of equilibrium, erratic and irregular swimming, rapid operculum movement, increase in surface breathing, air gulping, and fin tremors, Liver: congestion, necrosis of hepatocytes, and atrophy of hepatocytes, Gills: lamellar atrophy and fusion, congestion, epithelial cell necrosis of primary and secondary lamellae, secondary lamellar uplifting, telogenesis, Kidneys: degeneration of renal tubules, ceroid, atrophy of glomerulus, necrosis of renal tubules, Increased DNA damage , Increased morphological and nuclear changes, Rise in quantity of biomarkers of oxidative stress	(Wang *et al.*, 2022)
53	*Cteno-pharyngodon idella*	Grass Carp	Lambda-cyhalothrin	Blood, gills, muscles, brain, liver	Severe histopathological lesions in investigated organs, alterations in serum biochemistry, disturbed glucose, total protein, triglycerides, and amylase levels	(Niaz *et al.*, 2022)

Other insecticides and pesticide

Profenofos (LC50): Profenofos are new insecticide and neuro toxic molecules. Widely used in in India, Pakistan, Bangladesh for agriculture purpose. The pesticide is highly risk for aquatic organism like fish (Lundebye *et al.*, 1997).

λ-cyhalothrin: The λ-cyhalothrin used for Agriculture purposes such vegitable production and cotton cultivation. It observed in running water in irrigation canal.the toxicity clearly indicates acute and sub-acute toxicity test, toxicity of pesticide with species temperature, and size of the fish (Bibi *et al*., 2014).

Dichlorodiphenyltrichloroethane (DDT): The Dichlorodiphenyltrichloroethane is used pesticide and kill the Aquatic organism (vertebrates and invertebrates). Causes death in fish hatchery kill fry and effect on fish fecundity (Hopkins *et al*., 1969).

Pyriproxyfen: Pyriproxyfen is most sensitive pesticide, high concentration detected in Daphnia magna, effected reproductive organ such as, *Xiphophorus maculatus*, *Eurytemora affinis*, *Leander tenuicornis, Danio rerio* (zebrafish) and *Capitella* sp. (polychaete). highly detected from river water and effected 25.82% species (Moura and Souza-Santos, 2020).

Pendimethalin: Thy known as (N-(1-ethylpropyl)-2, 6-dinitro-3,4-xylidine) belong to dinitroaniline herbicide and commonly used in terrestrial system (Danion *et al*., 2014). High concentratin detected in river (840 ng/L) at France and effected biotic and abiotic components of ecosystem (Dupuy *et al*., 2019).

Triclosan: The 5-chloro-2-(2,4-dichlorophenoxy)-phenol commonly used in personal care products such as dental care products, deodorants and textiles (Liang *et al*., 2013). TCS higher concentration recorded in sediments then water. It has androgenic effects potential, altering swimming of (*Oryzias latipes*), reproductively effects of (*Closterium ehrenbergii*) and genotoxic effects on *C. ehrenbergii* has reported (Liang *et al*., 2013).

Acetochlor: Acetochlor is well known herbicide, effect the aquatic species including Bighead carp, there are different Scientific names base on divergent branchial row abdominal keel and Length, such as *Aristichthys nobilis*, *Cephalus hypothalamus*, *Leuciscus nobilis*, *Hypophthalmichthys mandschuricus*, and *Hypophthalmichthys simony*. *Hypophthalmichthys nobilis* (Ghaffar *et al*., 2017).

Hexachlorocyclohexane (HCH): Hexachlorocyclohexane is harmful pesticide mostly used in Pakistan. It cause serious health impact including reproductive, neurological, hematological and immunological disorder on animals (Kalyoncu *et al*., 2009).

Atrazine: Atrazine (2–18 chloro-4-ethylamino-6-isopropylamino-s-triazine) is toxic herbicide. Effect erythrocyte of *Lithobates catesbeianus*, *Dendrophryniscus minutus, Rhinella, schneideri Anaxyrus americanus*, *Xenopus laevis*, *Lithobates pipiens* (Khan *et al*., 2012).

Conclusions and Recommendations

This article concludes that increased and unplanned of pesticides renders great threat to environment, aquatic life, and humans. Pesticides causes different behavioral, hematological, histopathological, genotoxic, endocrine alterations in fish body, which is tolerated by fish only up to a certain level beyond which mortality of fish occurs, resulting in economic losses. On the other hand, these affected fishes cause different hematological and endocrine disorders and some even poses carcinogenic risk to humans when consumed. Regulations and awareness among masses should be developed for responsible utilization of pesticides and to control run-off of these pesticides to aquatic bodies. Furthermore, those fishes should be stocked in water bodies which are least vulnerable to pesticides and chemicals. Further research is needed to study the effects of newly introduced pesticides and to develop biodegradable pesticides that are environment friendly and have least toxicity to non-target organisms.

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Novelty Statement

The research and experimental work on the subject title recommends responsible utilization of pesticides and discourage unnecessary use of pesticides in aquatic environment.

Author's Contribution

Yaseen and Asad Ullah: Designed and prepared the manuscript.
Imad Khan and Maryam Begum: Supervised the write up.
Sumbal Bibi and Umber: Helped in data collection.

Namra and Abbas Khan: Technically assisted at every step.
Shumaila Gul and Raheela Taj: Proof reading.

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