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A Review on the Impact of Pesticide Toxicity on the Physiological and Behavioral Condition of Fish

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Abstract

Pesticides are an essential component of contemporary agriculture because they help keep unwanted insects and animals under control and boost crop yields. However, the widespread usage of pesticides has led to worries over the unexpected consequences that these chemicals have on non-target animals and ecosystems, particularly those that are aquatic. Fish, which play an essential role in aquatic food webs, are particularly vulnerable to the damaging effects of pesticides as a result of their direct contact with contaminated water bodies. The review covers acute and chronic pesticide effects on fish, including physiological and behavioral responses. It discusses population-level effects and biodiversity loss on fish reproduction, growth, development, immunological function, and locomotor activity. It also highlights pesticide toxicity's long-term effects on fish populations. Pesticide exposure may also alter foraging behavior, competitive aptitude, and predation vulnerability, according to the review. Pesticides harm fish health by accumulating toxins, causing genetic defects, and upsetting the aquatic ecology. These effects put biodiversity in jeopardy and upset the food chain's delicate balance, raising major environmental issues. It emphasizes the need for interdisciplinary research to better understand fish pesticide toxicity and guide environmental regulatory measures. Implementation of Integrated Pest Management (IPM) practices to ensure sustainable pesticide use in the environment. Use of non-chemical strategies such as crop rotation, natural predators, and resistant varieties. limit pesticide application to specific pests, thereby minimizing ecological damage and preserving ecosystem equilibrium. We can improve agriculture-aquatic biodiversity coexistence by supporting holistic pesticide management.

Keywords: Fisheries, Fish Health, Insecticides, Pesticides, Toxicity

1. Introduction

Aquatic toxicology studies how pollutants like pesticides, insecticides, and other chemicals affect fish and other aquatic creatures[1]. Pesticides are substances that can have a natural or synthetic origin and are used to control pests, weeds, and pathogens that are found in plants. It can contain insecticides, fungicides, rodenticides, bactericides, and larvicides[2]. It is widely agreed that pesticides play a significant role in the expansion of agriculture. This is due to the fact that pesticides can cut down on the number of agricultural products that are wasted while also increasing both the quantity and quality of food produced[3-5]. Additionally, beginning in the 1940s and continuing ahead, a growth in the usage of synthetic crop protection chemicals allowed for an even

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greater expansion of food production[6]. Within the past half-century, there has been a significant rise in the use of pesticides and fertilizers, both of which have significantly contributed to an improvement in the safety of the food supply[7]. In addition, the global production of pesticides expanded at a pace of approximately 11% per year, going from 0.2 million metric tonnes in the 1950s to more than 5 million metric tonnes by the year 2000[8].

Organochlorines, organophosphates, carbamates, and pyrethroids are the four primary categories that emerge from a classification system for pesticides that is predicated on the chemicals that make them up[9]. The neurological system of insects is disrupted by the activity of organochlorines, which then leads to convulsions and paralysis, which eventually result in death. Organochlorines include several different chemicals, some of the most well-known of which are Dichlorodiphenyltrichloroethane (DDT), lindane, endosulfan, aldrin, dieldrin, and chlordane[10]. Because humans and domestic animals depend on fish species as their primary source of proteins and lipids, maintaining the health of fish species is extremely important to the well-being of human beings. Large quantities of the pesticides that are still present either encompass or reach environmental media and plants that are not their targets. As a direct result of the contamination caused by pesticides, the environment has become polluted, and this has had a significant influence on human health[11]. The contamination of water with insecticides typically takes place within a few weeks of the application of the pesticides and is mostly caused by intensive agriculture mixed with surface runoff and surface drainage. Fish are especially vulnerable to the effects of water that has been contaminated by the environment. Therefore, contaminants such as pesticides may have a major impact on specific physiological and biochemical processes, and exposure to different types of insecticides may result in a significant deterioration of fishes' overall health state (Figure 1).

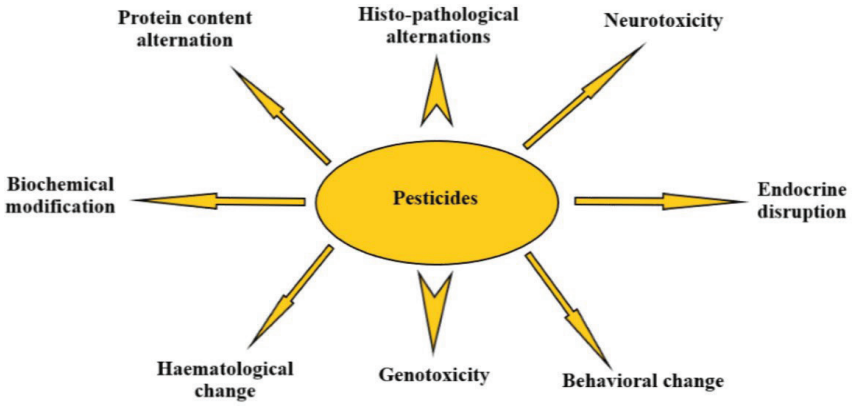


Figure 1. Different effect of pesticides in fish physiology and behaviors.

When these pollutants get into water bodies in higher amounts than what is allowed, they kill a lot of fish, shellfish, and other aquatic life. When these pollutants enter water bodies in lower concentrations, however, they lead to their bioaccumulation, which eventually reaches human beings through the food web[12-14]. When water is polluted, not only do aquatic organisms suffer, but the water also becomes unsafe for human consumption. This can have catastrophic results in regions already struggling with water constraints[15,16]. Most pesticides are extremely poisonous and can bioaccumulate, making them a danger to aquatic and terrestrial life[17]. This is a problem that strives to attract people's attention, and it needs to be dealt with and focused on properly and attentively in order to guarantee that eating fish will be safer on a priority basis[18].

2. Methodology

In order to conduct this review using the technique that was chosen, a comprehensive search was conducted, and relevant papers were then selected, after which data were extracted and analyzed. The findings shed light on the major effects that pesticide poisoning has on the physiology and behavior of fish, which in turn provides insights into the possible hazards and implications for aquatic ecosystems. This article provides a detailed

assessment of the research published between 1976 and 2023 on the effects of pesticide toxicity on the physiological and behavioral states of fish.

3. Pathway of Pesticide's Appearance in Aquatic Systems

The accumulation of pesticides in aquatic systems can be caused by a variety of different mechanisms, but their presence can be evaluated by determining the three primary pathways through which the chemicals reach water bodies[19,20]. These pathways include the water column, organic substrates like mosses and algae, leaf litter, vascular hydrophytes, and branches, and inorganic substrates such as materials derived from sediments of varied sizes[21].

4. Effects of Pesticides on Fish Indirectly

Concerns regarding the effects of pesticide usage on vertebrates have more recently shifted to the vast potential for indirect effects. This is despite the fact that indirect effects are rarely taken into account in ecological risk assessments[22]. Controlling plants that are considered weeds typically requires the application of herbicides. The control of macrophytes in aquatic systems makes use of some herbicides, while the vast majority of herbicides are applied to the control of weeds in terrestrial environments. Herbicides that kill macrophytes can have two unintended consequences, both of which are likely to be harmful to fish and other aquatic species. It is possible that the death of the macrophytes may result in an increased biological demand for oxygen, which will deprive fish and other species of oxygen if the biomass of the macrophytes is substantial and the herbicide acts quickly. When herbicides are sprayed directly on water for this purpose, the treated areas are often quite small. This lowers the probability that there will be a significant increase in biological oxygen demand. According to[23], the gradual decomposition of the macrophytes lowers the probability that the fish will be negatively affected by the biological oxygen demand. The removal of plants will, of course, result in changes to the environment, which may have an effect on fish either because there will be less food for fish (or their prey) or because there will be less physical habitat for fish to use as cover. There is no herbicide that is currently in use that has been documented to have effects through this mechanism; however, chlorate, which was historically used as an herbicide in terrestrial situations, was found in the effluent of pulp mills and was shown to have a negative impact on fish in the Baltic by removing shelter for larval fish[24].

5. Effects of Pesticides on Fish Directly

According to research by[25], many pesticides have a direct impact on fish. Changes in fish behavior are one of the many forms of toxicity that can be caused by exposure to pesticides[26,27]. Pesticides themselves can also cause many forms of toxicity in fish, including alterations in hematological characteristics[28-30], abnormalities on the histological level[31-33], enzyme changes, and genotoxicity[34-36]. Both biochemical changes and disruptions to the endocrine system were found[37-40]. Nutritional profile alteration[41-44]. Researcher found that there is a lot of variation in feeding biology[45]. Alterations in the antioxidant defence system[46-49]. Activity of the enzyme acetylcholinesterase that had been modified[51-53].

6. Lethal Effects of Pesticides

Sublethal concentrations of these pesticides lead to subtle changes in the biology of various fish, which in turn have an influence on the fish's ability to survive[54,55], (Table 1). This is in contrast to the lethality and mortality of fish that are caused by lethal doses of the pesticide. The pesticides potential on the freshwater edible fish *H. fossilis*, which has an LD 50 of 0.134 mL/L and causes a negative effect on *H. fossilis*, is unknown. The acute toxicity of trichlorfon to freshwater fish is between 1.67 and 180 ppm (17), and it is extremely harmful to species that live in both cold and warm water environments[56].

7. Behavioural Changes

Since the change in behavior is an integrated output of the nervous system at the organismal level in response to the underlying biochemical, morphological, or physiological disturbances, it is seen as a good endpoint that shows a sequence of toxic effects and compensatory responses.

Table 1. List of Some pesticides' Acute Toxicity (LC50) to Specific Fish Species[57,58].

Sl. No.	Pesticides Name	Name of Fish Species	Exposure Duration
1	Malathion	*Heteropneustess fossilis*	96 hrs 0.98ppm
2	Endosulfan	Channel catfish	96 hrs 1.5µg/l
3	Acephate	Feathed Minnow	96 hrs >1000µg/l
4	Malathion	*Labeo rohita*	96 hrs 15µg/l
5	Akton	Channel catfish	96 hrs 400µg/l
6	Methyl parathion	*Catla catla*	96 hrs 4.8ppm
7	Alaclor	Rainbow trout	96 hrs 2.4µg/l
8	Rogar	*Puntius stigma*	96 hrs 7.1 and 7.8 ppm
9	DDT	Rainbow Trout	96 hrs 8.7µg/l
10	Pyrethroid Lambela Cyhalothrin	*Danio rerio*	96 hrs 0.119µ/L
11	Elsan	*Channa punctatus*	4 hrs 0.43ppm
12	Endosulfan	*Channa striatus*	96 hrs 0.0035ppm
13	BHC	Gold fish	96 hrs 348(261- 466) µg/L
14	Cypermethrin	*Labeo rohita*	96 hrs 4.0µ/L
15	Metasystox	*Nemacheilus botia*	96 hrs 7.018ppm

This is because the underlying disturbances can be any of the three: biochemical, morphological, or physiological[59].

The activity of Acetylcholinesterase (AChE), which stops the transmission of nerve impulses by quickly breaking down a neurotransmitter, is one of the most commonly used ways to tell if brain function has changed. AChE is involved in the termination of impulse transmission by rapidly hydrolyzing the neurotransmitter. Changes in behavior are caused by pesticide-induced inhibition, which is caused mostly by organophosphates and carbamates. These changes include decreased swimming performance, increased excitability, and altered social behaviour[60]. An investigation has shown that both the behavioral and morphological characteristics of the fish, *Clarias batrachus*, are significantly altered as a result of being subjected to lethal and sub-lethal quantities of pesticides. The magnitude of the responses, both physical and behavioral, increased noticeably as the concentration of the pesticide used in the LC50 calculation was raised. The responses were virtually identical at various doses, with the exception that the size of the responses increased noticeably. The fish exhibited disrupted school behavior, localization to the bottom of the test tank, and independence in their swimming when exposed to a lower quantity of the pesticide. The movement of the fish to the vessel's corners, which may be interpreted as an avoidance behavior in response to the presence of the pesticide, was observed. At larger concentrations, it was noticed that the subject's swimming action became jerky, unpredictable, and darting and that they lost their equilibrium. There were moments when the fish were seen hanging vertically in the water. The fish gradually lost their appetite, got agitated, and exuded mucus all over their bodies[61].

The migratory behavior of fish that can move from one body of water to another can be altered by pesticides[62], which can disrupt the life cycle of some species of fish. One example of this is the ability of salmonid fish to go from freshwater to saltwater. However, additional research into this phenomenon is required, with a particular focus on the crucial transitional time that takes place in estuaries. Studies have shown that adult salmon avoid polluted and contaminated areas when migrating, which changes their migration behavior and causes them to delay spawning[63]. This results in a delay in the salmon's ability to reproduce.

8. Histopathological Changes

Pesticide-induced histopathological alterations in fish have been the subject of substantial research. The organ index was figured out by looking at how the different organs of *Anabastes tudineus* responded when they were exposed to sublethal amounts of monocrotophos for 30 days. The results showed that the gills were the organ that was most severely affected, followed by the liver, which was moderately affected, and then the kidney, which was the organ that was least affected. These results were consistent across all species of fish. Histopathology demonstrates flexibility to degeneration, and histopathological abnormalities can be used as indicators of organic compound contamination in the environment. Histopathology is the study of diseases caused by the breakdown of tissue. Histological changes in fish gills should develop into a quick "early warning system" for determining water quality in sublethal and chronic situations because toxicants produce changes at lower levels of biological organisation prior to organismic alterations. This would allow for a more accurate assessment of water quality[64].

From January to June, the liver of *Channa punctatus* that had been exposed to a safe dose (4.5 ppm) of the commercial carbamate pesticide carbofuran for six months showed different degrees of histopathological changes. These changes included cytoplasmolysis, nuclear pyknosis, and necrosis, which ultimately led to the complete exhaustion and disintegration of hepatocytes. The extensive degeneration of proliferated hepatocytes, which were found near blood sinuses and resembled the darkly stained debris of hepatomas, as well as the induction of tumors, were indicative of the carcinogenic action of this pesticide. This action may be attributed to the cumulative toxicity that occurs during chronic exposure to the pesticide. Aside from this, it is possible to observe the rupturing of the blood sinus, which results in the invasive infiltration of leukocytes, as well as the harmful localized necrosis that leads to the full dissolution of hepatocytes, which is shown by the presence of debris masses in the necrotic area. In addition, a significant drop in hepatosomatic index and ascorbic acid content, as well as an elevation in acid and alkaline phosphatase levels, were recorded in the livers of experimental fish. These changes correspond to cellular damage that was caused by the treatment[65]. Carofuran caused degeneration of connective tissues, follicular walls, and vacuolization in the ooplasm during stages 2 and 3. Malathion caused changes in ovigerous lamellae, follicular cell degeneration, atretic oocyte increment, clumping of cytoplasm, ruptured follicular epithelial lining, and nuclear materials' shrinkage. These alterations were attributed to endocrine and hormonal imbalances[66].

9. Haematological Changes

According to a researcher, pesticides typically bring about rather rapid changes in the hematological parameters of fish[67]. According to a researcher, a hematologic index is an excellent tool for evaluating the health of fish and other aquatic creatures as well as their response to various toxicants[68]. This index takes into account the ecological location of the habitat as well as a typical method for determining the sub-lethal impacts of the contaminant. According to research done by[69,70], blood parameters in fish are affected by characteristics such as their sex, age, size, reproductive stage, and overall health, as well as by external factors such as seasonal dynamics, water temperature, quality of the environment, diet, and stress. Pesticides have an effect on a wide variety of fish traits, with the blood parameters being particularly susceptible to change.

Researcher conducted the experiment on *Anabas testudineus* in order to evaluate the hematological impact of Cypermethrin at concentrations ranging from 0.015 to 0.04 mg/L[71]. It was found that the red blood cell count, hemoglobin level, hematocrit level, and platelet count all went down. After seven days, there was an increase in the WBC count, but after 14 and 21 days, there was a decrease in the WBC count due to the increased cypermethrin. Likewise,[72] investigated the same effects that triazophos had on blood parameters when it was administered to *Labeo rohita* at concentrations ranging from 0.010-0.200 ppm. Pesticides such as DDT, BHC, aldrin, dieldrin, chlordane, permethrin, cypermethrin, karate, delmethrin sulfane, endosulfan, and others have had an effect on the blood parameters of numerous species, including the histological variation in white blood cells and red blood cells, the amount of haemoglobin, and the packed cell volume. According to[73], haematological alterations were seen in both *Cyprinus carpio* and *Puntius ticto*.

10. Biochemical Changes

Clarias batrachus was exposed to carbofuran insecticide, which caused a delayed drop in the total protein content of liver and muscle tissues. By the time the recovery period came to an end, this decline had however reversed. The free amino acid content in the liver was not significantly altered, but it was found to be increased in the muscle. However, ammonia levels were found to be elevated in both tissues for the entirety of the exposure period, and these levels in the liver continued to be elevated throughout recovery. The amount of glycogen stored in the liver dropped significantly, but it quickly recovered after the fish were moved into clean water. During the time of exposure, it was found that the enzymes alanine aminotransaminase, aspartate aminotransaminase, glutamate dehydrogenase, and glycogen phosphorylase were more active in both types of tissue. Following carbofuran administration, an inhibition of glycogen phosphorylase ab activity was seen in the liver. Both the liver and the muscle tissues of *C. batrachus* had distinctively dissimilar patterns of enzyme recovery. The recurrent patterns of effects that carbofuran has on intermediate metabolism point in the direction of potential pathways for elucidating the mechanisms that are responsible for such effects[74].

According to a study, Atrazine (0.56 g L1), azoxystrobin (0.024 g L1), and imidacloprid (0.11 g L1) were the most commonly discovered herbicide, fungicide, and insecticide, respectively, in the river as well as when they were employed in the laboratory test. These results were based on the concentrations of these chemicals in the river. When compared to individualized exposure groups, *O. niloticus* which had been exposed to the pesticide mixture showed a greater number of biochemical impacts. Depending on the biomarker, this response may be the result of the combined actions of the pesticides, which could culminate in either an additive or synergistic effect. Atrazine exhibited the most significant changes among the individual exposure groups, followed by azoxystrobin and imidacloprid. In general, exposure to pesticides led to a rise in the levels of oxidative stress parameters, a reduction in the activities of antioxidant enzymes, and an increase in the activity of acetylcholinesterase. These findings bring to light the danger that may be posed to aquatic species as a result of the presence of a variety of hazardous substances in their natural habitat[75]. In the brain, liver, gills, and muscle fibers of *Tor putitora*[76], cyclomethrin significantly altered the enzymes catalase, glutathion reductase, peroxidase, and lipid peroxidase, but only in the liver of *Labeo rohita*[77].

11. Genotoxicity

Damage to the DNA of the freshwater fish *Oreochromis niloticus* is caused by the combination of the pesticides endosulfan and chlorpyrifos, as measured by the Comet test[78]. According to them, a dose-dependent reaction was found in the erythrocytes of fish, with the induction of the greatest DNA damage occurring at the concentration of the pesticide combination that was one third of the LC50. In treated fish, statistically significant effects were detected for both concentrations and times of exposure in terms of DNA damage when compared to the control group. The control group consisted of untreated fish. The toxicity of certain pesticides has been linked to alterations in the replication of DNA as well as DNA aberrations that can result in mutation[79]. Additionally, the toxicity of certain pesticides has been linked to the hyperproliferation of cells as a result of local irritation[80].

12. Endocrine Disruption Effect

Pesticides typically contain a number of compounds that have been discovered to be endocrine disruptors. It is possible to list around 105 different compounds. 46% of these are insecticides, 21% are herbicides, and 31% are fungicides; some of these were banned from widespread usage many years ago but can still be found in the environment (for example, DDT and atrazine in a number of nations)[81-84].

Research found that the oxons of methyl-parathion, chlorpyrifos, and diazinon were 15 to 10 times more dangerous to sperm DNA than the chemicals they came from[85]. Another illustration of this would be the fact that *in vitro* research has shown that the herbicide 2,4-dichlorophenoxyacetic acid, also known as 2,4-D, is a recognized estrogen receptor ligand[86]. This herbicide belongs to the organophosphate family and is widely used. It encourages the proliferation of androgen-sensitive cells[87]. Vinclozolin can be broken down into a number of different metabolites in the soil as well as in plant and animal organism[88]. Organochlorine pesticides, often known as OCPs, are pervasive environmental toxins that have the ability to alter endocrine function and are harmful to organ systems. These pesticides, such

as Dichlorodiphenyltrichloroethane (DDT), dieldrin, and toxaphene, amongst others, are considered to be among the most hazardous substances to the health of humans. These pesticides have several negative effects on human health, including acting as teratogens, disrupting neuroendocrine systems, inhibiting the immunological and reproductive systems, and causing lipid and metabolic imbalances[89].

When pesticides mess with the endocrine system, they often mimic the effects of sexually active steroids. This causes the Hypothalamic-Hypophyseal-Gonadal (HHG) system to be out of balance in many ways, both physiologically and functionally. Organochlorine and organophosphate insecticides have estrogenic rather than androgenic steroidal mimicking activities. This is one of the characteristics that distinguishes these families from other groups of pesticides. Compared to the effects of sex-steroid analogues on the HHG axis during gametogenesis in a few models of teleost fish, the effects of pesticides were worse. It is interesting to note that the impacts of these substances have created varied results in juveniles and adults, and that these effects also change depending on the dosage and the duration of the exposure. In addition, the therapies have induced sexually dimorphic effects on occasion, which is an indication that the activity of these chemicals has important implications for the development of sexuality. The potentially harmful effects of endocrine disruption caused by pesticides, with particular focus on endosulfan and malathion, are due to the fact that these chemicals are still used, or have been used in the past, for the purpose of preventing agricultural pests in a number of Asian nations, including India[90]. Also change in the teleost's endocrine system can be exploited as a biomarker for early delectation of these toxicants because pharmaceuticals are a developing endocrine disrupting substance in the aquatic environment[91].

13. Conclusion

Pesticides damage fish and aquatic environments. Pesticides eradicate pests in agricultural, industrial, and home contexts. While they improve crop productivity and human health, they harm aquatic life. Pesticides affect fish immediately and in the long term. Water-soluble pesticides can infiltrate waterways by runoff or direct application. They bioaccumulate in fish tissues in the water. Bioaccumulation can enhance fish toxicity, reducing reproduction, immune systems, and overall health and survival. Pesticides harm aquatic habitats. They damage fish, plankton, insects, and amphibians. Disruptions can reduce biodiversity and alter ecosystem dynamics, altering ecosystem stability and function. Pesticides affect more than fish and ecosystems. Fish pesticides can harm humans. Contaminated fish can accumulate chemicals in human tissues, producing developmental disorders, hormone imbalances, and possibly increased illness risk. Sustainable agriculture is essential to reduce pesticide damage to fish. Integrated pest management solutions, including biological treatments, crop rotation, and pest-resistant genotypes, reduce pesticide use. To protect fish populations and aquatic ecosystems, pesticide control, monitoring, and the development and marketing of less hazardous alternatives are needed. Pesticides harm fish and need prompt treatment. Healthy aquatic ecosystems and their interconnection are essential for fish populations, biodiversity, and our planet's well-being.

14. References

1. Pereira JL, Antunes SC, Castro BB, Marques CR, Gonçalves AM, Gonçalves F, *et al*. Toxicity evaluation of three pesticides on non-target aquatic and soil organisms: Commercial formulation versus active ingredient. Ecotoxicology. 2009; 18(4):455-63. PMID 19205879. https://doi.org/10.1007/s10646-009-0300-y
2. Abhilash PC, Singh N. Pesticide use and application: An Indian scenario. J Hazard Mater. 2009; 165(1-3):1-12. PMID 19081675. https://doi.org/10.1016/j.jhazmat.2008.10.061
3. Aktar MW, Paramasivam M, Sengupta D, Purkait S, Ganguly M, Banerjee S. Impact assessment of pesticide residues in fish of Ganga river around Kolkata in West Bengal. Environ Monit Assess. 2009; 157(1-4):97-104. PMID 18758975. https://doi.org/10.1007/s10661-008-0518-9
4. Fenik J, Tankiewicz M, Biziuk M. Properties and determination of pesticides in fruits and vegetables. TrAC Trends Anal Chem. 2011; 30(6):814-26. https://doi.org/10.1016/j.trac.2011.02.008
5. Strassemeyer J, Daehmlow D, Dominic AR, Lorenz S, Golla B. SYNOPS-WEB, an online tool for environmental risk assessment to evaluate pesticide strategies on field level. Crop Prot. 2017; 97:28-44. https://doi.org/10.1016/j.cropro.2016.11.036
6. Bernardes MFF, Pazin M, Pereira LC, Dorta DJ. Impact of pesticides on environmental and human health. In: Toxicology studies-cells, drugs and environment. London, UK: IntechOpen. 2015; 195-233. https://doi.org/10.5772/59710

7. Boliko MC. FAO and the situation of food security and nutrition in the world. J Nutr Sci Vitaminol (Tokyo). 2019; 65:S4-8. PMID 31619643. https://doi.org/10.3177/jnsv.65.S4
8. Carvalho FP. Pesticides, environment, and food safety. Food Energy Secur. 2017; 6(2):48-60. https://doi.org/10.1002/fes3.108
9. Buchel KH. Chemistry of pesticides. New York: John Wiley and Sons, Inc; 1983.
10. Garg PK, Chishi N, Kumar R, Latha TK, Rai S, Banerjee BD, *et al*. Organochlorine pesticide tissue levels in benign and malignant breast disease: A comparative exploratory study. J Environ Pathol Toxicol Oncol. 2021; 40(1):43-50. PMID 33639072. https://doi.org/10.1615/JEnvironPatholToxicolOncol.2020035783
11. Hernández AF, Gil F, Lacasaña M, Rodríguez-Barranco M, Tsatsakis AM, Requena M, *et al*. Pesticide exposure and genetic variation in xenobiotic-metabolizing enzymes interact to induce biochemical liver damage. Food Chem Toxicol. 2013; 61:144-51. PMID 23688862. https://doi.org/10.1016/j.fct.2013.05.012
12. Xie P, Zhuge Y, Dai M. Impacts of eutrophication on biodiversity of plankton community. Acta Hydrobiol Sin. 1996; 20:30-7.
13. Morel FMM, Kraepiel AML, Amyot M. The chemical cycle and bioaccumulation of mercury. Annu Rev Ecol Syst. 1998; 29(1):543-66. https://doi.org/10.1146/annurev.ecolsys.29.1.543
14. Abedi Z, Hasantabar F, Khalesi MK, Babaei S. Enzymatic activities in common carp; *Cyprinus carpio* influenced by sublethal concentrations of cadmium, lead, chromium. World J Fish Mar Sci. 2013; 5(2):144-51.
15. Nicolopoulou-Stamati P, Maipas S, Kotampasi C, Stamatis P, Hens L. Chemical pesticides and human health: The urgent need for a new concept in agriculture. Front Public Health. 2016; 4:148. PMID 27486573. https://doi.org/10.3389/fpubh.2016.00148
16. Rani S, Ahmed MK, Xiongzhi X, Keliang C, Islam MS, Habibullah-Al-Mamun M. Occurrence, spatial distribution and ecological risk assessment of trace elements in surface sediments of rivers and coastal areas of the East Coast of Bangladesh, North-East Bay of Bengal. Sci Total Environ. 2021; 801:149782. PMID 34467902. https://doi.org/10.1016/j.scitotenv.2021.149782
17. Beketov MA, Kefford BJ, Schäfer RB, Liess M. Pesticides reduce regional biodiversity of stream invertebrates. Proc Natl Acad Sci USA. 2013; 110(27):11039-43. PMID 23776226. https://doi.org/10.1073/pnas.1305618110
18. Ullah S, Akmal M, Aziz F, Ullah S, Khan KJ. Hand pumps' water quality analysis for drinking and irrigation purposes in the district. Khyber Pakhtunkhwa Pakistan. European. Academic research Lower, editor. 2014b;2(1):1560-71.
19. Kosygin L, Dharmendra H, Gyaneshwari R. Pollution status and conservation strategies of Moirang River, Manipur with a note on its aquatic bio-resources. J Environ Biol. 2007; 28(3):669-73. PMID 18380093.
20. Sarkar SK, Bhattacharya BD, Bhattacharya A, Chatterjee M, Alam A, Satpathy KK, *et al*. Occurrence, distribution and possible sources of organochlorine pesticide residues in the tropical coastal environment of India: A overview. Environ Int. 2008; 34(7):1062-71. PMID 18423595. https://doi.org/10.1016/j.envint.2008.02.010.
21. Murthy KS, Kiran BR, Venkateshwarlu M. A review on toxicity of pesticides in Fish. Int J Open Sci Res. 2013; 1(1):15-36.
22. Boatman ND, Brickle NW, Hart JD, Milsom TP, Morris AJ, Murray AWA, *et al*. Evidence for the indirect effects of pesticides on farmland birds. Ibis. 2004; 146:131-43. https://doi.org/10.1111/j.1474-919X.2004.00347.x
23. Stephenson GR, Solomon KR. Pesticides and the environment. Guelph, Ontario, Canada: Canadian Network of Toxicology Centres Press; 2007.
24. Lehtinen K-J, Notini M, Mattsson J, Landner L. Disappearance of bladder wrack (*Fucus vesiculosis* L.) in the Baltic Sea; Relation to pulp-mill chlorate. Ambio. 1988; 17:387-93.
25. Rao AS, Pillala RR. The concentration of pesticides in sediments from Kolleru lake in India. Pest Manag Sci. 2001; 57(7):620-4. PMID 11464794. https://doi.org/10.1002/ps.336
26. Scott GR, Sloman KA. The effects of environmental pollutants on complex fish behaviour: Integrating behavioural and physiological indicators of toxicity. Aquat Toxicol. 2004; 68(4):369-92. PMID 15177953. https://doi.org/10.1016/j.aquatox.2004.03.016
27. Krian A, Jha AK. Acute toxicity and behavioural responses of herbicide (Herboclin) to the fish *Clarias batrachus* (Linn). Indian J Environ Ecoplan. 2009; 16(1):185-8
28. Joshi PK, Pandey AK, Nagar RK. Eletrophoretic variation in the blood protein fractions in Malathion treated fish *Channa punctatus* (Bloch). Proceedings of the Nat Symp Anim Meta Pol L; 1988. p. 147-9.
29. Far MS, Roodsari HV, Zamini A, Mirrasooli E, Kazemi R. The effects of diazinon on behavior and some hematological parameters of fry rainbow trout (*Oncorhynchus mykiss*). World J Fish Mar Sci. 2012; 4(4):369-75.
30. Ullah R, Zuberi A, Tariq M, Ullah S. Acute toxic effects of cypermethrin on hematology and morphology of liver, brain and gills of mahseer (*Tor putitora*). Int J Agric Biol. 2014.
31. Anees MA. Intestinal pathology in a freshwater teleost, *Channa punctatus* (Bloch) exposed to sublethal and chronic levels of three organophosphorus insecticides. Acta Physiol Lattinoam. 1976; 26(1):63-7.

32. Rani S, Venkataramana GV. Effects of the organophosphorous Malathion on the branchial gills of a freshwater fish *Glossogobius giuris* (Ham). Int J Sci N Atl. 2012; 3(2): 324-30.
33. Deka S, Mahanta R. A study on the effect of organophosphorus pesticide Malathion on hepatorenal and reproductive organs of *Heteropneustes fossilis* (Bloch). Sci Probe. 2012; 1(1):1-13.
34. Helma C, Mersch-Sundermann V, Houk VS, Glasbrenner U, Klein C, Wenquing L, *et al*. Comparative evaluations of four bacterial assays for the detection of genotoxic effects in the dissolved water phases of aqueous matrices. Environ Sci Technol. 1996; 30(3):897-907. https://doi.org/10.1021/es950355w
35. Gartiser S, Stiene G, Hartmann A, Zipperle J. Einsatz von Desinfektionsmitteln im Krankenhausbereich Ursache fur okotoxische and gentoxische Effekte im Krankakenhausabwasser? (German). Wasser. 2001; 96:71-88.
36. Vargas VM, Migliavacca SB, de Melo AC, Horn RC, Guidobono RR, de Sá Ferreira IC, *et al*. Genotoxicity assessments in aquatic environments under the influence of heavy metals and organic contaminants. Mutat Res. 2001; 490(2):141-58. PMID 11342240. https://doi.org/10.1016/S1383-5718(00)00159-5
37. Dunier M, Siwicki AK. Effects of pesticides and other organic pollutants in the aquatic environment on immunity of fish: A review. Fish Shellfish Immunol. 1993; 3(6):423-38. https://doi.org/10.1006/fsim.1993.1042
38. Hoeger B, Hitzfeld B, Köllner B, Dietrich DR, van den Heuvel MR. Sex and low-level sampling stress modify the impacts of sewage effluent on the rainbow trout (*Oncorhynchus myckiss*) immune system. Aquat Toxicol. 2005; 73(1):79-90. PMID 15892994. https://doi.org/10.1016/j.aquatox.2005.03.004
39. Maskaoui K, Zhou JL, Zheng TL, Hong H, Yu Z. *Organochlorine micropollutants* in the Jiulong River Estuary and Western Xiamen Sea, China. Mar Pollut Bull. 2005; 51(8-12):950-9. PMID 16291197. https://doi.org/10.1016/j.marpolbul.2004.11.018
40. Murthy KS, Kiran BR, Venkateshwarlu M. A review on toxicity of pesticides in Fish. Int J Open Sci Res. 2013; 1(1):15-36
41. Palanisamy S, Bhaskaran P. Selected biochemical and physiological response of the fish *Channa striatus* as biomonitor to assess heavy metal pollution in freshwater environment. J Ecotoxicol Environ Monit. 1995; 5(2):131-8.
42. Thenmozhi C, Vignesh V, Thirumurugan R, Arun S. Impacts of Malathion on mortality and biochemical changes of freshwater fish *Labeo rohita*. Iran J Environ Health Sci Eng. 2011; 8(4):387-94.
43. Bose S, Nath S, Sahana SS. Toxic impact of thiamethoxam on the growth performance and liver protein concentration of a freshwater fish *Oreochromis niloticus* (TREWAVAS); Ind J Fundament [app]. Life Sci 1. 2011; 4:274-80.
44. Muthukumaravel K, Sivakumar B, Kumarasamy P, Govindarajan M. Studies on the toxicity of pesticide monocrotophos on the biochemical constituents of the freshwater fish *Labeo rohita*. Int J Curr Biochem Biotechnol. 2013; 2(10):20-6.
45. Roger PA, Bhuiyan SI. Ricefield ecosystem management and its impact on disease vectors. Int J Water Resour Dev. 1990; 6(1):2-18. https://doi.org/10.1080/07900629008722446
46. Joshi UM, Desai AK. Effects of sublethal concentration of monocrotophos on acid and alkaline phosphatase activities in the tissues of freshwater fish tilapia mossambica. J Anim Morphol Physiol. 1981; 28:221-8.
47. Milaeva ER. The role of radical reactions in organomercurials impact on lipid peroxidation. J Inorg Biochem. 2006; 100(5-6):905-15. PMID 16624415. https://doi.org/10.1016/j.jinorgbio.2006.02.014
48. Filipak Neto F, Zanata SM, Silva de Assis HC, Nakao LS, Randi MAF, Oliveira Ribeiro CA. Toxic effects of DDT and methyl mercury on the hepatocytes from *Hoplias malabaricus*. Toxicol Vitro. 2008; 22(7):1705-13. https://doi.org/10.1016/j.tiv.2008.07.006
49. Nwani CD, Lakra WS, Nagpure NS, Kumar R, Kushwaha B, Srivastava SK. Toxicity of the herbicide atrazine: Effects on lipid peroxidation and activities of Antioxidant Enzymes in the fresh water fish *Channa punctatus* (Block). Int J Environ Res Public Health. 2010; 7(8):3298-312. PMID 20948961. https://doi.org/10.3390/ijerph7083298
50. Minier C, Levy F, Rabel D, Bocquené G, Godefroy D, Burgeot T, *et al*. Flounder health status in the Seine bay. A multi markers study. Mar Environ Res. 2000; 50(1-5):373-7. PMID 11460721. https://doi.org/10.1016/S0141-1136(00)00059-3
51. Marigoudar SR, Ahmed RN, David M. Cypermethrin induced respiratory and behavioural responses in *Labeo rohita*. Vet Arh. 2009; 79(6):583-90.
52. Singh SK, Singh SK, Yadav RP. Toxicological and biochemical alterations of cypermethrin (synthetic pyrethroids) against freshwater teleost fish *Colisa fasciatus* at different season. World J Zool. 2010; 5(1):25-32.
53. Marigoudar SR, Ahmed RN, David M. Cypermethrin induced: *in vivo* inhibition of the acetylcholinesterase activity in functionally different tissues of the freshwater teleost, *Labeo rohita* (Hamilton). Toxicol Environ Chem. 2010; 91(6):1175-82. https://doi.org/10.1080/02772240802577282

54. Scott GR, Sloman KA. The effect of environmental pollutants on complex fish behaviour: Integrating behavioural and physiological indicators of toxicity. Aquat Toxicol. 2004; 68(4):369-92. PMID 15177953. https://doi.org/10.1016/j.aquatox.2004.03.016
55. Rani GI, Kumaraguru AK. Behavioural responses and acute toxicity of *Clarias batrachus* to synthetic pyrethroid insecticide, λ-cyhalothrin. J Environ App Biores. 2014; 2(1):19-24
56. Mishra A, Meshram L, Chubey K. Study of lethal effects of pesticides (trichlorfon) on fish *Heteropneustis fossilis*. J Ind Pollut Control. 2014; 30(2).
57. Sabra FS, Mehana ES. Pesticides toxicity in fish with particular reference to insecticides. Asian J Agric Food Sci. 2015; 3(1).
58. Murthy KS, Kiran BR, Venkateshwarlu M. A review on toxicity of pesticides in Fish. Int J Open Sci Res. 2013; 1(1):15-36.
59. Campbell HA, Handy RD, Sims DW. Shifts in a fish's resource holding power during a contact paired interaction: The influence of a copper-contaminated diet in rainbow trout. Physiol Biochem Zool. 2005; 78(5):706-14. PMID 16047292. https://doi.org/10.1086/432146
60. Colović MB, Krstić DZ, Lazarević-Pašti TD, Bondžić AM, Vasić VM. Acetylcholinesterase inhibitors: pharmacology and toxicology. Curr Neuropharmacol. 2013; 11(3):315-35. PMID 24179466. https://doi.org/10.2174/1570159X11311030006.
61. Kumar R, Kumari R, Mishra BK. Behavioural and morphological changes induced in the freshwater fish, *Clarias batrachus* exposed to chlorpyrifos 50%+ cypermethrin 5% EC.
62. Nagaraju B, Sudhakar P, Anitha A, Haribabu G, Rathnamma VV. Toxicity evaluation and behavioural studies of fresh water fish *Labeo rohita* exposed to Rimon. Int J Res Pharm Biomed Sci. 2011; 2(2):722-7.
63. Satyavardhan K. A Comparative Toxicity Evaluation and behavioral observations of fresh water fishes to fenvalerate. Middle East J Sci Res. 2013; 13(2):133-6.
64. Sulekha BT, Mercy TVA. Pesticide-induced histopathological Changes in the Freshwater Fishes of Kuttanand, Kerala-A Tool to Assess Water Quality and the Health Status of Fishes. Asian Fish Sci. 2009; 22(2):729-49. https://doi.org/10.33997/j.afs.2009.22.2.033
65. Ram RN, Singh SK. Carbofuran-induced histopathological and biochemical changes in liver of the teleost fish, *Channa punctatus* (Bloch). Ecotoxicol Environ Saf. 1988; 16(3):194-201. PMID 3229378. https://doi.org/10.1016/0147-6513(88)90050-4
66. Mohan RM. Malathion induced changes in the ovary of freshwater fish, *Glossogobins giuris* (Ham.). Pol Res. 2000; 19(1):73-5.
67. Rezania S, Park J, Md Din MF, Mat Taib S, Talaiekhozani A, Kumar Yadav K, *et al*. Microplastics pollution in different aquatic environments and biota: A review of recent studies. Mar Pollut Bull. 2018; 133:191-208. PMID 30041307. https://doi.org/10.1016/j.marpolbul.2018.05.022
68. Pimpão CT, Zampronio AR, Silva de Assis HC. Effects of deltamethrin on hematological parameters and enzymatic activity in *Ancistrus multispinis* (Pisces, Teleostei). Pestic Biochem Physiol. 2007; 88(2):122-7. https://doi.org/10.1016/j.pestbp.2006.10.002
69. Rios FS, Kalinin AL, Rantin FT. The effects of long-term food deprivation on respiration and haematology of the Neotropical fish *Hoplias malabaricus*. J Fish Biol. 2002; 61(1):85-95. https://doi.org/10.1111/j.1095-8649.2002.tb01738.x
70. Hrubec TC, Smith SA, Robertson JL. Age related differences in haematologic and plasma chemistry analytes of hybrid striped bass *Morore chrysops* x *Morore saxatilis*. Vet Clin Pathol. 2008; 30:8-15. https://doi.org/10.1111/j.1939-165X.2001.tb00249.x
71. Babu Velmurugan EI, Senthilkumaar P, Uysal E, Satar A. Hematological parameters of freshwater fish Anabas testudineus after sublethal exposure to cypermethrin. Environ Pollut Prot. 2016; 1:32-9. https://doi.org/10.22606/epp.2016.11004
72. Ghaffar A, Hussain R, Khan A, Abbas RZ. Hemato-biochemical and genetic damage caused by triazophos in fresh water fish, *Labeo rohita*. Int J Agric Biol. 2015; 17(3):637-42. https://doi.org/10.17957/IJAB/17.3.14.1016
73. Satyanarayan S, Bejankiwar RS, Chaudhari PR, Kotangale JP, Satyanarayan A. Impact of some chlorinated pesticides on the haematology of the fish *Cyprinus carpio* and *Puntius ticto*. J Environ Sci (China). 2004; 16(4):631-4. PMID 15495970
74. Begum G. Carbofuran insecticide induced biochemical alterations in liver and muscle tissues of the fish *Clarias batrachus* (linn) and recovery response. Aquat Toxicol. 2004; 66(1):83-92. PMID 14687981. https://doi.org/10.1016/j.aquatox.2003.08.002
75. Marins AT, Severo ES, Cerezer C, Leitemperger JW, Müller TE, Floriano L, *et al*. Environmentally relevant pesticides induce biochemical changes in Nile tilapia (*Oreochromis niloticus*). Ecotoxicology. 2021; 30(4):585-98. PMID 33770304. https://doi.org/10.1007/s10646-021-02368-8
76. Ullah R, Zuberi A, Ullah S, Ullah I, Ullah Dawar FU. Cypermethrin induced behavioral and biochemical changes in mahseer, *Tor putitora*. J Toxicol Sci. 2014; 39(6):829-36. PMID 25374374. https://doi.org/10.2131/jts.39.829
77. Marigoudar SR, Ahmed RN, David M. Ultrastructural responses and oxidate stress induced by cypermethrin in liver of *Labeo rohita*. Chem *E. coli* First. 2012; 1-13. https://doi.org/10.1080/02757540.2012.748754

78. Ambreen F, Javed M. Pesticide mixture induced DNA damage in peripheral blood erythrocytes of freshwater fish, *Oreochromis niloticus*. Pak J Zool. 2018; 50(1):339-46. https://doi.org/10.17582/journal.pjz/2018.50.1.339.346
79. Gilot-Delhalle J, Colizzi A, Moutschen J, Moutschen-Dahmen M. Mutagenicity of some organophosphorus compounds at the ade6 locus of *Schizosaccharomyces pombe*. Mutat Res. 1983; 117(1-2):139-48. PMID 6835257. https://doi.org/10.1016/0165-1218(83)90161-1
80. Mirsalis JC, Tyson CK, Steinmetz KL, Loh EK, Hamilton CM, Bakke JP, *et al*. Measurement of unscheduled DNA synthesis and S phase synthesis in rodent hepatocytes following *in vivo* treatment: Testing of 24 compounds. Environ Mol Mutagen. 1989; 14(3):155-64. PMID 2792091. https://doi.org/10.1002/em.2850140305
81. Vinggaard AM, Hnida C, Breinholt V, Larsen JC. Screening of selected pesticides for inhibition of CYP19 aromatase activity *in vitro*. Toxicol *In vitro*. 2000; 14(3):227-34. PMID 10806373. https://doi.org/10.1016/S0887-2333(00)00018-7
82. Andersen HR, Vinggaard AM, Rasmussen TH, Gjermandsen IM, Bonefeld-Jørgensen EC. Effects of currently used pesticides in assays for estrogenicity, androgenicity, and aromatase activity *in vitro*. Toxicol Appl Pharmacol. 2002; 179(1):1-12. PMID 11884232. https://doi.org/10.1006/taap.2001.9347
83. Kojima H, Katsura E, Takeuchi S, Niiyama K, Kobayashi K. Screening for estrogen and androgen receptor activities in 200 pesticides by *in vitro* reporter gene assays using Chinese hamster ovary cells. Environ Health Perspect. 2004; 112(5):524-31. PMID 15064155. https://doi.org/10.1289/ehp.6649
84. Lemaire G, Mnif W, Mauvais P, Balaguer P, Rahmani R. Activation of alpha- and beta-estrogen receptors by persistent pesticides in reporter cell lines. Life Sci. 2006; 79(12):1160-9. PMID 16626760. https://doi.org/10.1016/j.lfs.2006.03.023
85. Salazar-Arredondo E, de Jesús Solís-Heredia M, Rojas-Garcıa E, Hernández-Ochoa I, Quintanilla-Vega B. Sperm chromatin alteration and DNA damage by methyl-parathion; chlorpyrifos and diazinon and their oxon metabolites in human spermatozoa. Reprod Toxicol. 2008; 25(4):455-60. PMID 18595656. https://doi.org/10.1016/j.reprotox.2008.05.055
86. Blair RM, Fang H, Branham WS, Hass BS, Dial SL, Moland CL, *et al*. The estrogen receptor relative binding affinities of 188 natural and xenochemicals: Structural diversity of ligands. Toxicol Sci. 2000; 54(1):138-53. PMID 10746941. https://doi.org/10.1093/toxsci/54.1.138
87. Kim HJ, Park YI, Dong MS. Effects of 2,4-D and DCP on the DHT-induced androgenic action in human prostate cancer cells. Toxicol Sci. 2005; 88(1):52-9. PMID 16107550. https://doi.org/10.1093/toxsci/kfi287
88. Kelce WR, Monosson E, Gamcsik MP, Laws SC, Gray LE. Environmental hormone disruptors, evidence that vinclozolin developmental toxicity is mediated by antiandrogenic metabolites. Toxicol Appl Pharmacol. 1994; 126(2):276-85. PMID 8209380. https://doi.org/10.1006/taap.1994.1117
89. Martyniuk CJ, Mehinto AC, Denslow ND. Organochlorine pesticides: Agrochemicals with potent endocrine-disrupting properties in fish. Mol Cell Endocrinol. 2020; 507:110764. PMID 32112812. https://doi.org/10.1016/j.mce.2020.110764
90. Senthilkumaran B. Pesticide-and sex steroid analogue-induced endocrine disruption differentially targets hypothalamo–hypophyseal–gonadal system during gametogenesis in teleosts- A review. Gen Comp Endocrinol. 2015; 219:136-42. PMID 25637674. https://doi.org/10.1016/j.ygcen.2015.01.010
91. Biswas C, Maity S, Adhikari M, Chatterjee A, Guchhait R, Pramanick K. Pharmaceuticals in the aquatic environment and their endocrine disruptive effects in fish. In Proceedings of the Zoological Society. Springer India; 2021. p. 1-16. https://doi.org/10.1007/s12595-021-00402-5