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Review Article

An overview of the pesticides' impacts on fishes and humans

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Abstract: Agrochemicals, also known as pesticides include nematicides, molluscicides, rodenticides, herbicides, fungicides and insecticides, can control pests, weeds, fungi, rodents, etc. The accumulation of pesticides in the food chain and water has harmful effects on humans and animals. Despite the advantages provided by pesticides, aquatic organisms and human health are affected as the results of continuous usage of pesticides and issues of building up of chemical substances in aquatic organisms, such as fish. Pesticides must be lethal to the targeted species without any effect on non-targeted ones. Pesticides have harmful effects on the nervous system. Other pesticides are known to be carcinogenic substances. This review discussed the effects of pesticides on the immune system, protein, chromosomes, behavior, enzymes, growth, bioaccumulation, genotoxicity and changes in blood biochemical parameters of fish and humans and suggested some possible ways of mitigating such effects.

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Introduction

The human population has rapidly increased in the last few decades leading to suburbanization, mechanization, or industrialization (Al-Mamun, 2017). The nutrient fortification of water environments, climate change, acid rain and contamination by insecticides, metals and manufactured toxic constituents cause such anthropogenic troubles (Kamble, 2014). The death of wildlife, including marine and freshwater organisms, a growing hazard to human wellbeing, includes chronic respiratory disease, damage to organs (e.g., brain, lung, heart, liver and kidneys) and algal bloom in many water bodies, are some of the pesticidal effects (Al-Mamun, 2017). Increasingly, water bodies are getting exposed to contaminants or pollutants owing to human actions, such as farming, industrialization and domestic activities (Lu et al., 2015; Al-Mamun, 2017). The use of agrochemicals is essential for controlling pests and increasing food production for the universal population (Khan et al., 2013; Al-Mamun, 2017). Globally, serious concerns have been raised about the existence of these toxic chemicals in both aquatic and terrestrial environments or ecosystems (Alrumman et al., 2016). According to recent studies, industrial chemicals, pesticides, and other metals affect the endocrine system of several organisms, including humans (Haseena and Malik, 2017). The presence of these chemicals may negatively affect the normal function of the endocrine system and cause growth disorders in many species, including invertebrates and complex animals, also in humans; it can cause cancer, genetic disorders, respiratory diseases and neurological effects (Bibi et al., 2016; Haseena and Malik, 2017).

This review discussed the effects of pesticides on fish and human focusing on the immune system, protein, chromosomes, behavior, enzymes, growth, bioaccumulation, genotoxicity and changes in blood biochemical parameters of fish and humans and suggested some possible ways for mitigating such effects.

Pesticides: Well-thought-out as a distinctive class of chemical compounds, according to WHO, pesticides are utilized to kill a wide array of pests that comprises

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rodents, weeds and insects. They are utilized with the objectives of improving yield and qualities of farm products (Sharma et al., 2020). Pesticides are well-thought-out as hypothetically toxic elements released into the environment to kill fungi, weeds, insects, rodents, etc. The physical and chemical properties of pesticides are different. They are categorized based on their properties (US Environmental Protection Agency, 2018). Currently, there are three most common categories of pesticides that are extensively used, and the categories are based on the type of the entrance, pesticide utility and the entity (Yadav et al., 2017). Based on the harmfulness of pesticides, The World Health Organization (WHO) grouped them into four categories, including exceedingly hazardous, greatly hazardous, abstemiously dangerous and considerably harmful (Al-Mamun, 2017). The most popular pesticides among these are herbicides (GRACE Communications, 2018). The majority of the pesticides is anticipated to aid as crop protection, which generally protects crops from weed growth, fungal infestation and insect attacks. Pesticides are categorized based on the target animal (organism) and chemical structure (organic, inorganic, synthetic and biological substances) (Yadav et al., 2017; Li and Jennings, 2017). Generally, pesticides are biological agents, such as a virus, bacterium, or fungus that discourages, debilitates, eradicates, or depresses pests (US Environmental Protection Agency, 2018). Despite the advantages, pesticides have harmful effects on humans and other organisms (Hong et al., 2019).

Benefits of pesticides: The beneficial effects of pesticides are important. Controlling of pests, weeds, rodents, etc. results in the high productivity and better quality of crops, which also results in additional economic revenue. The above benefits might help in the medical and educational needs of children of farmers, leading to better education and good health of the general public of a nation.

General acknowledged commercial incentives are dependent on the polluter pays standard or principle, comprising taxes, user fees and the licensing fees. Nevertheless, the benefits are mainly social benefits, including risk reduction and capacity to increase labour, hence by creating opportunities for employment (Popp et al., 2013).

The increases in outputs and production have been related to some factors comprising the use of pesticides (fertilizers). The reduction of losses caused by the diseases, insect pests and weeds can reduce the quality, market value and the number of harvestable crops (Aktar et al., 2009). Following Warren (1998), there was a remarkable increase in yield of crops in the USA during the 20th century, and considerable economic losses were observed without pesticidal use (Aktar et al., 2009). USA spent 9.2 billion USD yearly on pesticides for crop protection and saved approximately 60 billion USD on crops leading to a net profit of 6.5 USD for every donated dollar on pesticides (Gianessi, 2009).

The pesticides can generate substantial environmental and socio-economic remunerations in the form of safe, healthy and affordable food, which contributes to secure farm incomes and enable sustainable farm management by improving the efficiency of natural resources, such as soil, and water (Popp et al., 2013; Al-Mamun, 2017). It can be opposite when pesticides are inappropriately used.

The pesticides have many advantages and play a significant role in the management of weeds, rodents, fungi, etc. and improving crop quality, yield protection and food affordability, thereby providing economic benefits to farmers and the consumers. Certain ingredients of pesticides such as azadirachtin and/or glufosinate are compounds that occur naturally and are created using processes of synthetic chemistry (Schwartz et al. 2004; Ressel 2015; Fernandes et al., 2019; Mesnage et al., 2019). Additionally, several plants, of which several are utilized as eatable crops, have advanced resistance means against predators like microorganisms as well as insects through the production of compounds performing like pesticides (Ujváry, 2010). These naturally occurring pesticides are commonly established to have favorable wellbeing influences in humans due to the fact that they stimulate cellular stress adaption response pathways (Martel et al., 2019; Mesnage et al., 2019).

Since 1945, the utilization of pesticides has prevented approximately 7 million people from death as a result of killing pests, which spread diseases, including yellow fever, typhoid fever, bubonic plague and encephalitis (http://study.com/academy/lesson/use-of-pesticides-benefits-and-problems-associated-with-pesticides.html). The use of pesticides prevents the outbreaks of diseases, which contributes to improving human health. For example, malaria is reported to be responsible for the death of over 5000 a day worldwide (Ross, 2005).

Toxic nature of pesticides: World Health Organization (WHO) reported that approximately 300,000 people died per annum as a result of pesticide poisoning (Gunnell and Eddleston, 2003). This happened as a result of inhalations or consumption of pesticides by a person above the threshold via accident or occupation (Sharma et al., 2020). Pesticide poisoning occurs as a result of relatively ignorance or unawareness of detrimental effects via inhalation of these chemicals by people. The literature available has indicated that during the gestation period, when women are exposed to DDT, there were traces of the DDT in their breast milk and umbilical cord (Wolff et al., 2007; Debost-Legrand et al., 2016; Sharma et al., 2020). It has also been observed that there was some relationship between exposure to pesticides and changes in body weight at the birth time (Kezios et al., 2013). On the other hand, work-related poisoning known as occupational poisoning occurs as a result of the usage of these chemicals in the field of agriculture, manufacturing industries by the people in their daily activities (Gangemi et al., 2016; Darçın et al., 2017). Work-related poisoning of pesticides can happen in several ways, such as ingestion, skin contacts, and inhalation (Calvert et al., 2008; Sharma et al., 2020). The majority of people also consumed pesticides for suicide (Gunnell et al., 2007).

The existence of several agrochemicals popularly known as pesticides in water bodies such as dams, lakes, streams, and rivers generates a multifarious exposure of these chemicals hypothetically poisonous to aquatic organisms (Covert et al., 2020; Norman et al., 2020). When fish species are exposed to poisonous material such as pesticides, unexpected and extreme death may occur as the results of acute toxicity. The most ostensible signs of serious poisoning in fish as the result of pesticide usage consist of severe reaction to external stimuli, muscle spasms, and sudden fast swimming in circles, lethargy, pallor, and forward extension fins (Sabra and Mehana, 2015). Signs such as respiratory dysfunction and suffocation, disruption of nerve functions, and neurological disorder are some of the major clinical signs that can result in the mortality of fish (Banaee et al., 2011, 2012). WHO reported the median lethal dose (LD_{50}) of different pesticides in rats and other laboratory animals (Table 1).

Table 1. The hazard ratings of a lethal concentration of the relative toxicity of the agricultural pesticides.

Toxicity	LC50(mL)
Minimal	>100
Slight	10-100
Moderate	1-10
High	0.1-1.0
Extreme	0.01-0.1
Super	< 0.01

Source: https://www.beyondpesticides.org/programs/wildlife/fish

Pesticidal effects on humans: Pesticides and their residues can cause harmful effects on human health. The pesticides can enter into the human body and the food chain through direct contact, foods, and polluted air and water are not in dispute. As a result, human health is currently under threat of continuous use of pesticides. Pesticides from the agricultural field result in dire ailment in humans (Lee et al., 2011b). Many signs or symptoms, such as skin rashes, dizziness, poor concentration, nausea, body aches, cramps, impaired vision and headache occurred because of pesticide poisoning (Pan-Germany, 2012; Al-Mamun, 2017). These signs and symptoms are related to the amount and toxicity of the specific pesticide, mode of activity, application mode, frequency and duration of direct contact with person and chemicals. The direct contact or exposure to sub-lethal amount of these chemicals for a long period, such as several months, years and decades, could lead to chronic diseases (Pan-Germany, 2012). With regard to the chronic poisoning of pesticides, the signs cannot be observed.

Personnel working in the field of agriculture can be affected in great jeopardy, but others are also at risk through the food chain and polluted air and water (Al-Mamun, 2017). The prevalence of chronic illnesses has begun to increase as pesticide usage has grown in the last few decades. Several studies reported that pesticide exposure has harmful effects on the nervous system, reproduction, respiratory systems and cardiovascular system in humans (Mostafalou et al., 2012). Chronic illnesses, such as adult brain cancer, lymphocytic leukemia (CLL), prostate cancer, childhood cancer, Alzheimer's disease (AD), Parkinson's disease (PD), reproductive disorders and hormonal imbalance, respiratory diseases, breast pain and infertility were also reported in humans due to pesticide exposure (Lee et al., 2011a; Tanner et al., 2011; Abdullah et al., 2011; Andersen et al., 2012; Cocco et al., 2013; Zaganas et al., 2013; Schinasi and Leon, 2014; Al-Mamun, 2017; Polanco Rodriguez et al., 2017; Bonner et al., 2017; Sabarwal et al., 2018).

Some adverse effects of pesticides on aquatic ecosystems and pesticidal effects on fish: Currently, the use of herbicides has been increased tremendously and studies reported that it influences the environment and non-targeted organisms (Pérez et al., 2011; Pérez-Parada et al., 2018). Although it was first intended to control only unwanted plants (Stenersen, 2004), it has an adverse effect on non-targeted aquatic organisms and other animals according to the recent studies (Tulgar and Arınç, 2018; Pérez-Parada et al., 2018). Water sources, such as rivers, ponds, etc., hold pesticides at the bottom, which affects the reproduction and behaviors of living organisms in the aquatic ecosystem leading to the extinction of species (Tulgar, 2018). Several living organisms are dependent on planktons as food sources. These planktons mostly collect the pesticidal residues, which are transferred to fish and other invertebrates (Pereira et al., 2013; Tulgar, 2018). The entrance of pesticides into aquatic environments has many implications. Fish are affected directly or indirectly by the use of pesticides. The vulnerable parts of fish to chemical exposure are liver, kidney, brain and gills (Mahmood et al., 2016).

The widespread usage of chlorpyrifos increase the lethal load in aquatic ecosystems, causing antagonistic effects on non-targeted species, including fish (Palanikumar et al., 2014). Severe and long-lasting toxic effects of chlorpyrifos in diverse species of fish were widely observed (Anita et al., 2016). Sublethal toxic effect of chlorpyrifos in aquatic ecosystems can prompt developmental, hematological, histopathological, biochemical, neurobehavioral, oxidative and morphological changes, whereas the lethal intensities are responsible for mass mortalities of non-targeted species, weight loss, low disease resistance and sterility in fish (Sunanda et al., 2016; Banaee et al., 2019a, b, 2020; Hatami et al., 2019).

According to Jadhav and Pawar (2018), the concentration of endosulfan is more toxic to fish than any other aquatic organisms. One of the extensively used groups of insecticides in agriculture is organophosphates (OPs). Sublethal doses of organophosphates resulted in different physiological injuries, such as reproductive failure, predator avoidance and feeding problem (Little et al., 1990). The continuous utilization of fungicides, herbicides and insecticides have been associated with the reduction of animal and fish population. Due to overuse of pesticides, the population of different species (peregrine, falcon, bald eagle and osprey) are declining (Scholz et al., 2012). The extensive usage of pesticides has several implications, such as bioaccumulation, genotoxicity, the immune system effects, protein effects, chromosomal effects, behavioral effects, enzymes effects, growth and changes in blood biochemical parameters on fish and humans.

Bioaccumulation of pesticides: Pesticides could accrue in aquatic animals via several means; directly from water through skin or gills (bioconcentration), the ingestion of polluted/contaminated food (biomagnification) and suspended particles uptakes (ingestion) (Van der Oost et al., 2003; Banaee et al., 2015). Bioaccumulation of several kinds of pesticides directly affects fish (Rao and Pillala 2001; Clasen et al., 2018). The effect of pesticides in fish results in fish behavioral changes. Sluggish movement of fish and alteration of their swimming ability makes them more

susceptible to the predators, reduce their feeding ability, maintain their position and defend their territories (Ullah et al., 2014; Srivastava et al., 2016). The behavior of an organism offers an exceptional viewpoint to connect physiology and natural balance between animals and their surroundings (Srivastava and Singh, 2013; Srivastava et al., 2016). The behavior of the organism permits them to adapt internal and external stimuli, which enables them to adjust to ecological variables (Srivastava et al., 2016). According to Srivastava and Singh (2014) and Ullah et al. (2014), the sub-lethal concentration of pesticides in water ecosystems resulted in structural and functional variations in organisms. The bio-accumulation effects of several kinds of pesticides on aquatic organisms, such as fish, are immeasurable.

Immune system*:* The low concentration of pesticides disturbs the fish immune system (Farid and El-Sayed, 2015) and also work as an impersonator of sex hormones, and trigger uncharacteristic sex growth, the feminization of males, uncharacteristic sex ratios and infrequent coupling behavior. Indirectly, pesticides have impacts on fish through interfering with the diet source and sporadic habits (Satyavardhan, 2013). The function of the immune system is modified by the pesticides leading to immune depression, unrestrained cell growth and modification of host resistance comprising innate immunity and assimilated immunity. The most vital feature or possession of fish is its immune system against pathogens. Fish become vulnerable to infectious diseases and pathogens when sub-lethal concentrations of pesticides are introduced (Zelikoff et al., 2000).

Protein: Several studies have been reported the decrease of protein content under stress in fish and other organisms (Tiwari and Singh, 2009). As reported by Tiwari and Singh (2004), there was a significant reduction in the levels of protein in gills, blood, intestine, muscles and liver of *Channa punctatus* when exposed to oleandrin and the introduction of C. *carpio* to endosulfan. Also, there was a significant reduction in protein content of *Colisa fasciatus* and *Tor putitora* when exposed to cypermethrin (Singh et al., 2010; Ullah et al., 2014). There was a substantial reduction of protein content in *C. carpio* when exposed to endosulfan (Bibi et al., 2014). The introduction of *Clarias batrachus* and *Labeo rohita* to cypermethrin and malathion also revealed the reduction in the protein content (Thenmozhi et al., 2011). A study by Bose et al. (2011), revealed the decrease in protein content of the liver of *Oreochromis niloticus* when exposed to thiamethoxan. Several studies showed the reduction of protein contents in fish when exposed to pesticides.

Enzymes: All metabolic processes in the cell need enzyme catalysis to sustain. Metabolic pathways are dependent on enzymes. Enzymes help body to break down large complex molecules into small molecules, such as glucose. Pesticides in animals provoke some enzymatic pathways. As reported by Srivastava et al. (2016) and Das and Mukherjee (2003), brain acetylcholinesterase action was observed to be reduced after 45 days of exposure to cypermethrin. Lactate dehydrogenase action in the brain and liver were elevated but inhibited in the kidney, and succinate dehydrogenase (SDH) and ATPase activities were depleted in brain, kidney and liver because of the cypermethrin toxicity (Das et al., 2003). Ogueji and Auta (2007) reported the variations in biochemical parameters, such as alkaline phosphatase, glutamic oxaloacetic acid transaminase, glutamic pyruvic acid transaminase, triglycerides, cholesterol, protein and serum glucose in *C. gariepinus* under lamda-cyhalothrin exposure.

Genotoxicity*:* The genotoxic effect has become the key biomarkers for assessing contamination related damages. Biomonitoring programs have revealed the genotoxicity and wellbeing effects (Hughes and Hebert, 1991). Genotoxicity is defined as an asset possessed by specific elements, which is dangerous to the genetic evidence confined in animals. Several dynamisms can damage DNA, RNA and other genetic resources (Hong et al., 2020). The assets of genotoxicity can be applied only to the constituents that damage the genetic statistics. An element that causes genotoxicity is identified as genotoxin (Srivastava et al., 2016). Many studies revealed that genotoxins are mainly birth-defect factors, mutation-

causing agents, mutagens and carcinogens. However, there is evidence linked to pesticides (Srivastava et al., 2016). Cancer is the unrestrained development of cells inside the body (Kushwaha et al., 2012). The perfect model for checking wastewater quality and genotoxins is fish, since fish can metabolize toxic substances. Fish have small size micronuclei because their chromosomes are considerably small (Nagpure et al., 2007). The micronuclei are shaped in the fish cells. The development of micronuclei is based on the degree of propagation of cells that is also based on the fish species, target tissues, conditions of environments and the type of harmful waste. The RAPD profile and comet assay in *C. punctatus* was changed when the fish was introduced or exposed to sub-lethal concentration PFF, a sign of its genotoxic possibility to aquatic animals (Pandey et al., 2018). However, processes for the collaborative influence of contaminants in the cells of fish are still not completely understood.

Chromosomes: Chromosomal abnormalities are triggered by dichlorvos at 0.01 ppm concentration in the form of stubbed arms, extra fragments, attenuation, chromatid breaks, sub-chromatid breaks, chromatid gaps, centromeric gaps and pycnosis in kidney cells of *C. punctata* after 24, 48, 72 and 96 hours of exposure (Farid and El-Sayed, 2015). Similarly, dichlorvos toxicity was associated with the changes in DNA duplication that triggered the mutation and cellular hyper propagation (Sabra and Mehana, 2015).

Changes in blood biochemical parameters*:* The biochemical parameters of blood can be the indicators of pesticidal toxicity. When severe damages are caused to some tissues with special reference to the liver, a combination of various biochemical parameters could shrink considerably in cells, which can reduce specific biochemical dynamics in fish blood when introduced to pesticides (Banaee et al., 2008). Distractions and injuries of tissue in organs could lead to the reduction in survival, development, fitness and high probability of vulnerability to pathological alteration. The rate of recurrence and tissue lesion intensity is based on the pesticidal concentrations and the duration of the toxins introduced to fish (Sabra and Mehana, 2015). As reported by Fanta et al. (2003), histopathological lesions were noted in the liver of *C. carpio* and *Cirrhinus mrigala,* (Velmurugan et al., 2009). According to Banaee et al. (2012), the histopathological alterations were observed because of the exposure of dichlorvos and diazinon treated fish for 10 to 30 days.

Behavioral variations*:* Fish behavior is mostly affected by the uptake of contaminants. Fish eat and accumulate various pollutants, including pesticides, polychlorinated biphenyls, polycyclic aromatic hydrocarbons and heavy metals (Srivastava et al., 2016). According to Srivastava and Singh (2013), the acetylcholinesterase action of pesticides disturbed the existence and caused the death or mortality of *C. batrachus* when exposed to propiconazole and mancozeb. Srivastava and Singh (2013) also observed that compounds that hinder cholinesterase action disturbed the regular movements of fish. As a result, fish were further predisposed and vulnerable to infections and pathogens (Satyavardhan 2013; Gill and Raine, 2014; Srivastava et al., 2016). Imbalanced swimming, darting and erratic movements and hypoexcitability can be observed in *L. rohita, C. carpio, O. mossambicus, C. catla* and *C. mrigala* due to the introduction of sodium cyanide (Ullah et al., 2014).

Growth disorders*:* Deficiency in standard growth and development can diminish the fish survival rate. Larvae of fish can be directly exposed to pesticides through parenteral in viviparous fish (Viant et al., 2006). According to Todd and Leeuwen (2002), there was an influence of carbaryl pesticides on the fish embryo. Decreased development of fish comprises of anomalies in nourishing or eating behaviors, such as dysfunction in the metabolism process and waste of energy caused by insecticide exposure (Sabra and Mehana, 2015).

Conclusion and Future Directions: In the water cycle, chemicals contaminate groundwater, and most of these are transferred to lakes, rivers and ponds. They also hinder the existence of aquatic life by

polluting the sources of food of the aquatic organisms. Aquatic organisms and humans are affected directly or indirectly due to the ingestion of contaminated fruits, vegetables, fish and water (Simone et al., 2018; GRACE Communications, 2018), which are also the main sources of food and energy for organisms. Several studies have reported the activities of agriculture as the primary sources that release toxic components into the aquatic environments. The intake of pesticides by fish accumulates in human body systems and bio-intensification through the food chain causes environmental and health concerns. The non-target organisms have been continually affected by persistent organic pollutants in the ecosystem and increase probabilities of the disruption of the endocrine system, immune system, protein, chromosomes, behavior, enzymes, growth of fish and humans, bioaccumulation, genotoxicity and changes in blood biochemical parameters as long-term chronic effects. Biological sustainability of water environments is under serious threat due to heavy pesticidal usage (Mahmood et al., 2016).

Eliminating the risks from the use of pesticides is impossible. However, the risks can be reduced e.g. there is a need for environmentally friendly pesticide formulation, which can minimize the destructive effects of pesticide utilization. The appropriate dosage of pesticides is essential and required to reduce the risks. Crops that are grown without chemicals can be useful for human and aquatic organisms. Furthermore, the harmful pesticides, which are prohibited, must be strictly enforced by imposing jail terms and massive fines. It is believed that these approaches will help to save aquatic lives as well as humans.

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References

Abdullah N.Z., Ishaka A., Samsuddin N., Mohd Rus R., Mohamed A.H. (2011). Chronic organophosphate pesticide exposure and coronary artery disease: finding a bridge. IIUM Research, Invention and Innovation Exhibition, 9-10 February 2011, Cultural Activity Centre (CAC) and KAED Gallery IIUM, 223.

Aktar W., Sengupta D., Chowdhury A. (2009). Impact of pesticides use in agriculture: their benefits and hazards. Interdisciplinary Toxicology, 2(1): 1-12.

Al-Mamun A. (2017). Pesticide degradations, residues, and environmental concerns. In: Khan M., Rahman M. (Eds.). Pesticide Residue in Foods. Springer International Publishing. pp: 87-102.

Alrumman S.A., El-kott A.F., Kehsk M.A. (2016). Water pollution: Source and treatment. American Journal of Environmental Engineering, 6(3): 88-98.

Andersen H.R., Wohlfahrt-Veje C., Dalgård C., Christiansen L., Main K.M., Nellemann C., Murata K., Jensen T.K., Skakkebaek N.K., Grandjean P. (2012). Paraoxonase 1 polymorphism and prenatal pesticide exposure associated with adverse cardiovascular risk profiles at school age. PLoS One, 7: e36830.

Anita B., Yadav A.S., Cheema N. (2016). Genotoxic effects of chlorpyrifos in freshwater fish Cirrhinus mrigala using micronucleus assay. Advances in Biology, 1-6.

Banaee M., Akhlaghi M., Soltanian S. Sureda A., Gholamhosseini A., Rakhshaninejad M. (2020). Combined effects of exposure to sub-lethal concentration of the insecticide chlorpyrifos and the herbicide glyphosate on the biochemical changes in the freshwater crayfish *Pontastacus leptodactylus*. Ecotoxicology, 29: 1500-1515.

Banaee M., Akhlaghi M., Soltanian S., Gholamhosseini A., Heidarieh H., Fereidouni M.S. (2019a). Acute exposure to chlorpyrifos and glyphosate induces changes in hemolymph biochemical parameters in the crayfish, *Astacus leptodactylus* (Eschscholtz, 1823). Comparative Biochemistry and Physiology Part C: Toxicology and Pharmacology, 222: 145-155.

Banaee M., Mirvagefei A., Rafei G.R., Majazi A.B. (2008). Effects of sublethal Diazinon concentrations on blood plasma. Biochemistry. International Journal of Environmental Research, 2(2): 189-198.

Banaee M., Mirvaghefei A.R., Majazi Amiri B., Rafei G.R., Nematdost B. (2011). Hematological and histopathological study of experimental diazinon poisoning in common carp fish (*Cyprinus carpio*). Journal of Fisheries (Iranian Journal of Natural

Resources), 64(1): 1-14.

Banaee M., Mohammadipour S., Madhani S. (2015). Effects of sublethal concentrations of permethrin on bioaccumulation of cadmium in zebra cichlid (*Cichlasoma nigrofasciatum*). Toxicological and Environmental Chemistry, 97(2): 200-207.

Banaee M., Sureda A., Mirvagefei A.R., Ahmadi K. (2012). Histopathological alterations induced by Diazinon in Rainbow trout (*Oncohrynchus mykiss*). International Journal of Environmental Research, 7(3): 735-744.

Banaee M., Sureda A., Taheri S., Hedayatzadeh F. (2019b). Sub-lethal effects of dimethoate alone and in combination with cadmium on biochemical parameters in freshwater snail, *Galba truncatula*. Comparative Biochemistry and Physiology Part C: Toxicology and Pharmacology, 220: 62-70.

Basic Information about Pesticide Ingredients. US Environmental Protection Agency (2018). Retrieved Dec 1, 2018.

Begum G. (2004). Carbofuran insecticides induced biochemical alterations in liver and muscle tissues of the fish *Clarias batrachus* (Linin) and recovery response, Aquatic Toxicology, 66: 83-92.

Bibi N., Zuberi A., Naeem M., Ullah I., Sarwar H., Atika B. (2014). Evaluation of acute toxicity of karate and its sub-lethal effects on protein and acetylcholinesterase activity in *Cyprinus carpio*. International Journal of Agriculture and Biology, 16: 731-737.

Bibi S., Khan R.L., Nazir R. (2016). Heavy metals in drinking water of Lakki Marwat District, KPK, Pakistan. World Applied Sciences Journal, 34(1): 15-19.

Bonner M.R., Freeman L.E., Hoppin J.A., Koutros S., Sandler D.P., Lynch C.F., Hines C.J., Thomas K., Blair A., Alavanja M.C. (2017). Occupational exposure to pesticides and the incidence of Lung Cancer in the agricultural health study. Environmental Health Perspectives, 125: 544-551.

Bose S., Nath S., Sahana S.S. (2011). Toxic impact of thiamethoxam on the growth performance and liver protein concentration of a freshwater fish, *Oreochromis niloticus* (Trewavas). Indian Journal of Fundamental and Applied Life Science, 1: 274-280.

Calvert G.M., Karnik J., Mehler L., Beckman J., Morrissey B., Sievert J., Moraga-McHaley S. (2008). Acute pesticide poisoning among agricultural workers in the United States, 1998-2005. American Journal of Industrial Medicine, 51(12): 883-898.

Cholz N.L., Fleishman E., Brown L., Werner I., Johnson M.L., Brooks M.L., Mitchelmore C.L. (2012). A perspective on modern pesticides, pelagic fish declines, and unknown ecological resilience in highly managed ecosystems. Bioscience, 62(4): 428-434.

Clasen B., Loro V.L., Murussi C.R., Tiecher T.L., Moraes B., Zanella R. (2018). Bioaccumulation and oxidative stress caused by pesticides in *Cyprinus carpio* reared in a rice-fish system. Science of The Total Environment, 626: 737-743.

Cocco P., Satta G., Dubois S., Pili C., Pilleri M., Zucca M., Mannetje A.M., Becker N., Benavente Y., De Sanjose S., Foretova L., Staines A., Maynadie M., Nieters A., Brennan P., Miligi L., Ennas M.G., Boffetta P. (2013). Lymphoma risk and occupational exposure to pesticides: results of the Epilymph study. Occupational and Environmental Medicine, 70: 91-98.

Covert S.A., Shoda M.E., Stackpoole S.M., Stone W.W. (2020). Pesticide mixtures show potential toxicity to aquatic life in U.S. streams, water years 2013-2017. Science of The Total Environment, 141285.

Darçın E.S., Darçın M., Alkan M., Doğrul G. (2017). Occupational Risk Factors for Acute Pesticide Poisoning among Farmers in Asia. Poisoning - From Specific Toxic Agents to Novel Rapid and Simplified Techniques for Analysis. doi:10.5772/ intechopen.72006

Das B.K., Mukherjee S.C. (2003). Toxicity of cypermethrin in *Labeo rohita* fingerlings: biochemical, enzymatic and haematological consequences. Comparative Biochemistry and Physiology Part C: Toxicology and Pharmacology, 134(1): 109-121.

Debost-Legrand A., Warembourg C., Massart C., Chevrier C., Bonvallot N., Monfort C., … Cordier S. (2016). Prenatal exposure to persistent organic pollutants and organophosphate pesticides, and markers of glucose metabolism at birth. Environmental Research, 146: 207-217.

Fanta E., Sant Anna R., Romao F., Vianna A.C.C., Freiberger S. (2003). Histopathology of the fish *Corydoras paleatus* contaminated with sublethal levels of organophosphorus in water and food. Ecotoxicology and Environmenta Safety, 54: 119-130.

FAO, 2020. Pesticide Database Codex.

Farid S.S., El-Sayed E.M. (2015). Pesticides toxicity in fish with particular reference to insecticides. Asian Journal of Agriculture and Food Sciences, 3(1): Retrieved from https://www.ajouronline.com/index.php/AJAFS/article /view/2156.

Fernandes S.R., Barreiros L., Oliveira R.F., Cruz A., Prudêncio C., Oliveira A.I., Pinho C., Santos N.,

Morgado J. (2019). Chemistry, bioactivities, extraction and analysis of azadirachtin: state-of the-art. Fitoterapia, 134: 141-150.

Gangemi S., Miozzi E., Teodoro M., Briguglio G., De Luca A., Alibrando C., Libra M. (2016). Occupational exposure to pesticides as a possible risk factor for the development of chronic diseases in humans. Molecular Medicine Reports, 14(5): 4475-4488.

Gianessi L.P. (2009). The value of insecticides in U.S. crop production. Crop life Foundation, Crop Protection Research Institute (CPRI).

Gill R.J., Raine N.E. (2014). Chronic impairment of bumble bee natural foraging behaviour induced by sublethal pesticide exposure. Functional Ecology, 28: 1459-1471.

Gunnell D., Eddleston M. (2003). Suicide by intentional ingestion of pesticides: a continuing tragedy in developing countries. International Journal of Epidemiology, 32: 902-909.

Gunnell D., Eddleston M., Phillips M.R., Konradsen F. (2007). The global distribution of fatal pesticide self-poisoning: Systematic review. BMC Public Health, 7(1): 357.

Haseena M., Malik M.F. (2017). Water pollution and human health. Environ Risk Assess Remediate, 1(3): 16-19.

Hatami M., Banaee M., Nematdoost Haghi B. (2019). Sub-lethal toxicity of chlorpyrifos alone and in combination with polyethylene glycol to common carp (*Cyprinus carpio*). Chemosphere, 219: 981-988.

Hong Y., Huang Y., Yang X., Zhang J., Li L., Huang Q., Huang Z. (2020). Abamectin at environmentally-realistic concentrations cause oxidative stress and genotoxic damage in juvenile fish (*Schizothorax prenanti*). Aquatic Toxicology, 225: 105528.

Hong Y., Yang X., Huang Y., Yan G., Cheng Y. (2019). Assessment of the oxidative and genotoxic effects of the glyphosate-based herbicide roundup on the freshwater shrimp, *Macrobrachium nipponensis*. Chemosphere, 210: 896-906.

Hughes J.B., Hebert A.T. (1991). Erythrocyte micronuclei in winter flounder (*Pseudopleuronectes americanus*): results of field's surveys during 1980-1988 from Virginia to Nova Scotia and in Long Island Sound. Archives of Environmental Contamination and Toxicology, 20: 474- 479.

Jadhav T.J., Pawar, S.M. (2018). Organic pesticides effect on freshwater fish *Barbus ticto*. International Journal of Scientific Engineering and Research (IJSER), 7(8): 1-2.

Kamble S.M. (2014). Water pollution and public health issues in Kolhapur city in Maharashtra. International Journal of Scientific and Research Publication, 4(1): 1-6.

Kezios K.L., Liu X., Cirillo P.M., Cohn B.A., Kalantzi O.I., Wang Y., Factor-Litvak P. (2013). Dichlorodiphenyl-trichloroethane (DDT), DDT metabolites and pregnancy outcomes. Reproductive Toxicology, 35: 156-164.

Khan N., Hussain S.T., Saboor A. (2013). Physiochemica investigation of the drinking water sources from Mardan, Khyber Pakhtunkhwa, Pakistan. International Journal of Physical Sciences, 8(33): 1661-1671.

Kushwaha B., Pandey S., Sharma S., Srivastava R., Kumar R., Nagpure N.S., Dabas A., Srivastava S.K. (2012). *In situ* assessment of genotoxic and mutagenic potential of polluted river water in *Channa punctatus* and *Mystus vittatus*. International Aquatic Research, 4: 16-27.

Lee D.H., Lind P.M., Jacobs D.R., Salihovic S., van Bavel B., Lind L. (2011a). Polychlorinated biphenyls and organochlorine pesticides in plasma predict the development of type 2 diabetes in the elderly. The prospective investigation of the vasculature in Uppsala seniors (PIVUS) study. Diabetes Care, 34: 1778-1784.

Lee S.J., Mehler L., Beckman J., Diebolt-Brown B., Prado J., Lackovic M., Waltz J., Mulay P., Schwartz A., Mitchell Y., Moraga-McHaley S., Gergely R., Calvert G.M. (2011b). Acute pesticide illnesses associated with off-target pesticide drift from agricultural applications: 11 states, 1998-2006. Environmental Health Perspectives, 119(8): 1162-1169.

Li Z., Jennings A. (2017). Worldwide regulations of standard values of pesticides for human health risk control: A review. International Journal of Environmental Research and Public Health, 14(7): 826.

Little E.E., Archeski R.D., Flerov B.A., Kozlovskaya V.I. (1990). Behavioral indicators of sublethal toxicity in rainbow trout. Archives of Environmental Contamination and Toxicology, 19: 380-385.

Lu Y., Song S., Wang R., Liu Z., Meng J., Sweetman A.J. (2015). Impacts of soil and water pollution on food safety and health risks in China. Environment International, 77: 5-15.

Mahmood I., Imadi S.R., Shazadi K., Gul A., Hakeem K.R. (2016). Effects of Pesticides on Environment. Plant, Soil and Microbes, 253-269.

Martel J., Ojcius D.M., Ko Y.F., Ke P.Y., Wu C.Y., Peng H.H., Young J.D. (2019). Hormetic effects of phytochemicals on health and longevity. Trends in Endocrinology and Metabolism, 30: 335-346.

Mesnage R., Tsakiris I.N., Antoniou M.N., Tsatsakis A.

(2019). Limitations in the evidential basis supporting health benefits from a decreased exposure to pesticides through organic food consumption. Current Opinion in Toxicology, 19: 50-55.

Mostafalou S., Abdollahi M. (2012). Concerns of environmental persistence of pesticides and human chronic diseases. Clinical and Experimental Pharmacology and Physiology, S5: e002.

Nagpure N.S., Kumar R., Kushwaha B., Singh P.J., Srivastava S.K. (2007). Genotoxicity Assessment in Fishes: A Practical Approach. National Bureau of Fish Genetic Resource, Lucknow. 63 p.

Norman J.E., Mahler B.J., Nowell L.H., Van Metre P.C., Sandstrom M.W., Corbin M.A., Qian Y., Pankow J.F., Luo W., Fitzgerald N.B., Asher W.E., McWhirter K.J. (2020). Daily stream samples reveal highly complex pesticide occurrence and potential toxicity to aquatic life. Science of the Total Environment, 715: 136795.

Oerke E.C. (2005). Crop losses to pests. The Journal of Agricultural Science, 144: 31-43.

Ogueji E.O., Ibrahim B.U., Auta J. (2013). Investigation of acute toxicity of chlorpyrifos-ethyl on *Clarias gariepinus* - (Burchell, 1822) using some behavioural indices. International Journal of Basic and Applied Sciences, 2(2): 176-183.

Palanikumar L., Kumaraguru A.K., Ramakritinan C.M., Anand M. (2014). Toxicity, biochemical and clastogenic response of chlorpyrifos and carbendazim in milkfish *Chanos chanos*. International Journal of Environmental Science and Technology, 11(3): 765-774.

Pandey A.K., Nagpure N.S., Trivedi S.P. (2018). Genotoxicity assessment of pesticide profenofos in freshwater fish *Channa punctatus* (Bloch) using comet assay and random amplified polymorphic DNA (RAPD). Chemosphere, 211: 316-323.

Pan-Germany. (2012). Pesticide and health hazards. Facts Figures. 1-16 (www.panGermany.org/download/ Vergift_EN-201112-web.pdf).

Pereira L., Fernandes M.N., Martinez C.B.R. (2013). Hematological and biochemical alterations in the fish *Prochilodus lineatus* caused by the herbicide clomazone. Environmental Toxicology and Pharmacology, 36: 1-8.

Pérez G.L., Vera M.S., Miranda L. (2011). Effects of herbicide glyphosate and glyphosate-based formulations on aquatic ecosystems. In: A. Kortekamp (Ed.), Herbicides and Environment. ISBN: 978-953-307-476-4.

Pérez-Parada A., Goyenola G., Teixeira de Mello F., Heinzen H. (2018). Recent advances and open questions around pesticide dynamics and effects on freshwater fishes. Current Opinion in Environmental Science and Health, 4: 38-44.

Pesticides in Our Food System. FoodPrint. GRACE Communications (2018). Retrieved 26 March 2018. Polanco Rodriguez A.G., Riba Lopez M.I., DelValls Casillas T.A., Araujo Leon J.A., Mahjoub O., Prusty, A.K. (2017). Monitoring of organochlorine pesticides in blood of women with uterine cervix cancer. Environmental Pollution, 220: 853-862.

Popp J., Pető K., Nagy J. (2013). Pesticide productivity and food security. A review. Agronomy for Sustainable Development, 33: 243-255.

Rao A.S., Pillala R.R. (2001). The concentration of pesticides in sediments from Kolleru Lake in India. Pest Management Science, 57: 620- 624.

Ressel H. (2015). Method for producing phosphinates. Patent number EP3356376A1. European Patent Office.

Ross G. (2005). Risks and benefits of DDT. Lancet, 366(9499): 1771-1772.

Sabarwal A., Kumar K., Singh R.P. (2018). Hazardous Effects of Chemical Pesticides on Human Health-Cancer and Other Associated Disorders. Environmental Toxicology and Pharmacology, 63: 103-114.

Satyavardhan K. (2013). A comparative toxicity evaluation and behavioral observations of freshwater fishes to fenvalerate. Middle-East Journal of Scientific Research, 13: 133-136.

Schinasi L., Leon M.E. (2014). Non-hodgkin lymphoma and occupational exposure to agricultural pesticide chemical groups and active ingredients: a systematic review and meta-analysis. International Journal of Environmental Research and Public Health, 11: 4449-4527.

Schwartz D., Berger S., Heinzelmann E., Muschko K., Welzel K., Wohlleben W. (2004). Biosynthetic gene cluster of the herbicide phosphinothricin tripeptide from *Streptomyces viridochromogenes* Tu494. Applied and Environmental Microbiology, 70: 7093-7102.

Sharma A., Shukla A., Attri K., Kumar M., Kumar P., Suttee A., … Singla N. (2020). Global trends in pesticides: A looming threat and viable alternatives. Ecotoxicology and Environmental Safety, 201: 110812.

Simone T., Costa C., Umberto V., Giancarlo Q., Giovanni G. (2018). A survey of honey bee-collected pollen reveals widespread contamination by agricultural pesticides. Science of the Total Environment, 615: 208-218.

Srivastava P., Singh A. (2014). Study of *in vivo e*ffects

caused by metabolites (1,2,4-Trizole Alanine) of steroid-inhibitor fungicide on aquatic life (fish). Journal of Aquaculture Research and Development, 4(4): 183.

Srivastava P., Singh A. (2013). Study on some neural and behavioral changes induced by carbamate (Mancozeb) fungicide on freshwater fish, *Clarias batrachus.* World Journal of Zoology, 8: 376-380.

Srivastava P., Singh A., Pandey A.K. (2016). Pesticides toxicity in fishes: biochemical, physiological and genotoxic aspects. Biochemical and Cellular Archives, 16(2): 199-218.

Stenersen J. (2004). Chemical Pesticides: Mode of Action and Toxicology. CRC Press, Boca Raton, Florida, USA. 296 p.

Sunanda M., Rao C.S.J., Neelima P., Rao G.K., Simhachalam G. (2016). Effects of chlorpyrifos (an organophosphate pesticide) in fish. International Journal of Pharmaceutical Sciences Review and Research, 39(1): 299-305.

Tanner C.M., Kamel F., Ross G.W., Hoppin J.A., Goldman S.M., Korell M., Marras C., Bhudhikanok G.S., Kasten M., Chade A.R., Comyns K., Richards M.B., Meng C., Priestley B., Fernandez H.H., Cambi F., Umbach D.M., Blair A., Sandler D.P., Langston J.W. (2011). Rotenone paraquat, and Parkinson's disease. Environmental Health Perspectives, 119: 866-872.

Thenmozhi C., Vignesh V., Thirumurugan R., Arun S. (2011). Impacts of malathion on mortality and biochemical changes of freshwater fish, *Labeo rohita*. Iranian Journal of Environmental Health Science and Engineering, 8: 387-394.

Tiwari S., Singh A. (2004). Toxic and sublethal effects of oleandrin on biochemical parameters of freshwater air-breathing murrel, *Channa punctatus* (Bloch). Indian Journal of Experimental Biology, 42: 413-418.

Tiwari S., Singh A. (2009). Changes in some biochemical parameters in the liver and muscle of *Colisa fasciatus* due to toxicity of ethanolic extract of *Narium indicum* (Lal Kaner) latex. Journal of Natural Products, 8: 48-54.

Todd N.E., Leeuwen, M.V. (2002). Effects of seven (Carbaryl insecticide) on early life stages of Zebra fish (*danio rerio*). Ecotoxicology and Environmental Safety, 53: 267-272.

Tulgar A. (2018). Pesticide Pollution and their adverse effects on aquatic ecosystems. International Journal of Science and Research (IJSR) 8: DOI: 10.21275/ART20194502

Ujváry I. (2010). Pest control agents from natural products. In: R. Krieger (Ed.). Hayes' handbook of pesticide toxicology. 3rd ed., Academic Press. pp: 119-229.

Ullah R., Zuberi A., Ullah S., Ullah I., Dawar F.U. (2014). Cypermethrin induced behavioural and biochemical changes in mahseer, *Tor putitora*. The Journal of Toxicological Sciences, 39: 829-836.

Van der Oost R., Beyer J., Vermeulen N.P. (2003). Fish bioaccumulation and biomarkers in environmental risk assessment: a review. Environmental Toxicology and Pharmacology, 13(2): 57-149.

Velmurugan B., Selvanayagam M., Cengiz E., Unlu E. (2009). Histopathological changes in the gill and liver tissues if freshwater fish (*Cirrhinus mrigala*) exposed to Dichlorvos. An International Journal of Brazilian Archives of Biology and Technology, 52(5): 1291-1296.

Viant M.R., Christopher A.P., Ronald S.T. (2006). Metabolic effects of dinoseb, diazinon and esfenvalerate in eyed eggs andalevins of Chinook salmon (*Oncorhynchus tshawytscha*) determined by1H NMR metabolomics. Aquatic Toxicology, 77: 359-371.

Warren G.F. (1998). Spectacular Increases in Crop Yields in the United States in the Twentieth Century. Weed Tech, 12: 752.

Wolff M.S., Engel S., Berkowitz G., Teitelbaum S., Siskind J., Barr D.B., Wetmur J. (2007). Prenatal Pesticide and PCB Exposures and Birth Outcomes. Pediatric Research, 61(2): 243-250.

Yadav Devi I., Ningombam. (2017). Pesticides Classification and its impact on human and environment. Environmental Science and Engineering, 6: 140-158.

Zaganas I., Kapetanaki S., Mastorodemos V., Kanavouras K., Colosio C., Wilks M.F., Tsatsakis A.M. (2013). Linking pesticide exposure and dementia: what is the evidence? Toxicology, 307: 3-11.

Zelikoff H.T., Raymond A., Carlson E., Anderson M. (2000). Biomarkers of immunotoxicity in fish: from the lab to the Ocean. Toxicology Letters, 325-331.