FUDMA Journal of Sciences (FJS)
ISSN online: 2616-1370
ISSN print: 2645 - 2944
Vol. 5 No. 1, March, 2021, pp 319 – 332
DOI: https://doi.org/10.33003/fjs-2021-0501-571

IMPLICATION OF PESTICIDES USAGE ON FRESHWATER FISH: A REVIEW

*[1]Nafi'u, S. A and [2]Ibrahim, S.

[1]Department of Science Laboratory Technology, Kano State Polytechnic, Kano- Nigeria
[2]Department of Biological Sciences, Bayero University, Kano

*Corresponding author's email: nafiune.sn@gmail.com, 07030918094

ABSTRACT

Pesticides play a significant role in improving food production through control against harmful pests with low labour and efforts while on the other hand are regarded as aquatic pollutants. These toxicants persist in aquatic environment and cause harmful effects to non- target organisms including fish. The development of pesticide tolerant species led to the need and use of varieties of pesticides with the risk of exposure to many compartments including water. Many pesticides have been proscribed for agricultural purposes by the regulatory agencies such as WHO (2020). However, It is unfortunate that many of these are sold in Nigeria or donated by donor agencies. The donated pesticides often become "obsolete" while in stock due to poor logistics and delays in receiving them at the point of need. The review on the classification, bioavailability, biotransformation, the direct and indirect effects of pesticides on freshwater fish was carried out. Biomarkers of pesticides toxicity that induce alterations in fish physiology were discussed; these include: behavioral changes such as erratic swimming, hyperactivity among other alterations. Other alterations include feeding behaviour, fluctuation in antioxidant enzyme activities, histology, haematology, growth performance and DNA damage.

Keywords: Bioavailability, Biotransformation, Pesticides Harmful Effect, Freshwater fish, Physiology,

INTRODUCTION

Pesticides are substances produced to control, mitigate, regulate the growth of harmful organisms (IPCS, 2010). They are employed globally in agricultural processes for reducing vector-borne ailments and preventing crops against pests with low labour and efforts (WHO, 2020). They are biocides, designed to regulate and control insect pests, unwanted grasses, fungi and other organisms which cause threat to crop plants (Das, 2013). PANA (2016) ascertained that majority of pests are insects, unwanted weeds, plant pathogens molluscs, birds, mammals, nematodes, and bacteria. However, variety of pests compete with higher organims for food, transmit diseases to animals and cause havoc to agricultural produce (Mazlan *et al*., 2017).

The principal classes of pesticides are designed on chemical contents; such as organochlorines, organophosphates, carbamates and pyrethroids. However, based on the targeted organism, several groups such as insecticides (insects), herbicides (weeds), avicides (birds), molluscicides (snails), nematicides (nematodes), algicides (algae) and rodenticides (rodents) have been reported (Annett *et al.*, 2014). Besides, selective pesticides kill the desired organism, while others remains unharmed (Veeraiah *et al*., 2015). Afful *et al*., (2010) ascribed the lipophilic, hydrophobic and ubiquitous nature of pesticides. Further, detected the chemicals far from their sources of application due to their persistency in nature and transport through atmospheric exchange, water, debris and other anthropogenic processes (Afful *et al*., 2010). Mazlan et al. (2017) reported that many groups of pesticides commonly used across African continent remain stable for many years after their application. Recently, contamination of the aquatic ecosystems by pesticides has received urgent attention (Adeboyejo *et al.*, 2011). Moreover, studies showed acute and sub-acute exposure to pesticides produced adverse effects in the exposed organisms and non-target organisms (Ezemonye *et al*., 2009; Reuters, 2011; Bartosz *et al*., 2018 and Ullah *et al*., 2019).

WHO (2020) classify pesticides by hazard into; Class Ia (extremely hazardous), Class Ib (highly hazardous), Class II (moderately hazardous), Class III (slightly hazardous) and Class U (unlikely to be hazardous under short-term use). Due to their impact, this necessitates investigation of their effects in different ecosystem with the view to identify their level. For instance, in some class Ia pesticides such as Parathion, Bromethalin and Disulfoton, 5 ml via the oral route is sufficient to kill an adult human being (WHO, 2020). Nine groups of persistent pesticides were officially proscribed for use in agriculture by WHO (2020). These include: heptachlor, toxaphene hexachlorobenzene, aldrin, chlordane, DDT, dieldrin, endrin and mirex. However, It is unfortunate that many of these are sold in Nigeria or donated by donor agencies. The donated pesticides often become "obsolete" while in stock due to poor logistics and delays in receiving them at the point of need (Joshua, 2016; FAO/WHO, 2018). Previous findings depicted that many farmers in African countries apply tremendous quantity of class Ia, Ib and class II pesticides mainly due to affordability and being cheaper than the less hazardous ones (Shaibu, 2008; Banjo *et al*., 2010; Yusuf, 2010; Adegbola *et al*., 2011; Ali and Muhammad 2016; Joshua, 2016 and Erhunmwunse *et al*., 2018). In given of the foregoing this research aimed to review the implication of pesticide usage on fresh water-fish species.

Bioavailability of Pesticides in the Aquatic Environment

Pesticides have direct contact with surface freshwater through accidental spills, aerial drift or runoff polluting aquatic environment which in turn cause havoc to aquatic habitats among others (Adeboyejo *et al.,* 2011). Many pesticides have been identified in various aquatic compartments such as within water column, biota and sediments (Banjo *et al*., 2010; Yusuf, 2010; Adegbola *et al*., 2011; Akan *et al*., 2013 and Ezenwosu *et al*., 2020). They can be determined by studying three major routes such as the organic substrates (epilithic, and epiphytic algal parts, hydrophytes, branches and leaf litter), water column and inorganic substrate (sediments and other debris) (Murthy *et al*., 2013).

Factors Related to Transport and Fate of Pesticides in the Aquatic Environment

Factors that facilitate pesticides toxicity in the aquatic environment include physical and chemical behaviors, microbial properties, nature of rainfall and frequency of application (Erhunmwunse *et al.,* 2012). Pesticides transfer from one vicinity to another via processes such as transfer (mobility) and biotransformation (degradation) (Annett *et al*., 2014). Transfer often occur through surface runoff, vapourization to the atmosphere, adsorption and plant uptake or soil water fluxes (Adegbola *et al*., 2011). Biotransformation happens mainly through microbial activity, photo-catalysis, oxidation, hydrolysis, volatilization and reduction; producing variety of metabolites that could be more or less toxic (Annett *et al*., 2014; Ullah *et al*., 2019). Their molecular size, stability, reactivity and solubility are other features of pesticides that determine their specific effects in an organisms (Annet *et al*., 2014).

Solubility is a vital feature in evaluating how, where and when a toxic pesticide moves through the aquatic domain or its mode of action (Sánchez-Bayo, 2011). Based on their solublity, pesticides can be divided into two groups. Some groups dissolve easliy in water and some in oil. Water–soluble pesticides such as glyphosate move rapidly through the environment because water is ubiquitous. They tend to have access to many cells organells since aqueous solutions bathe all cells (Lipok *et al.*, 2010).

Factors Related to Routes and Circumstances of Exposure of Pesticides in the Aquatic Environment

The quantity (dose), exposure duration, route of entry and sensitivity of an organism are important roles in pesticides toxicity investigation (Ullah *et al*., 2019). Pesticides applied during agricultural activities get into the environment via many routes. According to Sadowski et al. (2014), pesticides compounds leached with runoff together with soil particles or accidental spills into water body and/or direct application during fishing (Sánchez-Bayo, 2012). The mode of action of pecticides are responsible for their toxicity to non-target organisms. However, variation in susceptibility among array of animal taxa indicate that many biochemical properties peculiar to certain species are responsible to specific sensitivity level (Sánchez-Bayo, 2012).

Disruption of Ecological Balance by Pesticides to Freshwater Fish

Pesticides used currently in various aquatic ecosystems may endanger populations of different non-target species by reducing their habitat such as wetlands and irrigation areas (Akan *et al*., 2013). Pesticides have been reported to disrupt the food chain in the aquatic ecosytem by indirectly interrupting the fish food supply and habitat alteration (Olutona *et al*., 2016). In addition to habitat alteration, fish species can be subjected to predators by decreasing habitat suitability and behaviour changes. Pesticides can run off to water bodies affecting their quality and altering the biology of many non-target species (Ullah *et al.,* 2019). Disruption of the ecological balance of freshwater fish through biological controls, invariably produce pests that were previously of minor importance, leading to a new problem of resistance and unsustainable dependence on more pesticides (USEPA, 2017).

Direct Effects of Pesticides on Freshwater Fish

Pesticides have been reported to induce different kinds of toxicity to aquatic biota including fish. These changes include behavioural changes (Rani and Kumaraguru, 2014; Rakesh and Kumar, 2019), haematological alterations (Modesto *et al*., 2010; Ullah *et al*., 2014 and George *et al.,* 2017), histopathological changes (Dane and Sisman, 2017), enzymes alteration (Annett *et al*., 2014) genotoxicity (Ansari, 2011; Nwani *et al*., 2013 and Ullah *et al*., 2017), biochemical modifications (Banee, 2011 and Akan *et al.,* 2013) and changes in antioxidant enzymes activity (Nwani *et al*., 2010; Ezike *et al*., 2019)

Behavioural Responses Induced by Pesticide in Fish

Behavioural changes resulting from exposure to pesticides are one of the indicators used to evaluate their effect on aquatic fauna such as fishes (Dube and Hosetti, 2010). Behaviour is the cumulative manifestation of genetics, physiological and biochemical processes (Dube and Hosetti, 2010). It allows an organism to adjust itself to varying external and internal stimuli in many challenging environment. Observation on the swimming-oriented alterations, opercular movement, discolouration, loss of reflex, erratic swimming and schooling are among the abnormal behavioural changes recorded in many fish species (Rakesh and Kumar, 2019). The effect of pesticides on fish population and other non-target organisms often depends on concentrations and exposure period which ultimately manifest in their behaviour (Karates, 2016; Mishra and Verma, 2016). Ogamba et al. (2014) reported behavioural changes such as excessive mucus production, jerky movements and restlessness in *Clarias gariepinus* challenged with sub-chronic concentrations of 0.3, 0.4, 0.5 and 0.6mg/l of dichlorvos for 96h. Discolouration, surfacing activity, intense hyperactivity and convulsions were recorded in *Clarias batrachus* exposed to lambda cyhalothrin (Ogeleka *et al*., 2010). Omoniyi et al. (2013) examined lateral and upward movement, calmness, respiratory distress, spiral swimming and spontaneous air gulping in *Clarias gariepinus* (juveniles) exposed to dichlorvos 400, 450, 500 and 600 μg/L.

Abnormal behavioural changes in fish due to pesticides exposure have been reported (Alaa, 2014; Ullah *et al*., 2014; Annett *et al*., 2014 and Ahmad *et al*., 2018). Pesticides caused abnormal changes in fish by subjecting them to a sluggish pattern, alter swimming ability, reduction in feeding ability and loss of reflex (Ahmad *et al*., 2018). Ilavazhahan et al. (2010) reported that *Catla catla* on exposure to Methyl parathion resulted in elevated mucus secretion, rapid jerk movement, increased movements of opercula and equilibrium loss. Ramesh and Munniswamy (2009) reported that *Cyprinus carpio* (Linnaeus) on exposure to chlorpyrifos caused hyperexcitability, erratic and irregular swimming and equilibrium loss. Pesticides also alter the migratory behaviour of fish which led to disruption of their life cycle (Nagaraju *et al*., 2011). Ullah et al. (2014) reported that cypermethrin resulted in jumping, increased surface activity, balance loss, increased air gulping, equilibrium loss, abrupt swimming, sluggishness, motionlessness and internal haemorrhage in *Tor putitora*. With regards to environmental stress as a result of pesticides exposure, fish become stressed and immunocompromised, which makes them prone to diseases and among other secondary infections (Rakesh and Kumar, 2019).

Pesticides Induced Haematological Alterations in Fish

Prevoius researches carried out revealed the effect of many pesticides on haematological indices on aquatic organisms including fish (Ahrar *et al*., 2012). Haematological parameters such as WBC count, RBC count, heamoglobin concentrations and PCV exhibit secondary responses of fish to the toxicants (Hedayati and Hassan, 2015). Akinrotimi and Amachree (2016) and Ahmad et al. (2018) opined that when water quality is affected by toxicants, any physiological alterations will be reflected in the haematology of the aquatic biota. For instance, after exposure to sublethal concentration of chlorpyrifos decrease in RBC count, WBC count, hb and PCV mean was reported in *Channa punctatus* (Bloch) (Deka and Mahanta, 2012). The result obtained by George et al. (2017) during exposure of *C. gariepinus* to varying concentrations of metalochlor and atrazine revealed an increase in WBC, neutrophils, monocytes, Mean Cell Heamoglobin, Mean Cell Heamoglobin Concentrations in both male and female *C. gariepinus*. Akinrotimi et al. (2012) reported a rise in WBC, neutrophils and monocytes in African catfish (*Clarias gariepinus*) on exposure to cypermethrin.

The rise in WBC, neutrophils and monocytes indicate an immune response to the toxicants. Akinrotimi et al. (2012) also opined a dose-dependent decline in RBC count and considerable elevation in MCV, MCH, and MCHC in *C. gariepinus* treated with atrazine/metolachlor. *Tilapia* sp. exposed to pesticides revealed characteristic alteration in the blood indices (Kumari *et al*., 2018). Chandra et al. (2017) reported the effect of dichlorvos on freshwater fish (*Orieochromis niloticus*) for 96 hours of exposure. In their findings alterations in the mean value of packed cell volume (PCV), haemoglobin (Hb), Red Blood cell (RBC), neutrophil, monocyte and lymphocytes count were recorded. Toxicological effects of lethal and sub-lethal concentrations of Deltamethrin on haematological parameters in *Cirrhinus mrigala* (Hamilton) was investigated by David et al. (2015) and the results revealed that the RBC, Hb and Haematocrit values decreased significantly while WBC, MCV and MCH were increased in a dose-dependent manner. Alterations in WBCs and RBCs, haemoglobin contents and packed cell volume of many fish species were reported such as Saeedi et al. (2012) who studied the effect of diazinon on haematological parameters of fry rainbow trout (*Oncorhynchus mykiss*), Akinrotimi et al. (2013) on haematological alterations of *Tilapia guineensis* challenged to varying concentrations of industrial effluents, Abdul-majid et al. (2014) on dichlorvos to freshwater fish (*Cyprinus carpio*), (Ullah *et al*., 2014) on cypermethrin to the haematological and physiological alterations in liver, brain and gills of Mahseer (*Tor putitora*), Gopala et al. (2017) on *Cyprinus carpio* challenged to pyrethroid (Permethrin) and Chandra et al. (2017) on the toxicological effects of dichlorvos to the freshwater fish.

Ullah et al. (2015) reported an increase in white blood cells (WBCs) count and a decline in RBCs count on exposure of *Tor putitora* to cypermethrin. Previous related findings reported various alterations in haematological indices in many fish species after exposure to different synthetic pyrethroids. For instance, Vani et al. (2012) investigated the effect of cypermethrin on *Catla catla*, Karatas (2016) on *Salmo trutta fario* exposed to deltamethrin, Ozok et al. (2018) studied the effect of cypermethrin on *Alburnus tarichi* and Vieira and Martinez (2018) on the response of *Prochilodus lineatus* to lambda-cyhalothrin. Changes in hematological indices due to pesticides exposure have been attributed to the inhibition of haemosynthesis, RBCs disruption, RBCs decrease due to hypoxia, hematopoietic system's failure and stimulated defense mechanism which alters WBCs count (Ullah *et al*., 2019)

Pesticides Induced Histopathological Alterations in Fish Tissues

Histopathological investigations have been regarded as a bio-indicator of toxicity stress in many vertebrates (*in vivo* and *in vitro*) including fish (Revathy and Chitra, 2015). Histopathological alteration is the result of cumulative physiological changes which affect target organs and mechanism of action (Ramesh *et al*., 2014). On exposure to Malathion (pesticides), alterations were observed in the liver, ovary and kidney tissues of *Heteropneustes fossilis* (Deka and Mahanta, 2012). When the intestine of *H. fossilis* were challenged to a sublethal dose (1.42ppm) of chlorpyrifos, degeneration, atrophy on the villi structure and necrosis of mucosal epithelium of the intestine and depletion of lymphoid follicles were observed (Nazia *et al*., 2016). At 0.28 ppm there was complete disappearance of villi structures, focal areas of necrosis and mucosal epithelium. Karthigayani et al. (2014) reported disintegration of the intestinal tissue in the study of cypermethrin administered to *Oreochromis mossambicus*.

Bais and Lokhande (2012) also recorded degenerative change of mucosal epithelium necrosis in the intestine of *O. striatus* challenged to cadmium chloride. Degeneration of glomerulus, lymphocytes infiltration, cytoplasmic vacuolation, necrosis and blood congestion in kidney tissues of *Cyprinus carpio* after exposure to Sodium cyanide (David and Kartheek, 2014). Other investigations on the histological effects of pesticides in varying organs of fish include that of Rani and Venkataramana, (2012) who determined the effects of Malathion to *Glossogobius giuris*. Banaee et al. (2013) on Diazinon to Rainbow trout (*Oncorhynchus mykiss*), Karthigayani et al. (2014) on the effect of cypermethrin on *O. mossambicus*, Ullah et al. (2014) on Cypermethrin to *Tor putitora*, Pandey and Dubey (2015) on pentachlorophenol (PCP) to catfish (*Heteropneustes fossilis*), Raibeemol and Chitra (2016) on chlorpyrifos to freshwater fish (*Etroplus maculatus*) and Nazia et al. (2016) on Chlorpyrifos to catfish.

Pesticides Induce Oxidative Stress in Fish Tissues

Oxidative stress is the imbalance between the productions of free radicals (pro-oxidant) which leads to peroxidation of the cell's lipid bi-layer and the antioxidant defense of the body (Ansari and Ansari, 2014). It is attributed with the increased rate of cellular disruption caused by oxygen free radicals and other reactive oxygen species (ROS) such as hydrogen peroxide (H_2O_2), superoxide anion (O_2-) and hydroxyl radicals (OH^-), nitric oxide (NO) and lipid peroxyl (LOO−) (Wu *et al*., 2011; Agarwal, 2014 and Ahmad *et al*., 2017). Free radicals are molecules containing one unpaired valence electrons at their outer shell making them highly reactive (Ahmad *et al*., 2017). High concentration of free radicals and ROS by overcoming the antioxidant defense system causes a detrimental effect on normal cellular functions, inactivate the enzymes which eventually results in oxidative stress, peroxidation of cell constituents and DNA damage (Ameur *et al*., 2012; Ahmad *et al*., 2017). The toxicity of xenobiotics is directly related to the free radicals production in the organisms (Ansari and Ansari, 2014).

Superoxide dismutase is among the vital enzymes that produce the first step of defense against free radicals (pro-oxidants) (Oluwatosin *et al*., 2016). It breaks down the transformation of superoxide radicals to H_2O_2 and O_2 while catalase stimulates the removal of H_2O_2 into oxygen and water (Oluwatosin *et al*., 2016). However, Glutathione protects the cell against reactive oxygen (ROS) and Reactive nitrogen species (RNS) whose role in maintaining normal cellular activities such as fighting against toxins and regulating various intercellular pathways (Ahmad *et al*., 2017). However, a high concentration of ROS in a cell more than antioxidant defense enzymes, results in oxidative stress which causes cellular inactivity through lipid peroxidation and denatures proteins (Ahmad *et al*., 2017). Toxins (both endogenous and exogenous) of electrophilic nature are detoxified by Glutathione. It maintains and stores the essential thiol profile of proteins and other amino acids such as cysteine (Oluwatosin *et al*., 2016). Previous researches regarded pesticides as inducers of anomalous biochemical pathways where they change the redox cycles which results in oxidative stress in many organisms including fish (Ameur *et al*., 2012; Nwani *et al*., 2015 and Oluwatosin and Abiola, 2016). They also disrupt the intracellular electron transfer processes with reactive oxygen species (ROS) resulting in celllular damage (Ameur *et al*., 2012).

These enzymes protects cells against reactive oxygen species (ROS) by neutralizing their effect and prevent it against oxidative damage (Doherty *et al*., 2010). Wu et al. (2013) reported exposure of *Clarias gariepinus* to Paraquat caused oxidative stress in the fish tissue due to alterations in the electrolyte levels. Nwani et al. (2015) reported impaired physiological activities and biochemical pathways in plasma protein, plasma glucose and triglycerides of *C. gariepinus* exposed to Paraquat. Mastan and Shaffi (2010) opined that exposure to sub-lethal concentration of organophosphates led to disturbance in various enzyme activities such as glutaminases and L-Keto acid-activated glutaminase in brain tissue, which are related to brain regions metabolism. Malathion pesticides have been reported to cause alterations in Glutathione-S-transferase and Catalase activities in gills, liver and muscles of *Labeo rohita* (Thenmozhi *et al*., 2011).

Tor putitora when exposed to cypermethrin resulted in the alterations of Glutathion Reductase, Peroxidase, Lipid peroxidase and Catalase in brain, liver and muscle tissues (Ullah *et al*., 2014). Faheem and Lone (2017) reported an increase in lipid peroxidation and glutathione-S-transferase (GST) activity in the liver and kidneys of *C. idella* after 14 days of exposure to bisphenol. An increased GST activity was attributed to the detoxification of BPA (Wu *et al*., 2011). Wu et al. (2011) reported an increase in GST activity in zebrafish embryos challenged to 0.1μg/l BPA. Elevated activity in GST was also observed in hepatocytes of pearl mullet and Japanese medaka (liver and gills) exposed to BPA (Li et al. (2016). In another development, Prieto et al. (2006) observed the response of the antioxidant enzymes glutathione reductase (GSH), superoxide dismutase (SOD), catalase (CAT) and lipid peroxidation (LPO) as a biomarkers of oxygen-mediated toxicity in liver, kidney and gill of *Oreochromis* sp. Glutathione-S-transferase breaks down the correlation reaction between glutathione reductase and metabolites of xenobiotic accelerating their excretion (Doherty *et al*., 2010). When antioxidant activity cannot compensate for the generation of Reactive Oxygen Species, oxidative damage occurs (Glusczak *et al*., 2011).

The activity of SOD, Catalase, GSH and GST decreased in the liver, kidney and gills of *Clarias gariepinus* in Asejire River while malondialdehyde (MDA) increased significantly (Oluwatosin and Abiola, 2016). They concluded that decrease in the activity of these enzymes was attributed to the high concentration of toxicants in the River. In an aquatic environment, the significant level of oxidative damage happens in biota challenged to contaminants which facilitates the generation of ROS that impairs antioxidant enzymes leading to oxidative stress (Oluwatosin and Abiola, 2016).

Activities of antioxidant enzymes like CAT, SOD, GSH and GST have been used as biomarkers to assess the influence of aquatic pollution on the biochemical pathway and enzymatic function in fish (Correia *et al*., 2010). Glutathione peroxidase (GPx) activity was reduced in *Prochilodus lineatus* exposed to 10 mg/l of glyphosate. After 24hours activity SOD decreased while hepatic glutathione content increased (Modesto and Martinez, 2010). Wu et al. (2011) recorded an increase in LPO activity in zebrafish embryos challenged a range of 0.1-1000µg/L of bisphenol.

Molecular Alterations in Fish Tissue Induced by Pesticides Exposure

Genotoxic potential assessment in an aquatic domain is one of the major challenges to the environmental pollution control programmes (Alaa, 2014). Genotoxicological investigation involves the use of toxicants that damage DNA of the cell and subsequently impact the wellbeing of aquatic biota (Ullah and Zorriehzahra, 2015). The single-cell gel electrophoresis is a versatile techniques applied for assesing the effects of environmental contaminants for biomonitoring purposes (Boettcher *et al*., 2010; Guilherme *et al*., 2010; Akcha *et al*., 2012; Obiakor *et al*., 2012; Ghisi and Cestari, 2013; Alaa, 2014; Ullah *et al*., 2017; Tasneem and Yasmeen, 2018; Ullah *et al*., 2019). It is more sensitive compared to other techniques applied in genotoxicological studies, like chromosomal aberration, sister chromatid exchanges test, and micronucleus test (Ullah *et al*., 2016). Comet assay has been proved to be reliable and has the ability of examining minute DNA damage. It is used for single and double-strand breakage in DNA, cell death and incomplete excision repair sites induced by chemical or physical agents eukaryotic cells (Poletta *et al*., 2013; Ullah *et al*., 2016).

The biotransformation of toxicants stimulates the generation of Reactive Oxygen Species (ROS) which can be harmful to fish and another aquatic biota. Fish possess an antioxidant defense system against ROS, but an increase in the production of ROS overcomes the defence systems of fish which results in cellular lesions and DNA alteration (Ansari *et al*., 2011). ROS directly catalyze DNA via OH- by directly reacting with DNA molecules and H_2O_2 causes base oxidation of intracellular DNA (Akcha *et al*., 2013). Osman et al. (2012) reported a higher degree of DNA damage in the blood of *Oreochromis niloticus* and *Clarias gariepinus* in downstream of heavily polluted areas of the River Nile. The DNA damage was significantly elevated in peripheral blood erythrocytes of the fish examined (Osman *et al*., 2012; Meza-Joya *et al*., 2013). The *Corydoras paleatus* revealed an increase in micronuclei frequency as well as DNA damage in peripheral erythrocytes after exposure to glyphosate (Ghisi and Cestari, 2013).

Double-stranded DNA damages were examined in *Anguilla anguilla* challenged to 58 and 116 µg/L of glyphosate-based herbicide after 24-hour exposure (Guilherme *et al*., 2010). In another finding, Guilherme et al. (2012) reported that the type of DNA damage differs with exposure period and concentration with ROS-dependent DNA damage. Glyphosate exposure induces DNA quality in the Neotropical fish, after only 6 hours of exposure at the highest concentration of 10 mg/L. Other investigations on induced genotoxicity of pesticides include Ansari et al. (2011) on cypermethrin in *Channa punctatus*, Poletta et al. (2013) on DNA damage in the gills of *Prochilodus lineatus*, Ullah (2015) on the erythrocyte of *Labeo rohita* and Vieira and Martinez (2018) on DNA damage in the blood erythrocyte of *Prochilodus lineatus* induced by λ-cyhalothrin. Ateeq et al. (2005) evaluated the genotoxic potential of two commonly used herbicides; 2, 4-dichlorophenoxyacetic acid (2, 4-D) and 2-chloro-2, 6-diethyl-N-(butoxymethyl) in erythrocytes of freshwater catfish, *Clarias batrachus*. The marked increase in comet tail length indicating DNA damage was observed at all concentrations of both herbicides compared to the control. Cypemethrin induced alterations in DNA and RNA in gonadal tissue of *Colisa fasciatus* (Singh *et al*., 2016).

CONCLUSION AND RECOMMENDATIONS

It is concluded that pesticides cause tremendous economic loss by fish death and rendering them unfit for human consumption, indicating a threat to fish biodiversity. Various ecotoxicological investigations revealed the detrimental effects of pesticides on fish such as behavioural change, haematological, biochemical, histological alterations, anti-oxidant enzyme activities and genotoxicity. It is therefore recommended that more investigation concerning new introduced harmless pesticides should be carried out in both *in-vivo* and *in-vitro*. Environmental friendly pesticides should also be employed in agricultural production.

REFERENCES

Abdul-Majid, T., Bhat, F. A and UlfatJan, M. S. G. (2014). Sublethal haematological effects of dichlorvos on the freshwater fish, *Cyprinus carpio* var. Communis. *International Journal of Recent Scientific Research Research*, 5 (7): 1334-1337.

Adeboyejo, O. A., Clarke, E.O. and Olarinmoye, M.O. (2011). Organochlorine Pesticide Residues in water, sediments, Fin and Shell-fish samples from Lagos Lagoon Complex, Nigeria. *Researcher*, 3(3):38-45.

Adegbola, J.A., Bamishaiye, E.I., and Olayemi, F.F. (2011). Merchants' Attitude Towards the use, and Ban of the Pesticide Gammalin in Dawanau International Grain Market, Kano, Nigeria. *Advances in Bioresearch,* 2(2): 47 -51.

Adeyemi, D., Ukpo, G., Anyakora, C. and Unyimandu, J. (2008). Organochlorine pesticides residues in fish samples from Lagos Lagoon, Nigeria. *American Journal of Environmental Science,* 4(1): 649-653.

Afful, S; Anim, A. and Serfor-Armah, Y. (2010). Spectrum of organochlorine pesticide residues in fish samples from the Densu Basin. *Research Journal of Environmental and Earth Sciences,* 2(3):133-138.

Agarwal, A. (2014). Mechanisms of oligozoospermia: an oxidative stress perspective. *Systematic Biology and Reproductive Medicine,* 60(4):206–216.

Ahmad, G., Almasry, M., Amolak, S., Dhillon, M. M., Abuayyash, N. K., Zeynep, C. (2017). Overview and Sources of Reactive Oxygen Species (ROS) in the Reproductive System. *Springer International Publishing*, pp1-5.

Ahmad, P. G., Dar, J. Y., Raja, A. H., Bhat, I. A., Bhat, K. K., Pandey, P. K and Debajit, S. (2018). Investigation of acute toxicity and behavioral response of Indian major carp, *Cirrhinus mrigala* (Hamilton, 1822) in response to Cypermethrin (25% EC). *Journal of Entomology and Zoology Studies*, 6(5): 194-199.

Ahrar, K. L. A and Muhammad, Z. K. (2012). Hemoto - Biochemical changes induced by pyrethroid insecticides in Avian, fish and mammalian species. *International Journal of agriculture* and *Biology*, 14(5): 834-842.

Akan, J. C., Mohammed, Z., Jafiya, L., Ogugbuaja, V. O. (2013) Organochlorine Pesticide Residues in Fish Samples from Alau Dam, Borno State, North Eastern Nigeria. *J Environ Anal Toxicol* 3(3): 171-178.

Akcha, F., Spagnol, C and Rouxel, J. (2012). Genotoxicity of diuron and glyphosate in oyster spermatozoa and embryos. *Aquatic Toxicology*, 106(1): 104–113.

Akinrotimi, O.A., Amachree, D. (2016) Changes in haematological parameters of *Tilapia guineensis* exposed to different concentrations of detergent under laboratory conditions. *Journal of Aquatic Science*, 31(1): 95-103.

Akinrotimi, O.A., Gabriel, U.U. (2012) Haematological profile of Nile Tilapia (*Oreochromis niloticus*) from ARAC Reservoir Aluu, Port Harcourt, Nigeria. *Advances in Students Research,* 2 (1): 31-37.

Akinrotimi, O.A., Gabriel, U.U., and Ariweriokuma, S.V. (2012) Haematotoxicity of cypermethrin to African catfish *Clarias gariepinus* under Laboratory Conditions. *Journal Environmental Engineering Technol.,* 1: 20-25.

Akinrotimi, O.A., Orlu, E.E., Gabriel, U.U. (2013) Haematological Responses of Tilapia guineensis treated with industrial effluents. *Applied Ecology and Environmental Science,* 1(1):10-13.

Akinwande, A.A., Abdulkadiri, J.O. and Adesina, B.T. (2016). Oxidative Stress and Antioxidant Response in the Giant African Catfish (*Heterobranchus bidorsalis* Geoffroy SaintHilaire, 1809) under Chronic Paraquat Exposure. *Nigerian Journal of Fisheries and Aquaculture,* 4(2): 30 – 37.

Alaa, G. M. O. (2014). Genotoxicity Tests and Their Contributions in Aquatic Environmental Research. *Journal of Environmental Protection*, 5(1):1391-1399.

Ali, D and Kumar, S. (2012). Study on the effect of chlorpyrifos on acetylcholinesterase and hematological response in *Channa punctatus*. *Bloch*, 3(5): 12-18.

Ali, J and Rani, V.J. (2009). Effect of Phosalone on Haematological Indices in the Tilapia, (*Oreochromis mossambicus)*. *Turkish Journal of Vetenary Animal science*. 33(1): 407-411.

Ali, S and Muhammad, K. (2016) Acute Toxicity of Herbicide (Glyphosate) in *Clarias gariepinus* (Juveniles). *Toxicology Reports,* 3(1): 513–515.

Al-Sarar, A. S., Abobakr, Y., Bayoumi, A. E., Hussein, H. I and Ghothemi, A. (2012). Reproductive toxicity and histopathological changes induced by lambda cyhalothrin in male mice. *Environ Toxicology,* 29(1): 750-759.

Ameur, W. B., Lapuente, J., El Megdiche, Y., Barhoumia, B., Trabelsi, S., Camps, L., Serret, J., Ramos-López, D., GonzalezLinares, J., Driss, M.R., Borràs, M. (2012). Oxidative stress, genotoxicity and histopathology biomarker responses in mullet (*Mugil cephalus*) and sea bass (*Dicentrarchus labrax*) liver from Bizerte Lagoon (Tunisia). *Mar Poll Bull*., 64(2): 241-251.

Ani, L.C., Nwamba, H.O., Ejilibe, C.O. and Nwani, C. D. (2017). Acute toxicity of glyphosate-based herbicide glycot on Juvenile African catfish *Clarias gariepinus* (Burchell 1822). *Journal of Fisheries and Livestock Production*, 5(1): 252-259.

Annett, R; Hamid, R. H and Alice, H. (2014). Impact of glyphosate and glyphosate-based herbicides on the freshwater environment. *Journal of Applied Toxicology*, 34(1):458-567.

Ansari, R. A., Rahman, S., Kaur, M., Anjum, S., Raisuddin, S. (2011). *In vivo* cytogenetic and oxidative stress-inducing effects of cypermethrin in freshwater fish, *Channa punctata* Bloch. *Ecotoxicol Environ Saf*, 74(1):150–156.

Ansari, S and Ansari, B. A. (2014). Temporal variations of CAT, GSH, and LPO in gills and livers of zebrafish, *Danio rerio*, exposed to dimethoate. *Arch Pol Fish*., 22:101-109.

Ateeq, B., Farah, M.A. and Ahmad, W. (2005) Detection of DNA Damage by Alkaline Single Cell Gel Electrophoresis in 2,4-Dichlorophenoxyacetic-Acid- and Butachlor-Exposed Erythrocytes of Clarias batrachus. *Ecotoxicology and Environmental Safety*, 62(1): 348-354.

Awoyemi, O. M., Bawa-Allah, K. A and Otitoloju, A. A. (2014). Accumulation and Anti-oxidant Enzymes as Biomarkers of Heavy Metal Exposure in *Clarias gariepinus* and *Oreochromis niloticus*. *Applied Ecology and Environmental Sciences*, 2(5): 114-122.

Bais U.E. and Lokhande M.N. (2012) Effect of cadmiumchloride on histopathological changes in the freshwater fish *Ophiocephalus striatus* (Channa). *International Journal Zoological Research*, 1(1): 23-32.

Bamidele, A; Germaine, A. O; Ebenezer, A; Oluwatosin, C. F and Abiodun, E. (2018). Effects of sub-Lethal Toxicity of Chlorpyrifos and DDforce pesticides on Haematological Parameters of *Clarias gariepinus. International Research Journal of Public and Environmental Health*, 5 (5): 62-71.

Banaee, M., Sureda, A., Mirvagefei, A.R. and Ahmadi, K. (2013). Histopathological Alterations Induced by Diazinon in Rainbow trout (*Oncorhynchus mykiss*). *International Journal of Enviromental Research*, 7(3): 735-744.

Banjo, A.D, Aina, S.A and Rije, O.I. (2010). Farmers Knowledge and Perception Towards Herbicides and Pesticide usage in Fadama area of Okun-owa, Ogun State of Nigeria. *African Journal of Basic and Applied Sciences*, 2(5-6): 188-944.

Banjo, A.D., Aina, S.A and Rije, O.I. (2010). Farmers knowledge and perception towards herbicides and pesticide usage in Fadama area of Okun-owa, Ogun State of Nigeria. *African Journal of basic and applied sciences* 2(**5-6**): 188-944.

Barkat, A.O. (2005). Assessment of persistent organochlorine pollutants in sediments. *Marine Pollution Bulletin*, 64(8): 1713–1720.

Bartosz, B; Mateusz, J; and Małgorzata, W. (2018) Physiological and Histological effects of herbicides in fish. *Annals of Warsaw University of Life Sciences, Animal Science*, 57 (3): 207–217.

Bhandare, R.Y., Pathan, T.S., Shinde, S.E., More, P.R and Sonawane, D.L. (2011). Toxicity and behavioural changes in fresh water fish *Puntius stigma* exposed to pesticide (Rogor). *Am-Euras. J. Toxicol. Sci*, 3(3): 149-152.

Boettcher, M., Grund, S., Keiter, S., Kosmehl, T., Reifferscheid, G., Seitz, N., Rocha, P.S., Hollert, H. and Braunbeck, T. (2010) Comparison of in Vitro and in Situ Genotoxicity in the Danube River by Means of the Comet Assay and the Micronucleus Test. *Mutation Research*, 700, 11-17.

Carson, R. (2009). Memorial Lecture. Pesticides *News*, 86:12-18.

Cavusoglu, K., Yalcin, E., Turkmen, Z., Yapar, K and Cicek, F. (2011). Investigation of Toxic Effects of the Glyphosate on *Allium cepa*. *Journal of Agricultural Sciences*, 17(1): 131-142.

Chandra, S. J., Neelima, P and GovindaRao, K. (2017). A review on the toxicity and other effects of Dichlorvos, an organophosphate pesticide to the freshwater fish. *Bioscience Discovery*, 8(3):402- 415.

Chitra, K. C and Sajitha, R. (2014). Effect of bisphenol-A on the antioxidant defense system and its impact on the activity of succinate dehydrogenase in the gill of freshwater fish, *Oreochromis mossambicus. Jounal of Cell Tissue Research*, 14(2):4219-4226.

Correia, T.G., Narcizo, A.M., Bianchini, A and Moreira, R.G. (2010). Aluminum as an Endocrine Disruptor in female Nile tilapia (*Oreochromis niloticus*). *Comparative Biochemistry and Physiology,* Part C, 151(1): 461-466.

Dahunsi, O.S., and Oranusi, U.S. (2013). Haematological Response of *Clarias gariepinus* to Rubber Processing Effluent. *Annual Review & Research in Biology*, 3(4):624-635.

Dane, H and Sisman T (2017). A Histopathological Study on the Freshwater fish Species Chub (*Squalius cephalus*) in the Karasu River, Turkey. *Turkish Journal of Zoology*, 41(1):1-11.

Dar, S. A., Yousuf, A. R., Balkhi, M. H., Ganai, F. A and Bhat, F. A. (2015) Assessment of Endosulfan Induced Genotoxicity and Mutagenicity Manifested by Oxidative Stress pathways in freshwater cyprinid fish crucian carp (*Carassius carassius L*.). *Chemosphere,* 120: 273-283.

Das, S. (2013). A review of dichlorvos toxicity in fish. *Current world environment*, 8 (1): 143-149.

David, A., Grace U., Chimezie, A and John, P. U. (2008). Organochlorine Pesticide Residues in Fish Samples from Lagos Lagoon, Nigeria. *American Journal of Environmental Sciences,* 4(6): 649-655.

David, M and Kartheek, R. M. (2014). Sodium cyanide induced Histopathological changes in kidney of fresh water fish *Cyprinus carpio* under sublethal exposure. *Int. J. Pharma. Chem. Biol*. *Sci*. 4(3): 634-639.

David, M., Sangeetha, J., Shrinivas, J., Harish, E. R., Naik, V.R. (2015). Effects of deltamethrin on haematological indices of indian major carp, *Cirrhinus mrigala* (Hamilton) *International Journal of Pure and Applied Zoology,* 23 (1): 37-43.

Deka, S and Mahanta, R (2015). Dichlorvos toxicity on fish – A review. *European Journal of Biological Research,* 5 (3):78-85.

Deka, S and Mahanta, R. (2012). A study on the effect of organophosphorus pesticide Malathion on Hepato-Renal and Reproductive organs of *Heteropneustes fossilis* (Bloch), *The Science Probe,* 1(1):1-13.

Devi, Y and Mishra, A. (2013). Study of behavioural and morphological anomalies of fry fish of freshwater teleost, *Channa punctatus* under chlorpyrifos intoxication. *Int. J. Pharma Bio Sci*., 4(1B): 865-874.

Devis, M. S and Gupta, A. (2014). Sublethal Toxicity of Commercial Formulations of Deltamethrin and Permethrin on Selected Biochemical Constituents and Enzyme Activities in Liver and Muscle Tissues of *Anabas testudineus*. *Pestic. Biochem. Physiol.,* 115: 48-52.

Dey, C and Saha, S. (2014). A comparative study on the acute toxicity bioassay of dimethoate and lambda-cyhalothrin and effects on thyroid hormones of freshwater teleost fish *Labeo rohita* (Hamilton). *Intetnational Journal of Environmental Research,* 8(1):1085–1092.

Doherty, V.F., Ogunkuade, O.O. and Kanife, U.C. (2010). Biomarkers of Oxidative Stress and Heavy Metal Levels as indicators of Environmental Pollution in Some Selected Fishes in Lagos, Nigeria. *American-Eurasian Journal of Agriculture & Environmental Science*. 7 (3): 359-365.

Doherty, V.F., Ladipo, M.K. & Oyebadejo, S.A. (2011). Acute Toxicity, Behavioural changes and Histopathological Effect of paraquat Dichloride on Tissues of Catfish (*Clarias gariepinus*). *International Journal of Biology*, 3(2): 67-74.

Dube, P. N., Alavandi, S., Hosetti, B. B. (2013). Effect of exposure to sublethal concentrations of sodium cyanide on the carbohydrate metabolism of the Indian Major Carp *Labeo rohita* (Hamilton, 1822). *Pesquisa Veterinária Brasileira*. 33(7): 914-919.

Dube, P.N., Hosetti, B.B. (2010). Behaviour surveillance and oxygen consumption in the freshwa ter fish *Labeo rohita* (Hamilton) exposed to sodium cyanide. *Biotechnology and Animal Husbandry*, 26(1-2): 91-103.

Dumont, S and Rivoal, J. (2019). Consequences of Oxidative Stress on Plant Glycolytic and Respiratory Metabolism. *Front. Plant Sci*., 10(1): 1-16.

Edge, B. E., Gahl, M. K., Thompson, D. G., Houlahan, J.E (2013). Laboratory and field exposure of two species of juvenile amphibians to a glyphosate-based herbicide and *Batrachochytrium dendrobatidies Science and Total Environment*, 444(1): 145–152.

Erhunmwunse, N. O; A. Dirisu, A and Olomukoro, J. O. (2012). Implications of Pesticide Usage In Nigeria *Tropical Freshwater Biology,* 21 (1):15- 25.

Erhunmwunse, N.O., Ogbeide, O.S., Tongo, I., Enuneku, A.A and Adebayo, P.O (2018) Acute Toxicity of Glyphosate-based Isopropylamine formulation to Juvenile African catfish (*Clarias gariepinus*). *Nigerian Journal of Basic and Applied Science,* 26(2): 97-101.

Etonihu, A. C.; Aminu, B. A.; Ambo, A. I.; Etonihu, K. I. (2011). Iodine content and pesticide residues of some Nigerian food grains. *Continental Journal of Agricultural Science,* 5(1): 26-32.

Ezemonye, L.; Ikpetsu, T. and Tongo, I. (2009). Distribution of propoxurin in water, sediment and fish from Warri River, Niger Delta, Nigeria. *Turkish Journal of Biochemistry,* 34(3): 121-127.

Ezemonye, L.I.N., Ikpesu, T O. and Ileshie, I. (2008). Distribution of Diazinon in Water, Sediment andFish from Warri River, Niger Deltal Nigeria. *Jordan Journal of Biological Sciences*, 1(2): 31 – 37.

Ezenwosu, S. U., Emmanuel, I. N., Gregory, E. Odo., Ogonna, C. A., Obiageli, C. E., Gladys, U. O and John, F. E. (2020). Lambda-Cyhalothrin induced hepato-nephro toxicity potentials and post treatment recovery in *Clarias garipinus*. *African Journal of Biochemistry Research,* 14(1):18-26.

Ezike, C. O; Felix, O. E; Nicholas, C. U and Godwin, E. O. (2019). Haematology, Oxidative Stress and Micronuclei Frequency of *Clarias gariepinus* Exposed to Glyphosate based Herbicide Glycot GBHG. *International Journal of Advanced Fisheries and Aquatic Science*, 4(1): 106-121.

Faheem, M and Lone, K. P. (2017). Oxidative stress and histopathologic biomarkers of exposure to bisphenol-A in the freshwater fish, (*Ctenopharyngodon idella*). *Brazilian Journal of Pharmeutical Sciences*, 53(3): 1-9.

FAO/WHO, (2018). Pesticide residues in food 201 8 Joint FAO/WHO Meeting on Pesticide Residues. Pp. 234-256.

Farah, M.A., Ateeq, B., Ali, M. N., Sabir, R and Ahmad, W. (2004). Studies on lethal concentrations and toxicity stress of some xenobiotics on aquatic organisms. *Chemosphere*, 55 (2): 257-265.

Fayinminmu, O. O; Tijjani, S. O and Fadina, O. O (2017). Toxicity Assessment of Sub Lethal Doses of Chlorpyrifos on the Kidney and Liver Organs of Male Wistar Rats. *International Journal of Biochemistry Research and Review*, 17(3):1-15.

Fetoui, H., Makni, M., Garoui, E. M and Zeghal, N. (2010). Toxic effects of lambda-cyhalothrin, a synthetic pyrethroid pesticide, on the rat Kidney: involvement of oxidative stress and protective role of ascorbic acid. *Exp Toxicol Pathol*, 62(1): 593-602.

Food and Agricultural Organization/ World Health Organization Food Standards CODEX alimentarius, (2013). Pesticide Residues in Food and Feed-Pesticide index. CODEX Pesticides Home. Available at http:// FAO%20WHO%20pesticide%20MRLs.html Accessed 19 August, 2019.

FAO/WHO, (2018). Pesticide residues in food 201 8 Joint FAO/WHO Meeting on Pesticide Residues. Pp. 234-256.

Gabriel, U.U., Uedeme-Naa, B., Akinrotimi, O.A. (2011) Pollutant induced altered behaviours in fish: A review of selected literature. *J Technol Education Nigeria*, 16(1): 9-23.

George, A. D., Akinrotimi, O. A and Nwokoma UK. (2017). Haematological Changes in African Catfish (*Clarias gariepinus*) Exposed to Mixture of Atrazine and Metolachlor in the Laboratory. *Journal of FisheriesSciences.com*, 11(3): 48-54.

Ghisi, N.C and Cestari, M. M. (2013). Genotoxic effects of the herbicide Roundup® in the fish *Corydoras paleatus* (Jenyns 1842) after short-term, environmentally low concentration exposure. *Environ. Monit. Assess*. 185(1): 3201–3207.

Gilden, R .C; Huffling, K and Sattler, B. (2010). Pesticides and Health Risks. *J. Obstet. Gynecol. Neonatal Nurs*., 39(1):103-109.

Gill, R.J and Raine, N.E. (2014). Chronic impairment of bumble bee natural foraging behaviour induced by sublethal pesticide exposure. *Functional Ecology* 28(6): 1459-1471.

Glusczak, L., dos Santos Miron D., Moraes B.S., Simoes R.R., Schetinger M.R.C., and Morsch V.M., Loro V.L. (2007): Acute effects of glyphosate herbicide on metabolic and enzymatic parameters of silver catfish (*Rhamdiaquelen*). *Comprehensive Biochemistry and Physiology*, 146(1): 519–524.

Glusczak, L., Loro, V.L., Pretto, A., Moraes, B.S., Raabe, A., Duarte, M.F, da Fonseca, M.B., de Menezes, C.C and Valladao, D.M.D. (2011). Acute exposure to glyphosate herbicide affects oxidative parameters in Piava (*Leporinus obtusidens*). *Arch. Environ. Contam. Toxicol*., 61(1): 624–630.

Gopala, R. N., Bala, K., Naik, R and Srinivasa R., G. (2017). Haematological changes in the fish *Cyprinus carpio* exposed to a synthetic pyrethroid [Class I], Permethrin and its 25% EC. *Current Trends in Technology and Science*, 6 (5): 759-763.

Gour, T.B and Sridevi, D. (2012). Chemistry. Toxicity and Mode of Action of Insecticides. *1st ed. Kalyani Publisher*.pp 134-136.

Graziana, I. N., Schiavulli, D. C., Francesco, B. P. Cocco, L. V., Linda, M., Annamaria, G. T., Perrone, G. I., Patrizio, M. M., Strusi, C. S., Giorgina, S and Giovanni. M. F. (2018) Assessment of DNA damages in lymphocytes of agricultural workers exposed to pesticides by comet assay in a cross-sectional study, *Biomarkers*, 23(5): 462-473.

Grewal, A.S., Ashish, S., Pradeep K and Jagdeep, S. D. (2017) Pesticide Residues in Food Grains, Vegetables and Fruits: A Hazard to Human Health. *J Med Chem Toxicol*., 2(1): 40- 46.

Grover, P., Danadevi, K., Mahboob, M., Rozati, R., Saleha, B. and Rahman, M.F., (2003). Evaluation of genetic damage in workers employed Insecticide production utilizing the Comet Assay. *Mutagenesis*, 18: 201-205.

Guilherme S, Gaivao I, Santos MA, Pacheco M. (2010). European eel (*Anguilla anguilla*) genotoxic and pro-oxidant responses following short-term exposure to Roundup - a glyphosate-based herbicide. *Mutagenesis* 25(1): 523–530.

Guilherme, S., Gaivao, I., Santos, M.A and Pacheco, M. (2012). DNA damage in fish (*Anguilla anguilla*) exposed to a glyphosate-based herbicide elucidation of organ-specificity and the role of oxidative stress. *Mut. Res. - Gen. Toxicol. Environ. Mutagen*, 743(1): 1–9.

Guner, U. (2016) Behavioral differentiation induced by insecticide Lambda-cyhalothrin in Mosquito Fish, *Gambusia affinis*. *Limnology Freshwater and Fisheries Research,* 2(1): 11–17.

Hedayati, A and Hassan, N. E. (2015). Hematological changes of silver carp in response to Diazinon pesticide. *Journal of Environmental Health Science and Engineering*, 13(52): 1-5.

Henderson, A. M.; Gervais, J. A.; Luukinen, B.; Buhl, K.; Stone, D.; Cross, A.; Jenkins, J. (2010). *Glyphosate General Fact Sheet*; National Pesticide Information Center, Oregon State University Extension Services. http://npic.orst.edu/factsheets/glyphogen.html. accessed on 18/9/2020.

Hernández, A.F.; Lacasaña, M.; Gil, F.; Rodríguez-Barranco, M.; Pla, A.; López-Guarnido, O. (2013). Evaluation of pesticide-induced oxidative stress from a gene–environment interaction perspective. *Toxicology*, 307: 95–102.

Ilavazhahan, M., Tamil, S.R., Jayaraj, S.S. (2010). Determination of LC_{50} of the Bacterial Pathogen, Pesticide and Heavy Metal for the Fingerling of Freshwater Fish *Catla catla*. *Glob. J. Environ. Res*. 4 (2): 76-82.

IPCS, (2010). The WHO recommended classification of pesticides by hazard and guidelines to classification, Geneva: WHO; 2010. *International Programme on Chemical Safety* (IPCS) Available:http://www.who.int/ipcs/publication ns/pesticides_hazard_2010 accessed 0n 10/6/2020.

Ishi, S.S and Patil, R. D. (2017). Acute toxicity bioassay of new tech biopesticide on fresh water cyprinid (*Danio aequipinnatus* (Ham Buch). *Intern. J. Fish. Aquat. Stud.*, 5(3): 584-586.

Ize-Iyamu, O.K., Asia, I. O. and Egwakhide, P.A. (2007). Concentrations of Residues from Organochlorine Pesticide in Water and Fish from Some Rivers in Edo state, Nigeria. *International Journal of Physical Sciences*, 2(9): 237-241.

Jayaprakash C and Shettu N. (2013). Changes in the hematology of the freshwater fish, *Channa punctatus* (Bloch) exposed to the toxicity of deltamethrin. *Journal of Chemical & Pharmaceutical Research*, 5(6):178-183.

Jerald, F. F and Saradhamani, N (2015). Impact of the herbicide glyphosate roundup (41%) on the haematology of the freshwater fish, *Catla catla* (Hamilton). *Journal of Environmental Science, Toxicology and Food Technology*, 9 (4) 3: 56-60.

Jones, D. K., Hammond, J. I and Relyea, R. A. (2011). Competitive stress can make the herbicide Roundup more deadly to larval amphibians. *Environmental Toxicology and Chemistry*, 30(2): 446-454.

Joshua, O. (2016). Pesticides Use and Health In Nigeria. *Ife Journal of Science,* 18(4): 981-991.

Karatas T (2016) Effects of deltamethrin on some haematological parameters of brown trout (*Salmo trutta fario*). *Indian Journal Animal Research,* 50(1): 89–92.

Karthigayani, T, Denis M, Andrew Remy AR and Shettu, N. (2014). Histological study of the intestine and liver tissues in the fish *Oreochromis mossambicus* exposed to cypermethrin. *Journal of Modern Biotechnology*, 3(4): 48-54.

Kaur, M and Rajinder, J. (2017). Oxidative stress response in liver, kidney and gills of *Ctenopharyngodon idellus* (cuvier & valenciennes) exposed to chlorpyrifos. *Molecular Journal of Biology and Medicine*, 1(4): 103–112.

Kumari, S., Kumar, R. V and Gopala Rao. N. G. (2018). Haematological changes induced in the fish *Ctenopharyngodon idella* (Valenciennes) exposed to organophosphate Dichlorvos both technical and 76% EC (Nuvan). *Journal of Innovations in Pharmaceutical and Biological Sciences*, 5(2): 58-63.

Kuruganti, K. (2005). Effects of Pesticide Exposure on Developmental Task Performance in Indian Children. *Children, Youth and Environments* 15(1): 83-114.

Li, D., Chen, Q., Cao, J., Chen, H., Li, L., Cedergreen, N., Xie, H., Xie, L. (2016). The chronic effects of lignin-derived bisphenol and bisphenol A in Japanese medaka *Oryzias latipes*. *Aquatic Toxicology*, 170(1):199-207.

Lipok, J., Studnik, H and Gruyaert S. (2010). The toxicity of Roundup 360 SL formulation and its main constituents: Glyphosate and isopropylamine towards non-target water photoautotrophs. *Ecotoxicology and Environmental Safety*, 73: 1681–1688.

Lushchak, O.V., Kubrak, O. I., Storey, J. M., Storey, K. B and Lushchak, V. I. (2009). Low toxic herbicide Roundup induces mild oxidative stress in goldfish tissues. Chemosphere 76: 932–937.

Mastan, S and Shaffi, S. (2010). Sub-lethal Effect of Pesticides on the Distribution of Glutaminases in the Brain of *Labeo rohita* (Ham.). *International Journal of Toxicology*, 7(2). 1-9.

Maton, S. M., Dodo, J. D., Nesla, R. A and Ali, A.Y. (2016) Environmental Impact of Pesticides Usage on Farmlands in Nigeria. *International Journal of Innovative Research and Development*, 5(4): 311-317.

Mazlan, N; Mohammed, A; Farrah, M; Muharam, M. D and Amirul Alam, A. (2017). Status of Persistent Organic Pesticide Residues in Water and Food and their Effects on Environment and Farmers: a comprehensive review in Nigeria. *Ciências Agrárias, Londrina*, 38 (3): 2221-2236.

Meza-Joya, F.L., Ramírez-Pinilla, M.P., Fuentes-Lorenzo, J. L. (2013). Toxic, cytotoxic, and genotoxic effects of a glyphosate fromulation (RoundupSL-Cosmosflux411F) in the direct-developing frog *Eleutherodactylus johnstonei*. *Environmetal and Molecular Mutagenesis*, 54(1): 362–373.

Mineau, P. (2004). Birds and Pesticides: Are Pesticide Regulatory Decisions Consistent with the Protection Afforded Migratory Bird Species Under the Migratory Bird Treaty Act? 28- 313pp.

Mishra A. (2017). Toxic impact of pesticides on the morphological characteristics of blood cells of fish *Channa punctatus* (Bloch*) Indian Journal of scientific Research*, 12 (2): 068-072.

Mishra, A. and Verma, S. (2016). Acute toxicity bioassay of organophosphorus pesticide, chlorpyrifos on fresh water catfish, *Heteropneustes fossilis* (Bloch, 1794). *International Journal of Fisheries and Aquatic Studies*, 4(6): 388-393.

Modesto, K.A and Martinez, C.B.R. (2010). Effects of Roundup Transorb on fish: Hematology, antioxidant defenses and acetylcholinesterase activity. *Chemosphere* 81(1): 781–787.

Mohamed, A. H. (2011). Sublethal toxicity of Roundup to immunological and molecular aspects of *Biomphalaria alexandrina* to *Schistosoma mansoni* infection. *Ecotoxicology and Environmental Safety*, 74(4): 754–760.

Murthy, K. S., Kiran, B. R and Venkateshwarlu, M. (2013). A review on toxicity of pesticides in Fish. *International Journal of Open Science Research,* 1(1): 15-36.

Nagaraju, B., Sudhakar, P., Anitha, A., Haribabu, G., Rathnamma, V.V. (2011). Toxicity evaluation and behavioural studies of fresh water fish *Labeo rohita* exposed to Rimon. *Int. J. Res. Pharma. Biomed. Sci*., 2(2): 722-727.

Nahed, S. G. (2011). Oxidative Stress and Antioxidant Enzymes in *Oreochromis niloticus* as Biomarkers of Exposure to Crude oil Pollution. *International Journal of Environmental Science and Engineering,* 1(1): 49-58.

Nazia, K., Taibur, R and Rita, M. (2016).Histopathological Studies of Chlorpyrifos Toxicity in Catfish. *Global Journal of Medical Research Microbiology and Pathology*, 16(3): 48-54.

Nehemia, A., Maganira, J. D and Rumisha, C. (2012). Length-Weight relationship and condition factor of Tilapia species grown in Marine and Freshwater Ponds. *Agriculture and Biology Journal of North America*, 3(3): 117-124.

Nte, M. E and Akinrotimi O. A. (2011). Biochemical Changes in Black Jaw Tilapia (*Sarotherodon melanotheron*) treated with sub lethal Levels of Industrial Effluents. *Sci. Edu. Develop. Inst.*, 1(1): 25-33.

Nnamonu, L.A. and Onekutu, A. (2015). Green Pesticides in Nigeria: An Overview. *Journal of Biology*, *Agriculture and Healthcare*, 5(9):48- 62.

Nwani, C. D., Ivoke, N., Ugwu, D.O., Atama, C., Onyishi, G.C., Echi, P.C., Ogbonna, A. (2013). Investigation on Acute Toxicity and Behavioral Changes in a Freshwater African Catfish, *Clarias gariepinus* (Burchell, 1822), Exposed to Organophosphorous Pesticide, Termifos. *Pakistan Journal of Zoology*, 45(4): 959-965.

Nwani, C.D., Ekwueme H.I., Ejere, V.C., Onyeke, C.C., Chukwuka, C.O., Peace, O.N. and Nwadinigwe, A.O. (2015). Physiological effects of Paraquat in juvenile African catfish *Clarias gariepinus* (Burchell, 1822). *Journal of Coastal Life Medicine*, 3(1):35-43.

Nwani, C.D., Nagpure, N.S., Kumar, R., Kushwaha, B., Kumar, P and Lakra, W.S. (2010). Lethal concentration and toxicity stress of Carbosulfan, Glyphosate and Atrazine to freshwater air breathing fish *Channa punctatus* (Bloch). *Int. Aquat. Res*., 2(1): 105-111.

Obiakor, M.O., Okonkwo, J.C., Nnabude, P.C. and Ezeonyejiaku, C.D. (2012) Eco-Genotoxicology: Micronucleus Assay in Fish Erythrocytes as in Situ Aquatic Pollution Biomarker: A Review. *Journal of Animal Science Advances*, 2(1): 123-133.

Ogamba, E.N, Inyang, I.R. and Azuma, I.K. (2014). Effect of paraquat dichloride on some metabolic and enzyme parameters of *Clarias gariepinus*. *Curr. Res. J. Bio. Sci*, 3(1):186- 190.

Omoniyi, I.T., Kazeem, L.A and Samuel O.O. (2013). Lethal Effects Of 2,2-Dichlorovinyl Dimethyl Phosphate .Ddvp • On Fingerling And Juvenile *Clarias gariepinus* .Burchell, 1822 *Croation Journal of Fisheries*, 71(1):19-24.

Ogundiran, M.A., Fawole O.O., Adewoye, S.O. and Ayandiran, T.A (2010). Toxicological impact of detergent effluent on juvenile of African Catfish (*Clariasgariepinus*). *Agriculture and biology journal of North America,* 1(1): 330 - 342.

Olutona, G. O., Olatunji, S.O and Obisanya, J. F. (2016) Downstream assessment of chlorinated organic compounds in the bed-sediment of Aiba Stream, Iwo, South-Western, Nigeria. *SpringerPlus*, 5(1): 67-73.

Oluwatosin, A.A; Olajumoke, O.N; John, A.A and Jacob, K.A. (2016). Induction of Oxidative Stress in *Clarias gariepinus* from Eleyele River in Nigeria. *Advances in Environmental Research*, 5(3): 179-187.

Osibanjo, O. (2002). Organochlorine in Nigeria and Africa. In: Fieldler, H. (ed.) *The Handbook of Environmental Chemistry. Persistent Organic Pollutants*. Heidelberg, Berlin: *Springer*

Osibanjo, O. and Adeyeye, A. (1999). Residues of organochlorine pesticides in fruits, vegetables and tubers from Nigerian markets. *Science of the Total Environment*, 231(2): 227-233.

Osman, A.G., Abuel-Fadl, K.Y. and Kloas, W. (2012) In Situ Evaluation of the Genotoxic Potential of the River Nile: II. Detection of DNA Strand-Breakage and Apoptosis in *Oreochromis niloticus* (Linnaeus, 1758) and *Clarias gariepinus* (Burchell, 1822). *Mutation Research*, 747(1): 14-21.

Ozok, N., Oguz, A. R., Kankaya, E., Yeltekin, A.C. (2018) Hemato-biochemical responses of Van fish (*Alburnus tarichi* Guldenstadt, 1814) during sublethal exposure to cypermethrin. *Human Ecology Risk Assessment International Journal*, 24(1): 2240–2246.

PAN, (2012). Pesticides and Health Hazards. Facts and Figures. Translation of the German publication "pesticized Gesundheitsgefahren: Daten und Fakten". PestizidesAktions-Netzwerk. www.pan-germany.org, Hamburg. Accessed on 18/9/2020.

PANA, (2016). The Lynchpin of Industrial Ag. Pesticides Action Network, North America. http:// www.panna. Org/pesticides-big-picture/lynchpinindustrial-ag (Accessed August 1, 2020).

Pandey, R.K., Singh, R.N., Singh, S., Singh, N.N., Das, V.K. (2009). Acute toxicity bioassay of dimethoate on freshwater airbreathing catfish, *Heteropneustes fossilis* (Bloch). *J. Environ. Biol.* 30(3): 437-440.

Pandey, A. K and Dubey, S. (2015). Histological changes in liver and kidney of cat fish, *Heteropneustes fossilis*, exposed to pentachlorophenol (PCP). *Plant Archives*, 15(2):1117-1120.

Patnaik, L., Patra A.K. (2006) Haematopoietic alterations induced by Carbary, in *Clarias batrachus Linn*). *J Applied Sci Environment Management*, 10: 5-7.

Poletta, G.L., Gigena, F., Loteste, A., Parma, M.J., Kleinsorge, E.C., Simoniello, M.F. (2013) Comet assay in gill cells of Prochilodus lineatus exposed in vivo to cypermethrin. *Pest Biochem Physiol*, 107(1): 385– 390.

Prieto, A.I.; Jos, A.; Pichardo, S.; Moreno, I.; Cameán, A.M. (2006). Differential oxidative stress responses to microcystins LR and RR in intraperitoneally exposed Tilapia fish (*Oreochromis* sp.). *Aquat. Toxicol*., 77: 314–321.

Raibeemol, K. P and Chitra, K. C. (2016). Histopathological alteration in gill of the freshwater fish *Etroplus maculatus* (Bloch, 1795) under chlorpyrifos toxicity. *Int. J. Adv. Res. Biol. Sci.*, 3(12): 141-146.

Rakesh, S. and Kumar, S.V. (2019). Acute toxicity and behavioural responses in *Clarias batrachus* (*Linnaeus*) exposed to herbicide pretilachlor. *Heliyon,* 5: 2405-8440.

Ramesh, H. and Munniswamy, D. (2009). Behavioral responses of the fresh water, Cyprinus carpio (Linnaeus) following sub-lethal exposure to chlorpyrifos. *Turkish J Fisheries Aquat Sci*., 9(1): 233-238.

Ramesh, R. C., Manjunatha, B., Jaffer, M. G., Srinivasulu, M., Juan, O. T., Shambanagouda, R. M. (2014). Histopathological Alterations in the Gill, Liver and Brain of *Cyprinus Carpio* on Exposure to Quinalphos. *American Journal of Life Sciences*, 2(4): 211-216.

Rani, G. I and Kumaraguru, A. K. (2014). Behavioural responses and acute toxicity of Clarias batrachus to synthetic pyrethroid insecticide, λ-cyhalothrin. *J. Environ. App. Biores*. 2(1): 19-24.

Rani, S and Venkataramana, G. V. (2012). Effects of the organophosphorous Malathion on the branchial gills of a freshwater fish *Glossogobius giuris* (Ham), *Int. J. Sci. Nat*. 3(2): 324-330.

Rekhadevi, P.; Rahman, M.; Mahboob, M.; InduKumari, S.; Chinde, S.; Dumala, N.; Grover, P. (2017). Assessment of genotoxicity in female agricultural workers exposed to pesticides. *Biomarkers*, 22: 446–454.

Remor, A.P.; Totti, C.C.; Moreira, D.A.; Dutra, G.P.; Heuser, V.D.; Boeira, J.M. (2009). Occupational exposure of farm workers to pesticides: Biochemical parameters and evaluation of genotoxicity. *Environ. Int*., 35: 273–278.

Reuben, I. I. (2016). "Effects of Lambda Cyhalothrin on Protein and Albumin Content in the Kidney and Liver of *Parpohiocephalus Obscurus*". EC *Pharmacology and Toxicology* 2(3): 148-153.

Reuters, (2011). Roundup: cancer cause or crucial for food production. ''The Huffington http://www.huffingtonpost.com/2011/04/11/roundupcancercouse_n_84743.html. Accessed on 18/9/2018.

Revathy, V and Chitra, K.C. (2015). Di (2-ethylhexyl) phthalateinduced histopathological changes in gill and liver of freshwater fish, *Oreochromis mossambicus* (Peters, 1852). *International Journal Advanced Research*, 3(9): 263–270.

Saeedi, F.M., Roodsari, H.V., Zamini, A., Mirrasooli, E and Kazemi, R. (2012). The Effects of Diazinon on Behavior and Some Hematological Parameters of Fry Rainbow Trout (*Oncorhynchus mykiss*). *World Journal of Fisheries and Marine Sciences*, 4(4): 369-375.

Saglam, D, Atli G, Dogan Z, Baysoy E, Gurler C, Eroglu A, Canli M. (2014). Response of the antioxidant system of freshwater fish *(Oreochromis niloticus*) exposed to metals (Cd, Cu) in different hardness. *Turkish Journal of Fisheries and Aquatic Sciences*, 14(1) 43-52.

Salbego, J., Pretto, A., Gioda, C. R., de Menezes, C. C., Lazzari, R., Neto, J.R., Baldisserotto, B and Loro, V.L. (2010). Herbicide formulation with glyphosate affects growth, acetylcholinesterase activity, and metabolic and hematological parameters in Piava (*Leporinus obtusidens*). *Arch. Environ. Contam. Toxicol*., 58(3): 740–745.

Salem, N. M., Ahmad, R. and Estaitieh, H. (2009). Organochlorine pesticide Residue in Diary products in Jordan. *Chemosphere*, 77: 673-678.

Salgad, V. (2013). BASF insecticide mode of action technical training manual, pp 56

Sánchez-Bayo, F. (2012). Insecticides Mode of Action in Relation to Their Toxicity to Non-Target Organisms. *Journal of Environment Analytical Toxicology,* 5(2): 1-9.

Shaibu, I. (2008) 'NAFDAC bans 30 agrochemical products' Vanguard, May 14, 2008. www.allafrica.com. Accessed on Wednesday, 24th August 2020

Singh, P.B., Singh, V., and Nayak, P.K. (2008). Pesticide residues and reproductive dysfunction in different vertebrates from north India. *Food Chem Toxicol*., 46(7): 2533-2539.

Sufi, D.A. and Zainab, T. (2015). Evaluation of Onchocerciasis: A Decade of Post Treatment with Ivermectin in Zainabi and Ririwai Doguwa Local Government Area of Kano State. *Advances in Entomology*, 3: 1-5.

Sultana S. A., Abjal, P. S., Kaiser, J and Abbas, H. A. (2016). Evaluation of cytotoxicity and genotoxicity of pesticide mixtures on lymphocytes. *Toxicology mechanisms and methods*, 26 (8): 588–594.

Tak, A.M; Bhat, F.A; Jan, U and Shah, G.H (2014). Sublethalhaematological effects of dichlorvos on the freshwater fish, *Cyprinus carpio* var. communis. *International Journal of Recent Scientific Research*, 5(7): 1334-1337.

Tasneem, S and Yasmeen, R (2018). Evaluation of genotoxicity by comet assay (single-cell gel electrophoresis) in tissues of the fish *Cyprinus carpio* during sub-lethal exposure to Karanjin. *Journal of Basic and Applied Zoology*, 79(19): 1-13.

Thenmozhi, C., Vignesh, V., Thirumurugan, R and Arun S (2011). Impacts of malathion on mortality and biochemical changes of freshwater fish *Labeo rohita*. I*ran. J. Environ. Health Sci. Eng.* 8(4): 387-394.

Tijjani, A. A. (2006) Pesticide use practices and safety issues: the case of cocoa farmers in Ondo State, Nigeria. *Journal of Human Ecology*, 19 (3): 183-190.

Ullah, S., Mohammad, J and Zorrieh, Z. (2014). Ecotoxicology: A Review of Pesticides Induced Toxicity in Fish. *Advances in Animal and Veterinary Sciences*, 3(1): 40-57.

Ullah, R., Zuberi, A., Naeem, M and Ullah, S. (2015) Toxicity to hematology and morphology of liver, brain and gills during acute exposure of Mahseer (*Tor putitora*) to cypermethrin. *Int J Agric Biol*, 17(1): 199–204.

Ullah, S., Begum, M., Ahmad, S and Dhama, K. (2016) Genotoxic effect of endosulfan at sublethal concentrations in Mori (*Cirrhinus mrigala*) fish using single cell gel electrophoresis (comet) assay. *Int J Pharmacol* 12(1): 169–176.

Ullah, S., Hasan, Z., Zorriehzahra, M.J and Ahmad, S. (2017). Diagnosis of endosulfan induced DNA damage in rohu (*Labeo rohita*, Hamilton) using comet assay. *Iran J Fish Sci* 16(1):138–149.

Ullah, S., Li, Z., Hasan, Z., Khan, S.U. and Fahad, S. (2018). Malathion induced oxidative stress leads to histopathological and biochemical toxicity in the liver of rohu (*Labeo rohita*, Hamilton) at acute concentration. *Ecotoxicol Environ Safety*, 161(1): 270–280.

Ullah, S., Zhongqiu L., Amina, Z., Muhammad, Z. U. A., Mirza, M. F. A. B. (2019a). Biomarkers of pyrethroid toxicity in fish. *Environmental Chemistry Letters,* 1(1): 1-28.

USEPA, (2017). Office of Prevention, Pesticides and Toxic Substances, http://www.epa.gov/pesticides/ 12 May.

Veeraiah, K, Padmaja, B; Sai, R. V; Naga, P. M and VivekCh, P. (2015). Impact of Glyphosate on Biochemical Constituents of the Freshwater Fish, *Catla Catla*. *International Journal of Bioassays*, 4 (7): 4139-4144.

Vieira, C.E. D and Martinez, C. B. (2018). The pyrethroid λ-cyhalothrin induces biochemical, genotoxic, and physiological alterations in the teleost *Prochilodus lineatus*. *Chemosphere* 210:958–967.

WHO, (2010). *The WHO recommended classification of pesticide by Hazard and guidelines to classification*. WHO, Geneva. Assessed online on 8/6/2020.

WHO, (2020) WHO recommended classification of pesticides by hazard and guidelines to classification, 2019 edition. Geneva: World Health Organization; 2020 PP 22-58.

Wu M, Xu H, Shen Y, Qiu W, Yang M. (2011). Oxidative stress in zebrafish embryos induced by short-term exposure to bisphenol-A, nonylphenol, and their mixture. *Environ Toxicol Chem.*, 30(10): 2335-2341.

Xing, H., Wang, X., Sun, G., Gao, X and Xu, S. (2011). Effects of atrazine and chlorpyrifos on activity and transcription of glutathione S-transferase in common carp (*Cyprinus carpio L*). *Environ Toxicol Pharmacol.*, 33(2): 233-244.

Yadav, A.S and Sehrawat, G. (2011). Evaluation of genetic damage in farmers exposed to pesticide mixtures. *International journalof human genetics.* 11(1): 105-109.

Yonar, M. E. (2012). The effect of lycopene on oxytetracycline-induced oxidative stress and immunosuppression in rainbow trout (*Oncorhynchus mykiss W*.) Fish Shellfish *Immunol.*, 32(6): 994-1001.

Younes, M and H. Galal-Gorchev, H. (2000) Pesticides in drinking water—a case study. *Food Chem. Toxicol.* 38(1): 87–90.

Yusuf, U. (2010). Gammalin 20, not cholera caused of mass killing in Adamawa, says Government. Vanguard, December 17, 2010. www.vanguard.com. accessed on Wednesday 24th May, 2020.

©2021 This is an Open Access article distributed under the terms of the Creative Commons Attribution 4.0 International license viewed via https://creativecommons.org/licenses/by/4.0/ which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is cited appropriately.