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ENDOSULFAN, A GLOBAL PESTICIDE: A REVIEW OF ITS TOXICITY ON VARIOUS ASPECTS OF FISH BIOLOGY

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ABSTRACT

Pesticides are used in agricultural fields to regulate pest population. These pesticides are usually toxic to non-target organisms like fish. Three of the main classes of pesticides are organochlorines, organophosphorous and carbamates. Organochlorines are the most commonly found pesticides in the environment including water, sediments, atmospheric air and biotic environment. Endosulfan is a broad spectrum organochlorine pesticide which has been commercially in use for decades to control insect pest. It is primarily used to kill insects and mites on crops including fruits, vegetables and cereal grains as well as ornamental shrubs, vines and trees. Endosulfan passes via surface runoff into natural waters, where it is accumulated in different organisms living in water, especially in fish, thus making it vulnerable to several prominent effects. Endosulfan is known to inhibit acetylcholinesterase, cause behavioural, neurological, oxidative, endocrine and other effects. The present review analyses the various effects of Endosulfan in fish.

KEYWORDS: Endosulfan, Fishes, Toxicity

INTRODUCTION

Organochlorine pesticides consist of a variety of chemicals composed primarily of carbon, hydrogen and chlorine that include among others polychlorinated biphenyls (PCBs), polychlorinated dibenzofurans (PCDFs), dichlorodiphenyltrichloroethane (DDT), dieldrin, chlordane, heptachlor, toxaphenes, mirex, lindane, dicofol, hexachlorobenzene, chlordecone and endosulfan (1). Organochlorine pesticides have strong insecticidal properties and broad applications due to their low cost of large scale production. However, some organochlorine pesticides have been banned in many countries due to their persistent residual characteristics and unexpected toxicities to non-target organisms in the environment (2, 3). While much less persistent than other organochlorines, endosulfan is known to be highly toxic to fish (4, 5).

Endosulfan (6,7,8,9,10,10- hexachloro-1,5,5a,6,9,9a- hexahydro-6, 9-methano- 2,4,3-benzodioxanthiepine, 3-oxide) is a broad spectrum organochlorine insecticide (6). Endosulfan is a broad spectrum insecticide–acaricide of the cyclodiene subgroup which consists of two biologically active isomers: alpha and beta, respectively in ratio of 7:3 (7). Whereas, endosulfan sulfate is the main environmental metabolite found in water, sediments and tissues (8). It is one of the few cyclodiene pesticides still used throughout the world (9). It is most often used for pest control on a variety of agricultural and horticultural crops, including; vegetables, cereals, fruits and tobacco (10, 11). The use of endosulfan is currently a concern because of its ability to enter the aquatic environment and affect non-target organisms. In water, endosulfan has been found to be present anywhere from a few days to a couple of months, depending on the chemical properties of the receiving water (12). Endosulfan is believed to act directly on the central nervous system of fish, which can lead to detrimental effects such as convulsions, hyperactivity and in severe cases mortality (12, 13). Traditionally, aquatic toxicity experiments focus on continuous exposures of toxicants and the associated acute or chronic effects.

Endosulpan was first produced by Farbwerke Hoechst in 1950s and was manufactured in the USA by FMC. Endosulphan was first registered as a pesticide in the United States in 1954. It emerged as a leading chemical used against a broad spectrum of insects and mites in agriculture and allied sectors. In 1984, worldwide production was estimated at 10,000 metric tons annually. Currently within the UNECE region only one company has been reported to produce endosulphan located at a site in Germany the company produces approximately 5,000 tpa (tons per anum) of the pesticide (14). There are however further production sites reported in non UNECE countries such as Israel, India, Korea and most recently in China.

Genotoxic and Mutagenic Effects

Exposure to xenobiotics in animals can sometime result in heritable damage or inactivation of DNA such phenomenon is called genotoxicity. The genotoxic potential of endosulfan may be attributed to its capability to act on genetic information and altering the structure of DNA thus interfering in prime cellular processes like replication, transcription and translation. Genotoxic chemicals such as insecticides have similar physical and chemicals properties that enable them to interact with genetic materials (15, 16). There is growing a concern over the existence of these genotoxicants in the aquatic environment as they have severe negative impact on fish health. There is considerable evidence that endosulfan can induce genotoxicity in aquatic organisms through ROS mediated damage to DNA (17). In a study carried out on *Oreochromis mossambicus* (Peters) to study genotoxic effect of endosulfan on DNA integrity as molecular biomarker, increase in percentage of hyperchromicity has been reported suggestive of the structural changes introduced in DNA due to the binding of endosulfan (18). Sana et al., (2016) (19) reported endosulfan to induce concentration and time dependent DNA damage in mori fishes (*Cirrhinusmrigala*).

Endocrine Effects

Fish are susceptible to endocrine disrupting effects during early developmental stages and early stages of life. Exposure to endosulfan has resulted in both reproductive and developmental effects in non-target animals. Endosulfan exposure caused reduced cortisol secretion in fish (20). Also, Endosulfan has been shown to have hormone disruption activity on diverse animals ranging from newts to zebra fish (21). Anderson et al., (22) reported endosulfan to interact with androgen and estrogen receptors and interfere with sex steroid metabolism and has shown weak endocrine disruptor action. Endosulfan functions as endocrine disruptor by inducing vitellogen protein expression, which causes the gonads to release E2 and consequently interfering the estrogen-receptor interaction. A significant increase in vitellogen proteins has been exhibited by *O. latipesmale* fish treated with endosulfan at a concentration of LC_{10} (23). Further, Chakravarthy et al. (24) have reported the effect of endosulfan on vitellogenesis and its modulation by different hormones in the vitellogenic cat fishes, *Clarias batrachus*. Kumar and Reddy, (25) observed that endosulfan effects turnover of RNA and proteins thereby changing the levels of macromolecular constituents in the tissue of fish *Claris Batarachus.* Chronic exposure of endosulfan to *Labeo rohita* (Hamilton) resulted in alteration in level of T_3 (Triodothyronine) and thyroid stimulating harmone (TSH) (26).

Developmental Defects

It is important to study development disorders caused by insecticides as it links between the concentrations of toxins and dysfunction in normal development from embryonic to puberty periods. Interference in the normal development and the growth may reduce the fish's survival chance. Embryos and larvae may be directly exposed to insecticides, through the yolk or via parental transfer in viviparous fish (27). Published reports have shown that exposure to endosulfan during development can cause persisting neuro-behavioural dysfunction, at low as well as higher doses. Developmental effects of endosulfan on adult zebra fish were reported by et al., they reported that treatments of endosulfan for 21 days severely impaired their hatching rate, without effecting its fecundity. The reproductive changes observed are presumably associated with the occurrence of ova-testes in males. They found that the hatching time, the GSI value in females, and the HSI value of male fish were affected by endosulfan. Also, the embryos and larvae of zebra fish (*Danio rerio*) exposed to endosulfan exhibited an abnormal response to touching, suggesting that endosulfan is developmentally toxic to zebra fish (9, 28).

Neurotoxic Effects

Insecticides neuro-toxicity in fishes is often assessed by determining the alterations in Acetylcholine esterase (AChE) in brain, muscle, plasma and other tissues or perhaps GABA activity in brain. AChE is an enzyme responsible for inactivating the neurotransmitter acetylcholine (29). AChE inactivation results in the accumulation of the neurotransmitter acetylcholine in cholinergic synapses space, leading to synaptic blockage and disruption of signal transmission (30). Jia and Misra, (31), and few others reported that endosulfan, like other cyclodiene insecticides, cause neurotoxicity through GABA-gated chloride channel inhibition (6). Inhibition of these channels results in excitation because the neuron unable to repolarize (31). A mutation in an insect GABA receptor subunit gene has been shown to provide resistance to cyclodiene, including endosulfan, toxicity in some insects (32).

According to the previously published reports of (33) Sarma et al., exposure of bluegill sunfish (*Lepomisma crochirus*) and spotted murrel (*Channa punctatus*) to high concentrations of endosulfan for 96 h leads to the inhibition of brain AChE. In another study conducted by (34) Prakash and Muthulingam, a remarkable decline in glycogen levels in brain and muscle have been witnessed in *Channa striatus* (a species of snakehead fish) when subjected to low, medium and high sub-lethal concentration of endosulfan. Other studies have also shown that inhibition of AChE enzyme is associated with the toxic effects of endosulfan (35). Dutta & Arends, (36) reported that AChE activity was inhibited in brain of *Lepomis macrochirus*, similarly (37) Kumar et al., showed inhibition of AchE in *Labeo rohita*. Endosulfan induced inhibition of AchE in muscle of *Jenynsia multidentata* has also been observed (38). By affecting the AChE activity in fish, the swimming capability and performance of fish is hampered which can contribute to more harmful consequences (39, 40). Pereira et al., (41) reported Endosulfan exposed zebra fish (*Danio rerio*) showed a general decreased exploratory ability, including reduced mean speed which lead to lower distance travelled.

Behavioural Effects

Behavioural changes are recognised as most sensitive indicators of possible toxic effects. The behavioural and the swimming patterns of the fish exposed to different insecticides include changes in feeding activities, swimming behaviour, competition, predation, reproduction and species-species social interactions such as aggression.

The effect of certain insecticides on the activity of acetylcholinestrase may lead to a decreased mobility in fish (42). Gormley & Teather, (43) have reported the same alterations in *Oryzias latipes*, treated with endosulfan. Reduced feeding behaviours of *Thalassoma pavo* was reported with endosulfan (44) also changes in spontaneous swimming activity of *Jenynsia multidentata* are documented (45). In Zebra fish (*Danio rerio*) endosulfan exposure showed a general decreased exploratory ability, including reduced mean speed, it also affected animals swimming body turn angles, suggesting it significantly impairs animals' exploratory performance, and potentially compromises their ecological and interspecific interaction (46). Further endosulfan has been shown to effect behavioural pattern in *Labeo Rohita* at acute concentrations (17).

Reproductive Effect

Due to its potency and shorter duration in aquatic environment, endosulfan is widely employed as an organo-chlorinated insecticide. Majority of the previously conducted studies indicate that endosulfan may have a direct effect on fish population by affecting mobility, hunting success, growth and development and reproductive capability of vulnerable/exposed subjects (47, 48). Another study carried out by Susan & Sania (49) reported anti-estrogenic effects of endosulfan in fresh water catfish and reproductive problems caused by it in female teleost fish and opercoid fish. The reports are further supported by Singh and Singh, (50) who outlined the inhibitory role of endosulfan during reproductive growth thereby affecting phospholipid biosynthesis via hepatic enzyme systems as well as by hormonal imbalance. Evidences in favour of reproductive toxicity of endosulfan in fish include: lowered vitellogenin plasma levels in females (51), decreased clutch size (43), sex ratio skew towards females (52) in exposed Japanese medaka (*Oryzias latipes*), suppression growth and reproductive activity in zebra fish (53), decreased hatching rate, reduced gonadosomatic index in females, vitellogenin levels increase in males and histological gonadal alterations (54) in exposed zebra fish (*Danio rerio*), a relatively abnormal response of exposed embryos and larvae of zebra fish to touching indicating developmental toxicity (9, 28), altered expression of steroidogenic enzymes, gonad-related transcription factors and cfGnRH mRNAs in larvae (55, 56) of the Asian catfish (*Clarias batrachus*), toxic effect on ovary at sub-lethal concentrations leading to the arrest of oocyte maturation (57).

CONCLUSIONS

Exposure of aquatic life to pesticides means a constant health hazard for the population. So, human population is at huge risk by consuming these toxicated fishes. This implies that we should be careful in the application of pesticides to defend the life of fish and other aquatic fauna. Endosulfan toxicity in fish has been studied by many researchers who suggested that at chronic level, it causes diverse effects including oxidative damage, developmental changes, endocrine disruption, genotoxic/mutagenic effects and neurotoxic effects especially inhibition of AChE activity. With increasing incidences of endosulfan usage and its adverse effects on non-target organisms like fish, it has become necessary to regulate the use of this pesticide. Since endosulfan is present in the environment with other similar organochlorine compounds, it may induce lethal or sublethal effects in fish. It is, therefore, a matter of great public health concern to frequently monitor the endosulfan residues in foods and humans in order to assess the population exposure to this pesticide. Moreover, for a safe use of thispesticides more scientific experimental work must be performed to determine the exact concentration and time of exposure that do not induce prominent toxic effects on fish.

REFERENCES

1. Van Dyk JS, Pletschke B. Review on the use of enzymes for the detection of organochlorine, organophosphate and carbamate pesticides in the environment. Chemosphere. 2011;82: 291–307.
2. Brunelli E, Bernabo I, Berg C, Lundstedt-Enkel K, Bonacci A, Tripepi S. Environmentally relevant concentrations of endosulfan impair devel-opment, metamorphosis and behavior in Bufo bufo tadpoles. Aquatic Toxicology. 2009; 91: 135-142.
3. Sharma A, Mishra M, Ram KR, Kumar R, Abdin MZ, Chowdhuri DK. Transcriptome analysis provides insights for understanding the adverse effects of endosulfan in Drosophila melanogaster. Chemosphere. 2011; 82: 370-376.
4. Neuparth T, Bickham JW, Theodorakis CW, Costa FO, Costa MH. Endosulfan-induced genotoxicity detected in the Gilthead seabream, Spa-rusaurata L., by means of flow cytometry and micronuclei assays. Bulletins of Environmental Contamination and Toxicology. 2006; 76: 242-248.
5. USEPA (US Environmental Protection Agency). Reregistration eligibility decision for Endosulfan, EPA 738-R-02-013. US: USEPA. 2002.
6. Naqvi SM, Vaishnavi C. Bioaccumulative potential and toxicity of endosulfan insecticide to non-target animals. Comparative Biochemistry Physiology. 1993; 105: 347–361.
7. Wan MT, Kuo J, Buday C, Schroeder G, Van Aggelen G, Pasternak J. Toxicity of α-, β-, (α + β)-endosulfan and their formulated and degradation products to *Daphnia magna*, *Hyalella azteca*, *Oncorhynchus mykiss*, *Oncorhynchuc kisutch*, and biological implications in streams. Environment Toxicology Chemistry. 2005; 24:1146–1154.
8. Rand GM, Carriger JF, Gardinali PR, Castro J. Endosulfan and its metabolite, endosulfan sulfate, in freshwater ecosystems of south Florida: a probabilistic aquatic ecological risk assessment. Ecotoxicology. 2010; 19:879–900.
9. Stanley KA, Curtis LR, Simonich SLM, Tanguay LR. Endosulfan I and endosulfan sulfate disrupts zebrafish embryonic development. Aquatic Toxicology. 2009; 95 (4): 355–361.
10. Tuduri L, Harner T, Blanchard P, Li Y, Poissant L, Waite DT, Murphy C, Belzer W. A review of currently used pesticides (CUPs) in Canadian air and precipitation: part 1: lindane and endosulfans. Atmosphere Environment. 2006; 40:1563–1578.
11. Sutherland TD, Horne I, Weir KM, Russell RJ, Oakeshott JG. Toxicity and residues of endosulfan isomers. Rev. Environmental Contamination Toxicology. 2004; 183: 99–113.
12. ATSDR. Toxicological profile for endosulfan. Atlanta, GA: Agency for Toxic Substances and Disease Registry. 2000.
13. Harris ML, van den Heuvel MR, Rouse J, Martin PA, Struger J, Bishop CA, et al. Pesticides in Ontario: A critical assessment of potential toxicity of agricultural products to wildlife, with consideration for endocrine disruption. Volume 1: endosulfan, EBDC fungicides, dinitroanaline herbicides,1,3-dichloropropene, azinphos-methyl, and

pesticide mixtures. Canadian Wildlife Service 2000. Ontario Region: Environmental Conservation Branch; 2000. p. 11–33

14. Herrmann M. Preliminary risk profile of endosulfan. Berlin Germany: Umweltbundesamt; 2002.
15. Candioti JV, Soloneski S, Larramendy ML. Genotoxic and cytotoxic effects of the formulated insecticide Aficida on Cnesterodon decemmaculatus (Jenyns, 1842) (Pisces: Poeciliidae). Mutation Research. 2010; 703: 180–186.
16. Dogan D, Can C, Kocyigit A, Dikilitas M, Taskin A, Bilinc H. Dimethoate induced oxidative stress and DNA damage in *Oncorhynchus mykiss*. Chemosphere 2011;
17. Ullah S, Hassan Z, Dhama K. Toxic effect of endosulfan on behaviour, protein content, antioxidant enzymes system in gills, liver brain and muscles of rohu (*Labeo Rohita*). International Journal of pharmacology. 2016; 12: 1-10.
18. Rani APA, Kumaraguru AK. DNA integrity as molecular biomarker of genotoxic effect of Endosulfan in *Oreochromis mossambicus* (Peters) International Journal of Engineering Science Invention. 201; 2 (4): 58-61.
19. Ullah S, Begum M, Ahmad S, Dhama K. Genotoxic Effect of Endosulfan at Sublethal Concentrations in Mori (*Cirrhinus mrigala*) Fish Using Single Cell Gel Electrophoresis (Comet) Assay. International Journal of Pharmacology. 2016; 12: 169-176.
20. US-EPA. Reregistration Eligibility Decision for Endosulfan. EPA 738-R-02-013. Pollution, Pesticides and Toxic Substances (7508C), United States Environmental Protection Agency. 2002.
21. Grumfeld HT, Bonefeld-Jorgensen EC. Effects of *in vitro* estrogenis pesticides on human oestrogen receptor alpha and beta mRNA levels. Toxicology Letters. 2004; 151 (3): 467-80.
22. Andersen HR, Andersson AM, Arnold SF, et al. Comparison of short-term estrogenicity tests for identification of hormone-disrupting chemicals. Environmental Health Perspectives. 1999; 107 (1): 89-108.
23. Sung-Eun Lee, Choi Young-Woong, Hyoung-ho Mo, Jino Son, Kyeonghun Parkand Kijong Cho' Endosulfan-Induced Biomarkers in Japanese Rice Fish (*Oryzias latipes*) Analyzed by SELDI-TOF-MS. International Journal of Biological Science. 2013; 9 (4): 343-349.
24. Chakravarty G, Goyal RP, Sharma S, Sharma A. Haematological changes induced by a common non-permitted food colour Malachite Green (MG) in swiss albino mice. Indian Journal of Environmental Science. 2005; 92: 113-117 .
25. Kumar AV, Karemungikar A, Reddy SLN. A comparative study of sublethal effect of endosulfan and cypermethrin on blood serum profiles in air breathing catfish, *Clarias batrachus*. Journal of Environmental Pollution. 1997; 4: 131-135.
26. Saravanan TS, Rajesh P, Sundaramoorthy M. Studies on effects of chronic exposure of endosulfan to Labeo rohita. Journal of Environmental Biology. 2010; 31(5): 755-758 (2010).
27. Viant MR, Pincetich CA, Tjeerdema RS. Metabolic effects of dinoseb, diazinon and esfenvalerate in eyed eggs and alevins of Chinook salmon (Oncorhynchus tshawytscha) determined by H NMR metabolomics. Aquatic

Toxicology, 2006; 77: 359–371.

28. Velasco-Santamarı´a YM, Handy RD, Sloman KA. Endosulfan affacts health variables in adult zebra fish (*Danio rerio*) and induces alterations in larvae development. Comparative Biochemistry Physiology C. 2011; 153:372–380.

29. Fulton MH, Key PB. Acetylcholinesterase inhibition in estuarine fish and invertebrates as an indicator of organophosphorus insecticide exposure and effects. Environmental Toxicology and Chemistry. 2001; 20: 37-45.

30. Ferrari A, Venturino A, de D'Angelo AMP. Muscular and brain cholinesterase sensitivities to azinphos methyl and carbaryl in the juvenile rainbow trout *Oncorhynchus mykiss*. Comparative Biochemistry and Physiology, Part C. 2007;146: 308–313.

31. Jia Z, Misra HP. Developmental exposure to pesticides zineb and/or endosulfan renders the nigrostriatal dopamine system more susceptible to these environmental chemicals later in life. Neuro Toxicology. 2007; 28: 727–735.

32. Ffrench-Constant RH, Anthony N, Aronstein K, Rocheleau T, Stilwell G. Cyclodiene insecticide resistance: from molecular to population genetics. Annual Reviews Entomology. 2000; 45: 449–466.

33. Sarma K, Pal AK, Sahu NP, Mukherjee SC, Baruah K. Biochemical and histological changes in the brain tissue of spotted murrel, *Channa punctatus* (Bloch), exposed to endosulfan. Fish Physiology and Biochemistry. 2010; 36: 597-603.

34. Prakash SLJ and Muthulingam M. Impact of endosulfan on phosphatase activity in brain and muscle of freshwater fish channa striatus (bloch) International Journal of Development Research. 2013 ; 3(2): 1-4.

35. Rodriguez-Fuentes G, Gold-Bouchot G. Environmental monitoring using Acetylcholinesterase inhibition in vitro. A case study in two Mexican lagoons. Marine Environmental Research. 2000; 50(1-5): 357-360.

36. Dutta HM, Arends DA. Effects of endosulfan on brain acetylcholinesterase activity in juvenile bluegill sunfish. Environmental Research. 2003; 91:157–62.

37. Kumar N, Jadhao SB, Chandan NK, Kumar K, Jha AK, Bhushan S, et al. Dietary choline, betaine and lecithin mitigates endosulfan-induced stress in Labeo rohita fingerlings. Fish Physiology Biochemistry. 2011.

38. Ballesteros ML, Durando PE, Nores ML, Dı´az MP, Bistoni MA, Wunderlin DA. Endosulfan induces changes in spontaneous swimming activity and acetylcholinesterase activity of Jenynsia multidentata (*Anablepidae, Cyprinodontiformes*). Environmental Pollution. 2009; 157: 1573–80.

39. Rao JV. Sublethal effects of an organophosphorus insecticide (RPR-II) on biochemical parameters of tilapia, Oreochromis mossambicus. Comparative Biochemistry Physiology Part C. 2006; 143(4): 492- 498.

40. Rao JV, Kavitha P, Jakka NM, Sridhar V, Usman P. Toxicity of organophosphates on morphology and locomotor behavior in brine shrimp, Artemia salina. Archhives of Environmental Contamination and Toxicology. 2007; 53(2): 227- 232.

41. Pereira VM , Bortolotto JW, Kist LW , Barbieri de Azevedo M, Fritsch RS, Oliveira R, Pereira TCB, Bonan CD, Vianna MR, Bogo M. Endosulfan exposure inhibits brain AChE activity and impairs swimming performance in adult zebrafish (*Danio rerio*). NeuroToxicology. 2012; 33: 469–475.

42. Bretaud S, Toutant JP, Saglio P. Effects of carbofuran, diuron, and nicosulfuron on acetylcholinesterase activity in goldfish (*Carassius auratus*). Ecotoxicology and Environmental Safety. 2000; 47: 117–124.

43. Gormley KL, Teather KL. Developmental, behavioral, and reproductive effects experienced by Japanese medaka (*Oryzias latipes*) in response to short-term exposure to endosulfan. Ecotoxicology and Environmental Safety. 2003; 54: 330–338.

44. Giusi G, Facciolo RM, Alo` R, Carelli A, Madeo M, Brandmayr P, et al. Some environmental contaminants influence motor and feeding behaviors in the ornate wrasse (*Thalassoma pavo*) via distinct cerebral histamine receptor subtypes. Environmental Health Perspective. 2005; 113:1522–1529.

45. Ballesteros ML, Durando PE, Nores ML, Dı´az MP, Bistoni MA, Wunderlin DA. Endosulfan induces changes in spontaneous swimming activity and acetylcholinesterase activity of Jenynsia multidentata (*Anablepidae, Cyprinodontiformes*). Environmental Pollution. 2009; 157:1573–1580.

46. Pereira VM, Bortolotto JW, Kist LW, Barbieri de Azevedo M, Fritsch RS, Oliveira R, Branda TC, Pereira, Bonan CD, Vianna MR. Bogo M. Endosulfan exposure inhibits brain AChE activity and impairs swimming performance in adult zebra fish (*Danio rerio*). NeuroToxicology. 2012; 33:469–475.

47. Doving KB. Assessment of animal behaviour as a method to indicate environmental toxicity. Comparative Biochemistry Physiology C and Comparative Pharmacology. 1991; 100:247–252.

48. Jones J, Reynolds J. Effects of pollution on reproductive behavior of fishes. Review of Fish Biology and Fisheries. 1997; 7:463–491.

49. Susan S, Sania P. Endosulfan- A Review of its Toxicity and its Effects on the Endocrine System WWF (World Wild Life Fund – Canada). 1999.

50. Singh PB, Singh V. Impact of endosulfan on the profiles of phospholipids at sublethal concentration in the male *Heteropneustes fossilis* (Bloch). Journal of Environmental Biology. 2006; 27: 509-514.

51. Chakravorty S, Lal B, Singh TP, Effect of endosulfan (thiodan) on vitellogenesis and its modulation by different hormones in the vitellogenic catfish *Clarias batrachus*. Toxicology. 1992; 75: 191–198.

52. Teather K, Jardine C, Gormley K. Behavioral and sex ratio modification of Japanese medaka (*Oryzias latipes*) in response to environmentally relevant mixtures of three pesticides. Environmental Toxicology. 2005; 20:110–117.

53. Balasubramani A, Pandian TJ. Endosulfan suppresses growth and reproduc- tion in zebrafish. Current Science India. 2008; 94: 883–890.

54. Han Z, Jiao S, Kong D, Shan Z, Zhang X. Effects of B-endosulfan on the growth and reproduction of zebrafish (*Danio rerio*). Environmental Toxicology and Chemistry. 2011; 30: 2525–2531.

55. Rajakumar A, Singh R, Chakrabarty S, Murugananthkumar R., Laldinsangi C, Prathibha Y, Sudhakumari CC, Dutta-Gupta A, Senthilkumaran, B., 2012.

56. Chakrabarty S, Rajakumar A, Raqhuveer K, Sridevi P, Mohanachary A, Prathibha Y, Bashyam L, Dutta-Gupta A, Senthilkumaran B. Endosulfan and flu- tamide, alone and in combination, target ovarian growth in juvenile catfish, *Clarias batrachus*. Comparative Biochemistry and Physiology – Part C: Toxicology & Pharmacology.

2012; 155: 491–497.

57. Bhende AM, Sitre SR. Alterations in the Gonads of *Labeo Rohita* Exposed to Endosulfan At Sublethal Dose in Long Duration Experiments Online International Interdisciplinary Research Journal, {Bi-Monthly}. 2014; (4): 232-240.