A Review on Zebrafish (*Danio rerio*) and Zebrafish embryo as a tool to study pyrethroid compounds' toxicity

Kulkarni Khyati[1]*, Desai Jigna[1]

[1]*Department of Biosciences, Veer Narmad South Gujarat University, Surat, Gujarat, India-395007*

**E-mail: - kul_1910@yahoo.com*

Abstract:

Now Zebrafish is the best animal model proved to study various molecules, in addition to understand biological functions, also to know the mechanism underlying the effect of any compound which can contribute to therapeutic discoveries. Pyrethroids are a class of man-made pesticides similar with the naturally available pesticide pyrethrum, which is produced by Chrysanthemum flowers. Pyrethroid insecticides are very commonly used residential and agricultural insecticides. As per scientific data available, it is observed that insecticides as well as pesticides have been involved in several neurological disorders in experimental animals and in humans too. Never the less, some data gap exists as their toxicity assessment is complex. Reviewing the valuable researches on effects of pyrethroid compound's toxicity on Zebrafish provides the useful information and proves that the Zebrafish are excellent model for toxicity studies. Nevertheless, comparatively less studies there on Pyrethroid's developmental neurotoxicity on the developing Zebrafish embryo. Concerning about pyrethroids, it can be assumed that, there may be higher risk of using these pesticides than currently acknowledged, as general population is using them extensively and in unsupervised manner. The precautionary step will be to guide our action on usage of pyrethroids to prevent undesirable consequences. Further research on alternatives to synthetic pyrethroids may need support from authorised institutes or government.

Key Words: Zebra Fish, Embryo, Pyrethroids, Toxicity

Introduction:

Pyrethroids

Since 1940, synthetic Pyrethroids are in use. Synthetic pyrethroids are derived from natural substances called Pyrethrins found in the extract from the flower heads of *Chrysanthemum cinerariaefolium* (Ramchandra, A.M. et al., 2019). Pyrethroids are said to be less poisonous to wildlife which biodegrade more effectively than organochlorine. Pyrethroids are used to spray inside the houses, to pervadebednets, which protect us from malarial mosquito bites. Deltamethrin and Fenvalerate are relatively less harmful to the nature and maximum non-target organisms than other insecticides (Adelsbach, T. L. & Tjeerdema, R. S., 2003). Though Pyrethroids are said as safe, they are found to be toxic to some insects like dragonflies, bees, mayflies and some other invertebrates which are the base of terrestrial and aquatic food webs (Zaveri, M., 2010). There are two different types of synthetic pyrethroids on the basis of their chemical structure; type I and II (Rehman, H.*et al*., 2014).Type I includes Allethrin, Bifenthrin, Permethrin, Phenothrin, Resemethrin, Tefluthrin and Teramethrin; whereas Type

II includes Cyfluthrin, Cyhalothrin, Cypermethrin, Deltamethrin, Fenvalerate, Fenpropathrin, Flucythrinate, Flumethrin, Fluvalinate and Tralomethrin (Thatheyus, A. J., & Selvam, A. G., 2013).

Zebrafish

The *Daniorerio*, commonly known as Zebrafish is a member of the family Cyprinidae. It is a tropical freshwater fish. Together with other ten species of the genera *Danio*, Zebrafish was firstly described by Buchanan Francis Hamilton in 1822 (Hamilton F., 1822). It has a short reproduction cycle which reach the maturity age within 3-6 months. Though Zebrafish is a popular aquarium fish, these days it is one of very important vertebrate models for genetic, medicine, developmental sciences, pharmacology and ecotoxicology (Scholz, S. et al., 2008; Scalzo, F. M. & Levin, E. D., 2004; Rubinstein, A. L., 2006). Zebrafish is easy to maintain in a laboratory conditions. The male and female adults are easily identifiable. One female can produce average of 190 eggs per spawning; which provide an effortless stock maintenance and enable a high number of organisms for tests (Rhaul De Oliveira, 2009).

Why and how Zebrafish?

There are some important characteristics that make Zebrafish as a model system logistically attractive are: (a) reduced size, (b) short life cycle, (c) short generation time (2-3 months: egg to reproductive adult), (d) good reproduction in captivity (e) possible daily breeding, (f) external fertilization (g) easily available non-adhesive eggs obtained from abundant spawning (h) optically transparent eggs that enable external observation of the embryo development (i) rapid embryonic development (Rhaul De Oliveira, 2009). The homology between Zebrafish and humans is also observed. This fish shows similarities in many ways including sense modalities like vision, olfaction, taste, touch, balance, hearing and cognitive behavioural and their sensory pathways. There has been continuous development of new techniques (e.g., microarrays technology, hybridizations and transgenic organisms) and involvement of large scale screening assays are various tools that contribute to the increased use of Zebrafish (Rubinstein, A. L., 2006, Zon, L.I. and Peterson, R. T., 2005; Spitsbergen, J. M. and Kent, M. L., 2003; Langheinrich, U., 2003; Chico, T. J.et al., 2008). The Zebrafish toxicity test was first published in 1984 by The International Organization for Standardization. Then, varoius countries propagated other toxicity testing standards through their use. It has been recorded that many environmental pollutants, including pyrethroids, hinder with the operation of the endocrine system, affect development, produce DNA damage, and induce oxidative stress in

Zebrafish (Jin, Y. et al., 2010; Jin, Y. et al., 2011; Shao, B. et al., 2012; MA, Y. et al., 2012). The "*Fish Embryo Test (FET)"* (OECD, 2006) has emerged as an alternative to determine the toxicity of substances and the Zebrafish as an excellent model for understanding toxic mechanisms of the chemicals. The embryos, including Zebrafish embryos, are not classified as animals, and for that are not subjects to welfare issues described by this directive (Nagel, R., 2002). Researchers have been paying attention, in adults and embryos assays, in the evaluation of the potential of chemical and metabolites that can cause any damage in genes. In the past few years, a wide variety of genotoxicity assays using adult fish have been used in ecotoxicological evaluations of environmental pollutants. Detection of DNA strand breaks produced by the chemical exposure remains the major approach. In another instance, few studies about fish chronic exhibition to genotoxic chemicals are available. The long-term exposure to a genotoxic chemical may induce a cascade of events resulting in changes in gene frequency in populations and mutational events (Van der Oost R. et al., 2003). The mostly used technique is the DNA microarray, which permit the simultaneous monitoring of the expression of thousands of genes. So that it can be used as a highly sensitive and informative biomarker for toxicity (Lettieri, T., 2006; Neumann, N. F. and Galvez, F., 2002).

Various researches on Zebrafish embryo and Zebrafish as a suitable animal model to study toxicity of Pyrethroid compounds

The mechanism of action of Pyrethroids in vertebrates is similar to insects, mainly involving the nervous system. There have been many experiments proved the hazardous consequences of Pyrethroids on rats and other mammals. Now focus has been moved from such experimental animals to the tiny zebra fishes due to their homology with human beings as well as no ethical issues remains to be clear.

In mammals and especially rats, two acute poisoning syndromes are described. "T-syndrome" is chiefly induced by natural Pyrethrins and type I Pyrethroids that is characterized by tremors, extreme sensitivity to sensory stimuli, ataxia, convulsions and, in some cases, paralysis. The "CS-syndrome" isinduced by type II Pyrethroids that is characterized by hypersensitivity to external stimuli, choreoathetosis (sinuous writhing), salivation and sometimes paralysis (Narhasi, T. 2000).

De Micco, A. et al. investigated the developmental neurotoxicity of six common Pyrethroids; three compounds from type I (Permethrin, Resmethrin and Bifenthrin) and three compounds from type II (Deltamethrin, Cypermethrin, and l-Cyhalothrin). The study revealed that

Pyrethroidexposure to Zebrafish embryos provoked an increase in mortality and pericardial edema being dose dependent, which showed that type II compounds was the most influential. At the doses around the LC50, craniofacial abnormalities were observed in Permethrin and Deltamethrin exposure. The findings were accordant with mammalian studies exhibiting that Pyrethroids are mildly teratogenic at high doses. However, body axis curvature and spasms had been observed at lower doses, which were reminiscent of the classic syndromes occurring due to Pyrethroidtoxicity. Diazepam treatment improved spasms, whereas treatment with the antagonist of sodium channel improved spasms and body curvature both, indicating that Zebrafish and mammals share similar pyrethroid-induced neurotoxicity (DeMicco, A. et al., 2010).

Awoyemi, O. M. et al. (2019) assessed the effects of the two Pyrethroid types on embryo and larval Zebrafish at laboratory concentrations and environmental relevant condition. Embryos were exposed to both types of Pyrethroids i.e. type- I (Permethrin, Bifenthrin) and type-II (Deltamethrin, λ-Cyhalothrin, Fenvalerate, Esfenvalerate). Results showed that Bifenthrin-(10 μg/L) and esfenvalerate-(1000 μg/L) notably ($p < 0.05$) reduced total distance travelled by larvae. Dose of 1000 μg/L for Deltamethrin and λ-Cyhalothrin were lethal to larva which caused body axis curvature and pericardial edema. In comparison to control, Permethrin-(0.122μg/L) upregulated Nrf2a and Casp-9 expressions, whereas λ-cyhalothrin-(0.053μg/L) down regulated Nrf2a and Fenvalerate-(0.037μg/L) downregulated GST at environmentally relevant concentrations. At laboratory concentrations, Permethrin-(1000μg/L) upregulated Nrf2a, Casp-9 and p53 expressions, Bifenthrin-(10μg/L) upregulated Casp-9 while Fenvalerate-(0.1μg/L) and Esfenvalerate-(1000μg/L) down regulated GST. The concentration dependent increase in carboxyl esterase activity was observed which positively correlated to total ROS.

Although Deltamethringenerally considered safe to use around humans, it is still neurotoxic. It is an allergen and causes asthma in some people. Kung, T. S. et al., used the Zebrafish to examine the hypothesis that developmental exposure to low doses of the Deltamethrin results in constant alterations in dopaminergic gene expression, neurochemistry, and locomotors activity. The results showed decreased transcript levels of the D1 dopamine (DA) receptor (drd1) and increased levels of tyrosine hydroxylase at 72 hours post fertilization. Larval fish had increased levels of one of DA metabolite i.e. homovanillic acid. Elevated larval swim activity was impaired by associated knockdown of the DA transporter. Dopaminergic dysfunction seems to promotelocomotor deficits in larval Zebrafish. The results culminate the

need to understand the continuous effects of low-dose neurotoxicant exposure during development (Kung, T. S. et al., 2015).

Shabnam, K. R. et al. (2019), investigated the expression pattern of four genes, namely, you (you), yot (you-too), momo (mom) and ubo (u-boot) during early development of Zebrafish, that is, from 12 hpf to 48 hpf stages to two concentrations (100 and 200 µg/L) of Deltamethrin (DM). All four genes are known to play a vital role in development of notochord and somites. These four genes were analyzed by Reverse transcription (RT)-polymerase chain reaction and intensity of the bands showed induction in their expression after exposure to the toxicant. In spite of the expression of genes, it was noticed that DM caused abnormalities. It can be said from the results that translational pathway could have been affected.

Cyfluthrin is also a very common household pesticide. In a study by Kadiru, S. (2018),acute toxicity and developmental effects of Cyfluthrin were evaluated for embryo-larval Zebrafish at 24, 48, 72 and 96 hpf. The results showed that at 96 hpf, LC50 of Cyfluthrin to embryos was 3.443 µg/L. Cyfluthrin increased spontaneous contractions frequency and hatching rate, whereas it significantly reduced the body length in a dose and time-dependent manner. Morphological abnormalities including yolk sac edema, tail deformities and curved body axis were also observed. This study stated that short term exposure of Cyfluthrin causes lethality and significant developmental defects in Zebrafish in early life stages.

Cypermethrin (Cyp), is one of the most common contaminants in freshwater aquatic systems. Though Cypermethrin neurotoxicity has been deliberated in adult rodents, less information is available concerning the developmental toxicity of Cypermethrin inearly life stages of fish.

A study by Shi, X. et al. (2011) revealed that 400 µg /LCypermethrinremarkably increased malondialdehyde production.Their results demonstrated that Cypermethrin could induce oxidative stress and generate apoptosis through the involvement of caspases in Zebrafish embryos.In addition, antioxidative enzymes activity including superoxide dismutase and catalase were significantly persuaded in Zebrafish larvae in a concentration-dependent manner. Cypermethrin also down-regulated ogg1 and increased the expression of p53 gene and the caspase-3 activity.

Jin, Y. et al. (2011) showed that exposure of Zebrafish embryos to 3 and 10 µg/L Cypermethrin (cyp) for 3 days induces apoptosis and immunotoxicity, also confirmed an increase in the activity of caspase-3 and -9 after exposure. By analyzing mRNA levels of different genes related to programmed cell death (p53, Apaf-1 and caspase-3), they reported

that Cyp induces oxidative stress, DNA damage, and apoptosis. These parameters were significantly increased, whereas the ratio between Bcl-2/Bax genes decreased significantly after exposure to 1 and 3 μg/L Cyp for 8 days.

Paravani, E. V. & Casco, V. H. (2018) also suggested that Cypermethrin inducesDNA damage and oxidative stress by evaluating the possible genotoxic effect of Cyp and oxidative stress in retinal cells of adult Zebrafish exposed to 0.3μg/L and 0.6 μg/L Cyp. Histological and immunofluorescence (IF) techniques were performed on Zebrafish which showed that there was presence of apoptotic cells in retina after 9 days of exposure with 0.6 μg/L Cyp. A double-stranded DNA damage marker i.e. histone γ-H2AX, was immunodetected in both the outer and inner nuclear layer after treatment of 0.6 μg/L Cyp, for 12 days; whereas the apoptotic antibody anti-caspase- 3 was detected in the outer nuclear layer. From these results, it was confirmed that the activities of superoxide dismutase and catalase increased markedly after exposure to 0.6 μg/L Cyp. The similar treatment caused a positive regulation of the mRNA levels of both genes.

In a research by Chow, W. S. (2009), Zebrafish embryo-larvae were used as a model to investigate the responses of biomarker gene expression to pesticides. The biomarkers selected include the biotransformation phase I cytochrome P450 (CYP) enzymes, CYPIA and 3A65, enzymes for the antioxidant defense system pi-class glutathione S-transferase (GST) and catalase (CAT), the multiple drug resistance gene (MDRl) which encodes P-glycoprotein and the yolk precursor protein vitellogenin (VTGl) which is an in vivo biomarker for estrogenicity in oviparous vertebrates. Inductions of CAT and GST demonstrated oxidative-stress-inducting potential of chlorpyrifos and cypermethrin.

Due to great photo stability and insecticidal action, Bifenthrin (BF) is majorly used as a miticide in nurseries, orchards and homes. In one of the studies, the developmental effects of Bifenthrin were analysed in embryo and larval Zebrafish. The hatching process of larva was accelerated by Bifenthrin in a concentration-dependent way, associated with increased spontaneous movement. Assays for locomotor activity showed that 96 hpf larvae revealed impaired swimming behaviour after treatment with 50, 100, and 200 μg/ L from 3 to 84 hpf. Furthermore, expression of vitellogenin I were remarkably induced in larvae exposed to 150 μg/ LBifenthrin for 72 hours, suggesting the disruption in the level of endocrine. In summary, these studies exhibited that Bifenthrin was developmentally toxic to early life stages of Zebrafish. It could alsoimpair the behaviour having much importance in the assessment of their ecological fitness (Jin, M. et al., 2009).

Fenvalerate (FV) is one of the most dynamic Pyrethroid insecticides as it can constrain a wide range of insects in public health situations, animal houses and agricultural fields. Gu, A. et al. (2010) studied Fenvalerate toxicity on Zebrafish. Their results demonstrated that larvae treated with Fenvalerate for 24–96 h displayed obvious morphological abnormalities. The LC50 concentrations were 131.95 µg/L, 107.18 µg/L, 21.76 µg/L, and 6.25 µg/L for 24,48,72 and 96 hrs respectively. Acridine orange staining showed notable signs of apoptosis mainly in the brain. Furthermore, FV induced alterations in Superoxide dismutase activity in larvae were concentration dependent and correlated to the length of treatment. FV also down-regulated the ogg1 and dlx2 genes' expression in a concentration dependent manner, suggestive of oxidative-DNA repair system as well as neurogenesis were impaired.

Sometimes two or more than two compounds induce more damages when introduced simultaneously. In previous study by Yang, Y. et al. (2014), embryo-larval Zebrafish were used to explore the combined effects of lethal concentrations of Permethrin and Cypermethrin. Their data exhibited that the mixture of Permethrin and Cypermethrin caused higher occurrence of morphological defects, higher inhibition in expression of proneural gene and more oxidative stress when compared to only one chemical at the equivalent doses. The results suggest that the combination of both types of pyrethroids produce a higher risk to fishes in the water column.

A commercial product called Pesguard FG161™ is a mixture of d-tetramethrin and cyphenothrin (in a 1:3 ratio), is widely used for quick control of dengue vector, i.e. *Aedesaegypti*, in the disease outbreaks. In one of the research, Zebrafish embryos were exposed to a binary mixture of pyrethroids at different concentrations. This dual mixture was extensively poisonous to Zebrafish embryos being concentration and time dependent. The most common toxic effect observed was coagulation of embryos along with lack of heartbeat and lack of somite formation (Mendis, J. C. et al., 2018).

Pyrethroids were hypothesised to affect their reproductive capacity along with other behavioural, morphological and genetic changes. In one of the research, both male and female Zebrafish, were exposed to 96-h LC5 values of Deltamethrin (DM) (0.016 µg dm-3) and Achook (0.025 µg dm-3) for 3 months. To observe the fecundity and hatchability, the fish were returned back to normal water and permitted to breed. The results showed remarkable reductions in fecundity and hatchability compared to control group. It was concluded that lower concentrations (at 96-h LC5 values) of both of the pesticides can have a notable impact on the reproduction of Zebrafish (Sharma, D. K. & Ansari, B. A., 2010).

For last few years, enantioselectivity of chiral pollutants has attracted researchers due to the difference in toxicology and environment fate between enantiomers. Sps (Synthetic pyrethroids) are from a family of chiral germicides having a great number of stereoisomers.

Toxicity assays of each isomer and racemate of Fenvelarate (FV) were performed using *Daphnia magna* (*D. magna*), Zebrafish (*Daniorerio*) and Zebrafish embryo-larvalin a research by Ma, Y. et al. (2009).The examination of 4 day old Zebrafish embryo & larvae demonstrated that exposure to Fenvelarateenantioselectively convinced crooked body, yolk sacedema and pericardial edema; also other observation came out that the αS-2S-FV was 3.8 times stronger than the other isomers in 96-h mortality. The results showed that, in evaluating the ecological effects of SPs, the enantiomeric differences should also be considered.

In one of the studies, the individual enantiomers of beta cypermethrin were tested in Zebrafish embryo and it demonstrated that beta-Cypermethrinenantioselectively provoked yolk sac edema, pericardial edema and crooked body. The results suggest that, to evaluate ecotoxicological effects of Cypermethrin, enantio selective effects of beta-CP should also be considered (Xu, C. et al., 2010).

Bifenthrin (BF) has an adverse effect on the behaviour and development of other than target organisms. However, there have been very few researches generated on effects of various enantiomers on the locomotor behaviour for SPs in Zebrafish, and whether locomotor actions are associated with the developmental toxicities remains to be clear.

In another research, enantioselectivity of Bifenthrin (BF, 1S and 1R), on acute locomotor activity and embryonic–larval developmental toxicitiesin Zebrafish were primarily evaluated. Administration of 20 μg/L of one enantiomer of Bifenthrin had distinctive effects on locomotor activity of larvae at 4dpfs under required light conditions. The results indicated that the enantio selectivity in locomotor activity might be due to differential effects on development. Moreover, 1R-BF induced the spontaneous movement and hatching process, while 1S-BF seemed to be inhibitory. The results suggest that, to achieve more comprehensive health risk assessments of chiral pesticides, there is a need to link behavioral changes to developmental toxicities (Jin, M. et al., 2010). Other research suggests that cis-bifenthrin could increase the transcription of genes related to the immune system in Zebrafish, including IL-8, IL-1β, and CXCL-Clc (Jin,Y. et al., 2013).

Due to high lipophilic nature, Synthetic pyrethorids are demonstrated to bioaccumulate in fish (4938 ng/g) (Richards, J. et al., 2017). 3-Phenoxybenzoic acid (PBA) is an important metabolite formed after metabolism of Deltamethrin (DM). One research was conducted in

order to demonstreate the toxic reactions in Zebrafish embryos & larvae to DM and PBA. Deltamethrin treated embryos or larvae demonstrated increased mortality, delayed hatching time, decreased rate of hatched embryos, increased heartbeat rate and decreased blood flow; also reduced body and eye pigmentation in a dose dependent manner was observed. DM also induced pericardial and yolk sac edema. Together with crooked notochord, deformation of tail was also observed in hatched and unhatched embryos. Whereas in PBA exposed to embryos/larvae, increased embryos & larval length and yolk sac size were noticed. Other deformities such as yolksacedema and pericardial edema, in some embryos reduced eye and body pigmentation were too observed. These responses were not as critical as seen in parental compound suggesting that Deltamethrin is more noxious than metabolite PBA. The results give a better perception of the probable consequences of fish treated with Deltamethrin and PBA (Kuder, R. S.& Gundala, H. P., 2018).

Similarly total protein content was estimated in one of the research after exposure of 5µg/L of deltamethrin for 6 days to Zebrafish. Alterations of various proteins in 5 different tissues named liver, brain, kidney, ovary and testis in adult Zebrafish were identified. The protein content was increased in both male and female brain, kidney and ovary while it was decreased in male and female liver tissue and testis. Compared to their control groups, protein bands being more eminent in brain, kidney, ovary and testis in deltamethrin treated groups (Shamshad Begum S. et al., 2016).Some studies have indicated that endocrine disrupters, such as SPs and 17β-estradiol, could induce the mRNA expression of genes involved in the innate immune system of Zebrafish larvae (Jin, Y. et al., 2010; Jin, M. et al., 2010).

Conclusion

The extensive research on Zebrafish (*Danio rerio*) represents it as an ideal model organism with diverse applications in the various fields of science. Specifically in developmental stages of life, researches give remarkable information unfolding various pathways. The review suggests that Zebrafish and Zebrafish embryo, as a model, gives better understanding to promote a change in conventional applications of Pyrethroid usage as well as its use in other similar toxicology studies.

References:

Adelsbach, T. L., & Tjeerdema, R. S., 2003. Chemistry and fate of fenvalerate and esfenvalerate. Reviews of Environmental Contamination and Toxicology, 137-154.

Awoyemi, O. M., Kumar, N., Schmitt, C., Subbiah, S., & Crago, J., 2019. Behavioral,

molecular and physiological responses of embryo-larval zebrafish exposed to types I and II pyrethroids. Chemosphere, 219, 526-537.

Chico, T. J., Ingham, P. W., & Crossman, D. C., 2008. Modeling cardiovascular disease in the zebrafish. Trends in cardiovascular medicine, 18(4), 150-155.

Chow, W. S., 2009. Effects of Pesticides on Biomarker Gene Expressions in Zebrafish Embryo-larvae (Doctoral dissertation, Chinese University of Hong Kong).

DeMicco, A., Cooper, K. R., Richardson, J. R., & White, L. A., 2010. Developmental neurotoxicity of pyrethroid insecticides in zebrafish embryos. Toxicological Sciences, 113(1), 177-186.

Gu, A., Shi, X., Yuan, C., Ji, G., Zhou, Y., Long, Y., & Wang, X., 2010. Exposure to fenvalerate causes brain impairment during zebrafish development. Toxicology letters, 197(3), 188-192.

Hamilton, F., 1822. An account of the fishes found in the river Ganges and its branches (Vol. 1). Archibald Constable.

Jin, M., Li, L., Xu, C., Wen, Y., & Zhao, M., 2010. Estrogenic activities of two synthetic pyrethroids and their metabolites. Journal of Environmental Sciences, 22(2), 290-296.

Jin, M., Zhang, X., Wang, L., Huang, C., Zhang, Y., & Zhao, M., 2009. Developmental toxicity of bifenthrin in embryo-larval stages of zebrafish. Aquatic Toxicology, 95(4), 347-354.

Jin, M., Zhang, Y., Ye, J., Huang, C., Zhao, M., & Liu, W., 2010. Dual enantioselective effect of the insecticide bifenthrin on locomotor behavior and development in embryonic–larval zebrafish. Environmental Toxicology and Chemistry, 29(7), 1561-1567.

Jin, Y., Chen, R., Liu, W., & Fu, Z., 2010. Effect of endocrine disrupting chemicals on the transcription of genes related to the innate immune system in the early developmental stage of zebrafish (*Danio rerio*). Fish & shellfish immunology, 28(5-6), 854-861.

Jin, Y., Pan, X., Cao, L., Ma, B., & Fu, Z., 2013. Embryonic exposure to cis-

bifenthrinenantioselectively induces the transcription of genes related to oxidative stress, apoptosis and immunotoxicity in zebrafish (*Daniorerio*). Fish & shellfish immunology, 34(2), 717-723.

Jin, Y., Zhang, X., Shu, L., Chen, L., Sun, L., Qian, H., & Fu, Z., 2010. Oxidative stress response and gene expression with atrazine exposure in adult female zebrafish (*Daniorerio*). Chemosphere, 78(7), 846-852.

Jin, Y., Zheng, S., & Fu, Z., 2011. Embryonic exposure to cypermethrin induces apoptosis and immunotoxicity in zebrafish (*Daniorerio*). Fish & shellfish immunology, 30(4-5), 1049-1054.

Jin, Y., Zheng, S., Pu, Y., Shu, L., Sun, L., Liu, W., & Fu, Z., 2011. Cypermethrin has the potential to induce hepatic oxidative stress, DNA damage and apoptosis in adult zebrafish (*Daniorerio*). Chemosphere, 82(3), 398-404.

Kadiru, S., 2018. Developmental toxicity of Cyfluthrin in Embryo – Larval stages of Zebrafish. International Journal of Advanced Scientific Research and Management,3(2).

Kuder, R. S., & Gundala, H. P., 2018. Developmental toxicity of deltamethrin and 3-phenoxybenzoic acid in embryo–larval stages of zebrafish (*Daniorerio*). Toxicology mechanisms and methods, 28(6), 415-422.

Kung, T. S., Richardson, J. R., Cooper, K. R., & White, L. A., 2015. Developmental deltamethrin exposure causes persistent changes in dopaminergic gene expression, neurochemistry, and locomotor activity in zebrafish. Toxicological Sciences, 146(2), 235-243.

Langheinrich, U., 2003. Zebrafish: a new model on the pharmaceutical catwalk. Bioessays, 25(9), 904-912.

Lettieri, T., 2006. Recent applications of DNA microarray technology to toxicology and ecotoxicology. Environmental health perspectives, 114(1), 4-9.

Ma, Y., Chen, L., Lu, X., Chu, H., Xu, C., & Liu, W., 2009. Enantioselectivity in aquatic toxicity of synthetic pyrethroid insecticide fenvalerate. Ecotoxicology and Environmental Safety, 72(7), 1913-1918.

Ma, Y., Han, J., Guo, Y., Lam, P. K., Wu, R. S., Giesy, J. P., & Zhou, B., 2012. Disruption of endocrine function in in vitro H295R cell-based and in in vivo assay in zebrafish by 2, 4-dichlorophenol. Aquatic toxicology, 106, 173-181.

Mendis, J. C., Tennakoon, T. K., & Jayasinghe, C. D., 2018. Zebrafish embryo toxicity of a binary mixture of pyrethroid insecticides: d-tetramethrin and cyphenothrin. Journal of toxicology, 2018.

Nagel, R., 2002. DarT: The embryo test with the ZebrafishDaniorerio--a general model in ecotoxicology and toxicology. Altex, 19, 38-48.

Narahashi, T., 2000. Neuroreceptors and ion channels as the basis for drug action: past, present, and future. Journal of Pharmacology and Experimental Therapeutics, 294(1), 1-26.

Neumann, N. F., & Galvez, F., 2002. DNA microarrays and toxicogenomics: applications for ecotoxicology?. Biotechnology advances, 20(5-6), 391-419.

OECD, OECD guideline for the testing of chemicals, draft proposal for a new guideline, Fish Embryo Toxicity (FET) Test, 2006. URL: https://www.oecd.org/chemicalsafety/testing/36817070.pdf

Paravani, E. V., & Casco, V. H., 2018. Genotoxicity Induced by Cypermethrin in the Zebrafish Retina. Genotoxicity-A Predictable Risk to Our Actual World, 41.

Ramchandra, A. M., Chacko, B., & Victor, P. J., 2019. Pyrethroid poisoning. Indian journal of critical care medicine: peer-reviewed, official publication of Indian Society of Critical Care Medicine, 23(Suppl 4), S267.

Rehman, H., Aziz, A. T., Saggu, S. H. A. L. I. N. I., Abbas, Z. K., Mohan, A. N. A. N. D., & Ansari, A. A., 2014. Systematic review on pyrethroid toxicity with special reference to deltamethrin. Journal of entomology and zoology studies, 2(6), 60-70.

Rhaul de Oliveira, 2009 (pp. 4-6) “Background, Aim and Scope,” Zebrafish early life-stages and adults as a tool for ecotoxicity assessment, Univversidade de Aveiro.URL: https://ria.ua.pt/bitstream/10773/8838/1/6237.pdf

Richards, J., Lu, Z., Fu, Q., Schlenk, D., & Gan, J., 2017. Conversion of pyrethroidinsecticides to 3-phenoxybenzoic acid on urban hard surfaces.

Environmental Science & Technology Letters, 4(12), 546-550.

Rubinstein, A. L., 2006. Zebrafish assays for drug toxicity screening. Expert opinion on drug metabolism & toxicology, 2(2), 231-240.

Scalzo, F. M., & Levin, E. D., 2004. The use of zebrafish (*Daniorerio*) as a model system in neurobehavioral toxicology. Neurotoxicology and teratology, 26(6), 707-708.

Scholz, S., Fischer, S., Gündel, U., Küster, E., Luckenbach, T., & Voelker, D., 2008. The zebrafish embryo model in environmental risk assessment—applications beyond acute toxicity testing. Environmental science and pollution research, 15(5), 394-404.

Shabnam, K. R., Gangappa, D., & Philip, G. H., 2019. Zebrafish embryos exposed to deltamethrin exhibit abnormalities despite induced expression of related genes (you, you-too, momo and u-boot). Toxicology and Industrial Health, 35(1), 11-19.

Shamshad Begam, S., Suvarchala, G., & Philip, G. H., 2016. Protein profile in tissues of zebrafish exposed to deltamethrin. Journal of Bio Innovation, 5(6), 914-922.

Shao, B., Zhu, L., Dong, M., Wang, J., Wang, J., Xie, H., & Zhu, S., 2012. DNA damage and oxidative stress induced by endosulfan exposure in zebrafish (*Daniorerio*). Ecotoxicology, 21(5), 1533-1540.

Sharma, D. K., & Ansari, B. A., 2010. Effect of the synthetic pyrethroidDeltamethrin and the neem-based pesticide Achook on the reproductive ability of zebrafish, *Daniorerio* (Cyprinidae). Fisheries & Aquatic Life, 18(3), 157-161.

Shi, X., Gu, A., Ji, G., Li, Y., Di, J., Jin, J., & Wang, X., 2011. Developmental toxicity of cypermethrin in embryo-larval stages of zebrafish. Chemosphere, 85(6), 1010-1016.

Spitsbergen, J. M., & Kent, M. L., 2003. The state of the art of the zebrafish model for toxicology and toxicologic pathology research—advantages and current limitations. Toxicologic pathology, 31(1_suppl), 62-87.

Thatheyus, A. J., &Selvam, A. G., 2013. Synthetic pyrethroids: toxicity and biodegradation. ApplEcol Environ Sci, 1(3), 33-36.

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

Xu, C., Tu, W., Lou, C., Hong, Y., & Zhao, M., 2010. Enantioselective separation and zebrafish embryo toxicity of insecticide beta-cypermethrin. Journal of environmental sciences, 22(5), 738-743.

Yang, Y., Ma, H., Zhou, J., Liu, J., & Liu, W., 2014. Joint toxicity of permethrin and cypermethrin at sublethal concentrations to the embryo-larval zebrafish. Chemosphere, 96, 146-154.

Zaveri, M., 2010. Study links pesticides to river contamination. The Daily Californian.

Zon, L. I., & Peterson, R. T., 2005. In vivo drug discovery in the zebrafish. Nature reviews Drug discovery, 4(1), 35-44.

Suggested citation:
Kulkarni K. & Desai J. (2022). A Review on Zebrafish (Danio rerio) and Zebrafish embryo as a tool to study pyrethroid compounds' toxicity. Prithivya, An Official Newsletter of WCB Research Foundation and WCB Research Lab. Vol 2(3) 34-47.