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SHORT COMMUNICATION

# Toxicity of fipronil insecticide on the early life stages of *Colossoma macropomum* (gamitana)

**Miguel Saldaña-Serrano . Dante Espinoza-Morriberon . Gabriel Enrique De-la-Torre . Guillermo Odilón Álvarez-Béjar . Alberto López**

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**Abstract** The present study was aimed to determine the lethality of the insecticide fipronil on two early life stages, post-larvae, and fingerling, of *Colossoma macropomum*, by determining the lethal concentration 50 ($LC_{50}$). Five nominal concentrations (0.12; 0.165; 0.21; 0.255 and 0.30 mg/L) and a control in 4 replicates per treatment for 48 hours of exposure were used for the post-larvae; and other nominal concentrations (0.22; 0.27; 0.34; 0.43 and 0.54 mg/L) and a control in 3 replicates per treatment for 96 hours of exposure were used for the fingerling stage. The $LC_{50}$ value was calculated as 0.22 mg/L and 0.33 mg/L for the post-larvae and fingerling stages, respectively. In addition, the maximum concentration that causes no mortality (MCNM) and the minimum concentration that causes mortality (MCM) for the post-larvae stage were determined as 0.12 and 0.15 mg/L, respectively; and 0.16 and 0.22 mg/L for the fingerling stage, respectively. *C. macropomum* showed erratic swimming, spasms in the region of the peduncle, caudal fin, and accelerated opercular movement in both life stages. The $LC_{50}$ values calculated in the present study are considered "highly toxic" for the early stages of life of this non-target organism, suggesting that *C. macropomum* may be a sensitive species to fipronil insecticide.

**Keywords** LC50 . Fipronil . Gamitana . Freshwater . Amazon fish . Aquaculture

## Introduction

Fipronil is a broad-spectrum phenylpyrazole insecticide registered in the 1990s and used for agricultural purposes ever since (Beasley 2020). This insecticide has been extensively used in seed-coasting formulations (Raveton et al. 2007) and direct soil treatment to control a wide range of underground pests (dos Santos et al. 2016). The worldwide popularity of fipronil is attributed to its effectiveness against pests that are resistant to conventional pesticides, such as pyrethroids and organophosphates (Pino-Otín et al. 2021). The action mechanism of fipronil acts by targeting and inhibiting the γ-aminobutyric acid (GABA) receptor chloride

Miguel Saldaña-Serrano (✉)
Universidad San Ignacio de Loyola, Lima - Peru
e-mail: miansaldana@gmail.com

Dante Espinoza-Morriberon
Universidad Tecnológica del Perú (UTP), Facultad de Ingeniería, Lima-Peru ; Facultad de Ingeniería Ambiental y de Recursos Naturales (FIARN). Universidad del Callao (UNAC), Callao – Peru

Gabriel Enrique De-la-Torre
Grupo de Investigación de Biodiversidad, Medio Ambiente y Sociedad, Universidad San Ignacio de Loyola, Lima, Peru

Guillermo Odilón Álvarez-Béjar
Laboratorio de Biología Acuática y Acuicultura. Departamento de Biología Celular y Genética. Facultad de Ciencias Biológicas. Universidad Nacional Mayor de San Marcos, Peru

Alberto López
Grupo de Investigación en Recursos Genéticos, Facultad de Ciencias Biológicas. Universidad Nacional Mayor de San Marcos. Lima, Peru

channels in the nervous system (Wang et al. 2016). Insect exposure to fipronil causes blockade of the inhibitory nerve transmission, resulting in hyperexcitability and death (Page 2008). The binding affinities of fipronil to mammalian gamma-aminobutyric acid ($GABA_A$) neurotransmitter receptors are significantly weaker than in insects (Zhao et al. 2003), demonstrating its low toxicity to mammals. However, fipronil can be highly toxic to other non-target organisms, such as terrestrial and aquatic species (Stehr et al. 2006; Gunasekara and Troung 2007; Taillebois et al. 2015). In terrestrial invertebrates, fipronil is known to cause lethal effects of the collembolan species *Folsomia candida* (Alves et al. 2014, Oliveira 2017), as well as sub-lethal effects in honeybees species *Apis mellifera* (Carrillo et al. 2013; Pisa et al. 2015; Holder et al. 2018). Concerning aquatic species, fipronil is known to cause acute lethal effects in *Cyprinodon variegatus*, *Lepomis macrochirus*, and *Oncorhynchus mykiss* (Beggel et al. 2010). The evidence regarding the toxicity of fipronil on non-target organisms led to its restricted use (Zhang et al. 2018).

On the other hand, the species "gamitana" (*Colossoma macropomum*) is an Amazonian fish of major importance to freshwater aquaculture in Southern and Central American countries (Sandre et al. 2017). The success of *C. macropomum* in Amazonian aquaculture relies on its relatively fast growth rate, diverse diet composition, and nutritional value (Ramos et al. 2016; Sousa et al. 2002). However, given the inherent exposure to chemicals associated with agriculture in the Amazon (Silva et al. 2019), the production of *C. macropomum* could be compromised. Recent studies have evaluated the ecotoxicological effects of common pesticides in *C. macropomum* (Soares et al. 2016; Rico et al. 2011). However, there are still no environmental regulatory standards of fipronil, especially for aquatic ecosystems, in Peru. This evidences the lack of information on the toxicity that this insecticide may cause on aquatic biota, such as organisms cultivated for human consumption or those that play key ecosystemic roles. In this sense, it is necessary to carry out acute and/or chronic toxicity tests that generate information and contribute with the Peruvian public environmental entities to establish maximum permissible limits for fipronil. Therefore, this study aimed to determine the lethal concentration 50 ($LC_{50}$) of the commercial insecticide Regent© in concentrated solution (SC) (A.I = fipronil 18.87%) in two early life stages (post-larvae and fingerlings) of *C. macropomum* with the purpose of establishing reference values for future toxicity studies and in this way, suggesting environmental regulatory measures for this insecticide in the Peruvian Amazon as it could pose a threat to freshwater aquaculture.

## Materials and methods

*C. macropomum* larvae with yolk-sac were acclimatized in glass aquariums of 150 L of volume, with temperature = 27 °C, dissolved oxygen = 9.83 mg/L, pH = 8.00, and water hardness = 80 mg/L. Then, during the post-larvae stage (20 days after hatching; 0.019 ± 0.01 g; 1.14 ± 0.05 cm), the organisms were fed with *Artemia sp.* nauplii for 10 days and co-fed with ground balanced food for 10 days (Álvarez et al. 2008). In the fingerling stage (40 days after hatching; 0.08 ± 0.01 g; 1.67 ± 0.06 cm), the organisms were fed with extruded balanced food (protein 28%) three times a day.

### Toxicity Test

Both toxicity tests followed the Fish Early Life Stage Toxicity Test (Organization for Economic Cooperation and Development – OECD 2013) guidelines. Feeding was suspended 24 hours before starting the toxicity tests to then transfer 10 organisms to aquariums (3 L) of soft water and finally, each aquarium was placed in larger aquariums (50 L) in a water bath system (temperature = 30 °C) controlled by thermostats. Two hours before starting the toxicity test a stock solution was prepared by diluting 0.1 ml of Regent© SC (A.I = 200 g/L) in 1 L of soft water, resulting in a final concentration of 20 mg/L. The final concentrations used in the toxicity test with the organisms in the post-larvae stage were determined through preliminary tests (Organization for Economic Cooperation and Development – OECD 2013), and the final concentrations for the toxicity test with the organisms in the fingerling stage were determined based on the results obtained in the final toxicity tests with the post-larvae. **First Acute Toxicity Test:** For the post-larvae stage, the nominals concentrations were: Control; 0.12; 0.165; 0.21; 0.255 and 0.30 mg/L with four replicates per treatment and 48 hours of exposure; **Second Toxicity Test:** For the fingerlings, the nominals concentrations

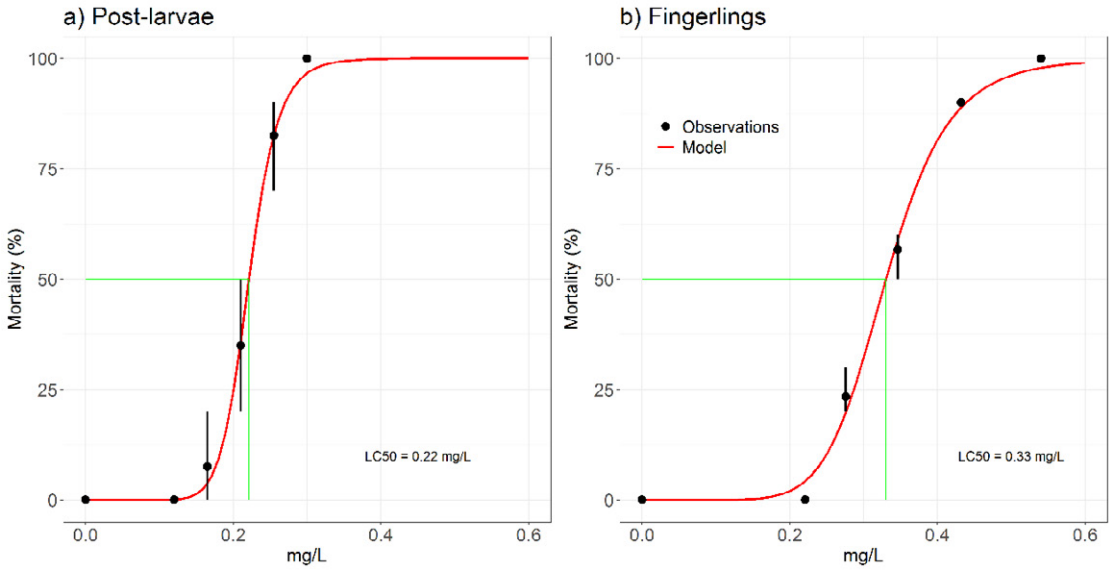


**Fig. 1** Concentration-mortality modeled curves (red line) and observation (black points) for both acute toxicity tests. The values of $LC_{50}$ are also indicated (green line).

were: Control; 0.22; 0.27; 0.34; 0.43 and 0.54 mg/L with three replicates per treatment and 96 hours of exposure. Both toxicity tests were carried out in a static system and the water quality parameters were monitored at the beginning and the end of the assay (temperature = 30 ± 0.5 °C; pH = 7.87 ± 0.05; dissolved oxygen = 4.15 ± 0.05 mg/L and hardness 80 mg/L as $CaCO_3$). The $LC_{50}$ values were calculated using the log-logistic model fixed with the "*drm*" function of the "*drc*" package from the R statistical software v. 4.0.2 (R 2019). The MCNM and MCM were calculated from the adjusted log-logistic model *i.e.* we calculated the difference between the mortalities corresponding to consecutive concentrations of fipronil (in our case every 0.01 mg/L). Thus, were defined as the limit concentration that the mortality is not greater than 0.1% (MCNM) and 1% (MCM). For our study, MCNM would represent the predicted no-effect concentration (PNEC), that is, the concentration that protects 99.9% of the species. In the case of the predicted environmental concentration (PEC), the environmental quality standards (ECA) of the Netherlands legislation (Tennekes 2018) were used, with the PEC of fipronil = 0.00007 µg/L. In this sense, the ecological risk was calculated using the hazard ratio (HQ) approach (HQ = PEC/PNEC) (EC 2011), which was considered significant when HQ> 1. In addition, the difference between the $LC_{50}$ of post-larvae and fingerlings was also evaluated, for that reason, the combination of all mortalities by treatments (T) and replicates by treatments (R) was used to obtain a set of $LC_{50}$ for post-larvae (4096 combinations) and fingerlings (729 combinations). The total combination was performed as $R^T$. The Kruskal-Wallis test was used to evaluate the statistical difference ($P < 0.05$) between the $LC_{50}$ values of the development stages and also, to determine statistical differences between the physicochemical parameters of the treatments ($P < 0.05$), using the *"pgirmess"* package from the R program.

## Results

In agreement with what was proposed by the Organization for Economic Cooperation and Development (OECD 2013), the control group presented 0% mortality in all cases. The lethal endpoints were calculated as $LC_{50\text{-}48h}$ = 0.22 mg/L for post-larvae and the $LC_{50\text{-}96h}$ = 0.33 mg/L for fingerlings (Fig. 1). Additionally, for the post-larval stage, the MNCM and MCM values were 0.12 mg/L and 0.16, respectively. In the case of the fingerling stage, the MNCM and MCM values were 0.15 mg/L and 0.22 mg/L, respectively.

The HQ for the post-larvae stage was 0.0005833 and for fingerlings, it was 0.0004375. No significant differences ($P > 0.05$) were found in the temperature, dissolved oxygen, and pH among treatments at the start and end of the toxicity tests (Fig. 2). There were significant differences ($P < 0.05$) in the mean $LC_{50}$ between post-larvae and fingerlings (Fig. 3).

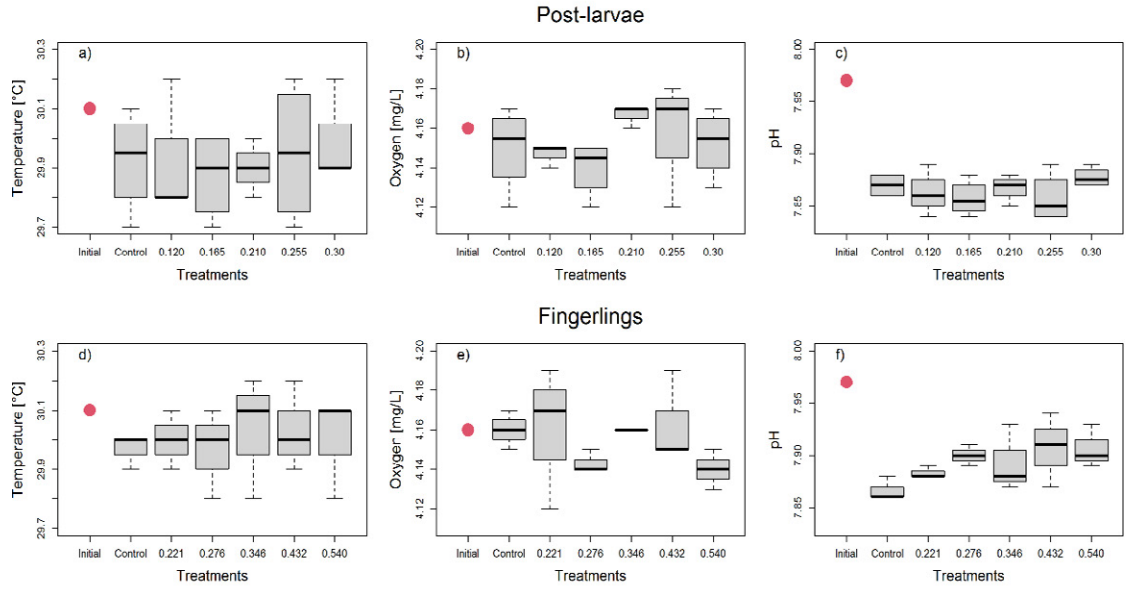


**Fig. 2** Variation of the physicochemical parameters for different treatments during toxicity tests post-larvae and fingerling stage

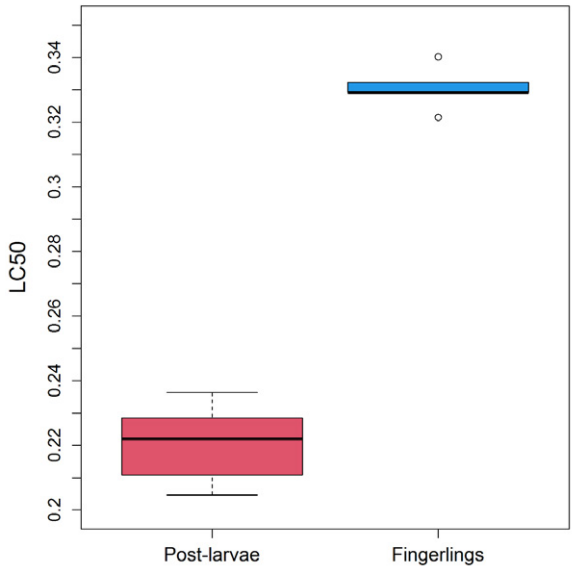


**Fig. 3** Comparison of $LC_{50}$ values calculated for post-larvae and fingerlings of *C. macropomum*

## Discussion

This is the first report to determine the $LC_{50}$ of fipronil insecticides on early life stages of freshwater fish *C. macropomum*. Comparing our results with other studies, Ardeshir et al. (2017) determined the $LC_{50\text{-}96h}$ (572 µg/L) in fingerlings of white Caspian, *Rutilus frisii kutum*, which was highly toxic to fish. Al-Badran et al. (2018) reported the $LC_{50\text{-}96h}$ (1.3 µg/L) of fipronil in juvenile brown shrimp *Farfantepenaeus aztecus*. Similarly, Gómez-Manrique (2009) determined the $LC_{50\text{-}96h}$ (0.08 mg/L) of fipronil in guarú *Poecilia reticulata* fingerlings, classifying these values as extremely toxic and Cella (2009) reported the $LC_{50\text{-}96h}$ (1.04 mg/L and 0.34 mg/L) of fipronil in juveniles of pacu *Piaractus mesopotamicus* and paulistinha *Danio rerio*, respectively. The $LC_{50}$ values calculated in post-larvae and fingerlings were compared to previous studies that evaluated the toxicity of different pesticides on *C. macropomum* (Table 1). Soares et al. (2016) reported a slightly higher $LC_{50\text{-}96h}$ (0.58 mg/L) of the pesticide Lufenuron in juveniles. Similarly, Duncan

**Table 1** Comparative studies of the acute tests of pesticides for *C. macropomum* in different stages of development

| Type of pesticide | Name | Stage | Duration | $LC_{50}$(CI) | Reference |
|---|---|---|---|---|---|
| Insecticide | Fipronil | Post-larvae | 48h | 0.22 mg/L (0.20 – 0.24 mg/L) | This study |
| Insecticide | Fipronil | Fingerling | 96h | 0.33 mg/L (0.29 – 0.36 mg/L) | This study |
| Insecticide | Malathion | Fingerling | 96h | 1.51 mg/L (1.36 – 1.67 mg/L) | (Rico et al. 2011) |
| Insecticide | Malathion | Juvenile | 96h | 15.8 mg/L | (de Souza et al. 2020b) |
| Antifungal | Carbendazim | Fingerling | 96h | 4.16 mg/L (3.43 – 5.04 mg/L) | (Rico et al. 2011) |
| Insecticide | Lufenuron | Juvenile | 96h | 0.58 mg/L (0.46 – 0.71 mg/L) | (Soares et al. 2016) |
| Insecticide | Deltamethrin | Fry | 96h | 6.69 µg/L (5.58 – 8.01 µg/L) | (de Souza et al. 2020a) |
| Insecticide | Trichlorfon | Juvenile | 96h | 0.87 mg/L (0.66 – 1.15 mg/L) | (Duncan et al. 2020; da Silva et al. 2020) |

et al. (2020) and da Silva et al. (2020) calculated the $LC_{50\text{-}96h}$ of the insecticide Trichlorfon as 0.87 mg/L in juveniles. The lowest $LC_{50\text{-}96h}$ calculated for the insecticide deltamethrin was reported by de Souza et al. (2020a), reaching 6.69 $10^{-3}$ mg/L in fry *C. macropomum*. In another study, the $LC_{50\text{-}96h}$ of the insecticide Malathion was evaluated by Rico et al. (2011), where the stage of development was not reported, and by (de Souza et al. 2020b), where the experiments were carried out on fingerlings. Furthermore, the rate of mortality showed significant differences among treatments ($P < 0.05$) for both toxicity tests, demonstrating the concentration-response behavior of *C. macropomum* mortality in the early stages of development.

On the other hand, several studies have determined chronic toxicity values and assessed sub-lethal effects for other pesticides in aquatic organisms (Soares et al. 2016; Salazar-Lugo et al. 2011). In this context, we found no observed effect concentrations (NOECs) and the lowest observed effect concentrations (LOECs). However, their use has been widely criticized, i.e. due to their computation only taking into account the concentrations of the test chemicals used in the treatments (Warne and Dam 2008). Therefore, we propose the values of the MCNM and MCM for post-larvae and fingerlings in our study. Both values may serve to set the ground for national legislation, specifically, determining the Maximum Permissible Limits for use in agricultural crops and Environmental Quality Standards in Peruvian waters, including Amazonian aquatic environments. Finally, we demonstrate the difference between the $LC_{50}$ of post-larvae and fingerlings, despite presenting similar experimental setups, the estimated values that differed in about an order of magnitude, may likely be due to the difference in the developmental stage of the test organisms used in this study. According to our results, the toxicity of fipronil for the post-larvae and fingerlings stage of *C. macropomum* is considered "high", since they are within the range of $LC_{50}$ = 0.11-1.0 mg/L in agreement with the classification for insecticides proposed by Helfrich et al. (2009). The toxicity of fipronil is based on its main mechanistic interaction with gamma-aminobutyric acid (GABA) receptors and other sublethal effects Wang et al. (2016). In that sense, several studies have demonstrated the sublethal effects of fipronil on *C. macropomum*. López et al. (2011) exposed *C. macropomum* fingerlings to 75 µg/L of fipronil, the frequency of nuclear aberrations (micronucleus) in peripheral blood samples was double than that of the control group after 48h of exposure. Dallarés et al. (2020) demonstrated that spiked food at a concentration of 10 mg/kg fipronil was metabolized by European sea bass *Dicentrarchus labrax, ultimately* causing metabolic disturbances and gonadal histological alterations. Sanahuja et al. (2020) demonstrated that fipronil exposure (7 and 14 days) caused a significant increase in brain acetylcholinesterase and carboxylesterases activities. Silva et al. (2019) demonstrated that Roundup®, a glyphosate-based herbicide, caused increased glutathione-S-transferase and catalase activities in the livers, as well as cellular and DNA damages, which were exacerbated by scenarios of hypoxia. Roundup© may also cause histopathological damage in gills and alterations in hematological parameters (Braz-Mota et al. 2015). A different pesticide, Trichlorfon, causes errand swimming and behavior shortly after exposure (da Silva et al. 2020), as well as brain and muscle acetylcholinesterase inhibition at low concentrations (~0.7 mg/L) (Duncan et al. 2020).

## Conclusion

This study showed that the commercial insecticide Regent SC (fipronil) is highly toxic for the early stages of life of this freshwater fish, demonstrating its sensitivity and suggesting *C. macropomum* as a test organism. In addition, the use of these acute toxicity values in monitoring programs is recommended, since they would represent a threat to Amazonian aquaculture areas and would serve in the development of

environmental regulations for Perú.

**Conflict of interest** The authors declare no competing interests.

**Authors' contribution** (M.A.S.S) conducted the toxicity tests and laboratory analysis, performed the statistical analysis, discussion and drafted the manuscript; (D.E.M) participated in statistical analysis, discussion and drafted the manuscript; (G.E.D.L.T) discussion and drafted the manuscript; (G.O.A.B) participated in the design and coordination of the project; (A.L) participated in the design and coordination of the project. All authors read and approved the final manuscript.

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