

Article

Tetraniliprole Triggers Transgenerational Hormesis in an Invasive Insect Herbivore: Molecular and Biological Insights

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Simple Summary

This study investigated the sublethal effects of tetraniliprole on the invasive tomato pest, *Tuta absoluta*. Although tetraniliprole caused high toxicity in third-instar larvae, sublethal (LC₁₀) and low lethal (LC₃₀) concentrations had complex effects across generations. The directly exposed generation (F₀) experienced decreased development and reproduction. However, its offspring (F₁ and F₂) showed a dual response: the LC₁₀ promoted faster development and increased population growth (hormetic-like effects), while the LC₃₀ continued to cause negative effects. These changes were linked to altered expression of key genes involved in reproduction, development, and detoxification. The results highlight a significant risk of unintended population resurgence at sublethal concentrations and emphasize the importance of considering these transgenerational effects in resistance management strategies.

Abstract

The South American tomato pinworm, *Tuta absoluta* (Meyrick), is among the most destructive invasive pests of tomato globally. The diamide insecticide tetraniliprole is increasingly used for its management. This study examines the sublethal effects of tetraniliprole on *T. absoluta* larvae, with a focus on its transgenerational impacts. Bioassays demonstrated that tetraniliprole was highly toxic to third-instar *T. absoluta* larvae, with an LC₅₀ of 0.029 mg/L. Sublethal (LC₁₀) and low lethal concentrations (LC₃₀) were used to investigate their impact on developmental, reproductive, and population parameters across two subsequent generations (F₁ and F₂). In the parental (F₀) generation, exposure to tetraniliprole at both concentrations significantly prolonged larval and pupal durations and reduced adult longevity and fecundity. In both F₁ and F₂ generations, concentration-dependent effects were observed—LC₁₀ accelerated development and enhanced fecundity and population growth, indicative of a hormetic response, whereas LC₃₀ delayed development and



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suppressed reproduction and survival. Life table analyses revealed significant changes in the r , λ , and T , particularly under LC₃₀. Additionally, the RT-qPCR analysis revealed the downregulation of development and reproduction-related genes (*Vg*, *VgR*, and *JHBP*) in the F₀ generation following exposure to tetraniliprole (LC₁₀ and LC₃₀). In contrast, these genes were upregulated in the progeny generations (F₁ and F₂) at LC₁₀. Furthermore, the overexpression of key detoxification genes, particularly *CYP4M116* and *CYP6AW1*, persisted across all three generations. Taken together, these findings reveal a substantial risk of unintended population resurgence (hormesis effects) at sublethal concentrations, underscoring the importance of integrating transgenerational consequences into insecticide resistance management programs for sustainable control of this key insect pest.

Keywords: diamide; *Tuta absoluta*; hormesis; sublethal effects; life table; insecticide resistance

1. Introduction

The South American tomato pinworm, *Tuta absoluta* (Meyrick) (Lepidoptera: Gelechiidae), is recognized as one of the most devastating insect pests of tomato crops [1,2]. Since its emergence in South America, *T. absoluta* has rapidly expanded its geographic range and now invades over 90 countries worldwide [2,3]. In addition to tomatoes, this invasive pest threatens other economically significant solanaceous crops such as potato, eggplant, pepper, and tobacco [4,5]. Its high reproductive capacity, cryptic larval behavior, and resistance to conventional insecticides contribute to its invasiveness and the extensive damage it causes to crops [6,7]. Infestations by *T. absoluta* result in substantial yield losses, reduced fruit quality, and increased pest management costs [2,8,9].

Although several eco-friendly approaches are available [10,11], chemical insecticides remain widely used against this pest due to their rapid results. Tetraniliprole, a third-generation anthranilic diamide insecticide, acts by targeting the ryanodine receptors in insects, disrupting calcium ion regulation and ultimately causing paralysis and death [12]. This mode of action is effective against a broad spectrum of insect pests, including Lepidoptera, Coleoptera, and Diptera, with the added advantage of minimal toxicity to non-target mammals [13–15]. However, insecticides are known to degrade over time following initial field application [16], potentially exposing arthropod populations to sublethal doses or concentrations [17]. Such exposures can induce a variety of physiological and behavioral changes, affecting insect survival, development, reproduction, and even resistance evolution [18–21]. Interestingly, sublethal doses or concentrations can sometimes paradoxically enhance certain biological traits, such as reproduction, a phenomenon known as hormesis [22,23].

Sublethal effects can also impact insect reproductive systems at the molecular level. For example, vitellogenin (*Vg*), the precursor of vitellin (*Vn*), and its receptor (*VgR*), which facilitates *Vg* transport into oocytes, play crucial roles in insect fecundity and are often disrupted under insecticidal stress [24,25]. These disruptions may affect both directly exposed individuals and their progeny, highlighting the need to assess both direct and transgenerational impacts of insecticides. Beyond reproductive genes, cytochrome P450 monooxygenases (CYPs) are central to insecticide detoxification and have long been implicated in resistance development. The upregulation of cytochrome P450 enzymes during resistance development in *T. absoluta* leads to decreased population growth rates since it creates substantial fitness costs, manifesting when insecticide pressure disappears. By investing metabolic resources in resistance mechanisms, insects suffer fitness costs that trigger reduced fecundity stress during development and growth, impairing total fitness [19–21].

Life table analyses offer a comprehensive framework to assess the cumulative effects of various stressors on insect populations, including survival, development, longevity, and reproductive potential [26,27]. Unlike traditional female-only life tables [28], the age-stage, two-sex life table approach incorporates both sexes and accounts for individual variability in developmental rates, thereby providing more accurate and holistic insights into population dynamics [27,29].

Given the widespread use of tetraniliprole and the growing concern about its sublethal impacts, it is essential to evaluate its effects not only on exposed individuals but also on their progeny. The current study investigates the sublethal and low-lethal effects of tetraniliprole on *T. absoluta* by assessing key biological traits across three generations (F_0 , F_1 , and F_2) using an age-stage, two-sex life table approach. The findings from this study will enhance our understanding of tetraniliprole's impact on population fitness and reproductive potential and offer valuable insights for the sustainable management of *T. absoluta*.

2. Materials and Methods

2.1. Insect

The initial colony of *T. absoluta* was established from larvae collected in tomato fields in Yuxi (24.3473° N, 102.5274° E), Yunnan Province, China, in June 2018. The population was subsequently maintained under laboratory conditions for several years without exposure to any insecticides to ensure a susceptible baseline strain. Rearing was conducted on pesticide-free tomato plants under controlled environmental conditions: 25 ± 1 °C, $60 \pm 5\%$ relative humidity, and a photoperiod of 16:8 h (light/dark).

2.2. Toxicity Bioassays

Adult *T. absoluta* were introduced onto fresh, pesticide-free tomato plants for a 12 h oviposition period. Following egg deposition, the infested plants were transferred to clean rearing cages to allow for hatching and larval development. This protocol ensured uniformity in larval age and developmental stage, with third-instar larvae subsequently selected for bioassay experiments. These larvae were designated as the parental (F_0) generation. The toxicity of tetraniliprole against third-instar *T. absoluta* larvae was evaluated using the standardized leaf-dip bioassay method described [30], under the same controlled laboratory conditions. A technical grade (95% purity) formulation of tetraniliprole was used to prepare a stock solution in analytical-grade acetone, which was serially diluted in distilled water containing 0.05% Triton X-100 (Sangon Biotech Co., Ltd., Shanghai, China) to obtain seven concentrations (0.0078, 0.0156, 0.0312, 0.0625, 0.125, 0.25, and 0.5 mg/L). The control treatment consisted of distilled water containing 0.05% Triton X-100 alone. Fresh tomato leaves were individually immersed in each insecticide concentration for 15 s and then air-dried at room temperature for 1–2 h. To maintain leaf turgidity, the petioles were wrapped in moistened cotton wool. Upon air-drying, treated leaves were placed in Petri dishes (diameter 9 cm $\times$ height 1.5 cm) lined with filter paper. For each replication under both treatment and control, 20 third-instar larvae were carefully transferred onto the treated leaves. Each treatment was replicated three times. Larval mortality was recorded 48 h post-treatment. Larvae unresponsive to gentle probing with a fine brush were recorded as dead. The mortality data were used for subsequent toxicity analysis.

2.3. Sublethal Effects of Tetraniliprole on Life-History Traits of the F_0 Generation

Uniform-aged third-instar *T. absoluta* larvae were used in life table studies and designated as the F_0 generation. Sublethal and low lethal concentrations of tetraniliprole (LC_{10} and LC_{30}) were applied to assess their effects on the life-history traits of directly exposed individuals. Tomato leaves were treated with the respective concentrations following the

procedure outlined in the toxicological bioassay section. After 72 h of exposure, seventy surviving larvae from each treatment group (LC₁₀, LC₃₀, and control) were individually transferred to separate Petri dishes containing untreated, pesticide-free tomato leaves. Each larva was treated as a single replicate. Moistened cotton wool was used to wrap the petioles of the leaves to prevent wilting and maintain turgor, and leaves were replaced as needed throughout rearing. Larval development and survival were monitored daily. Upon pupation, each individual was transferred to a clean glass tube (1.5 cm diameter × 8 cm height), where pupal duration and survival until adult emergence were recorded. After emergence, one male and one female were paired in a larger glass tube (3 cm diameter × 20 cm height) containing fresh, untreated tomato leaves and a cotton ball soaked in a 10% honey solution as a food source. The leaves with deposited eggs were collected and replaced daily. Adult survival and female fecundity were recorded daily until the death of all individuals. All experimental procedures were conducted under the same controlled environmental conditions.

2.4. Transgenerational Effects of Tetraniliprole on Biological Parameters of Subsequent Generations (F₁ and F₂)

Transgenerational effects of sublethal and low lethal concentrations of tetraniliprole (LC₁₀ and LC₃₀, respectively) on F₁ and F₂ generations of *T. absoluta* were evaluated using the same experimental protocol used for the F₀ generation. Eggs laid by F₀ adults were individually transferred to clean Petri dishes containing untreated tomato leaves and maintained under the same controlled conditions. Each egg served as a single replicate. All subsequent developmental, survival, and reproductive parameters were recorded daily throughout the life cycle. For the F₂ generation, eggs produced by the F₁ adults were similarly transferred to untreated tomato leaves and reared using the same procedure. Data collection on developmental duration, survival rates, adult longevity, and fecundity followed the standardized protocol used for the previous generations.

2.5. Tetraniliprole-Induced Transgenerational Effects on Developmental and Resistance Genes

The mRNA expression levels of development (juvenile hormone binding protein), reproduction (*Vg*, *VgR*), and resistance genes (*CYP15C1*, *CYP321C40*, *CYP339A1*, *CYP4M116*, *CYP4S55*, *CYP6AB327*, *CYP6AW1*, *CYP9A307v2*) were investigated in response to sublethal and low lethal exposure to tetraniliprole. Total RNA was extracted from third-instar *T. absoluta* larvae at F₀, F₁, and F₂ generations using the RNAsimple Total RNA kit (Tiangen Biotech (Beijing) Co., Ltd., Beijing, China) following the recommended protocol. The RNA quality and quantity were determined by the Bioanalyzer Agilent 2100 (Agilent Technologies, Santa Clara, CA, USA). 1 µg of total RNA was used to synthesize the cDNA using the iScript™ cDNA Synthesis Kit (Bio-Rad, Berkeley, CA, USA) according to the recommended instructions. RT-qPCR was conducted on a 10 µL total volume of a reaction consisting of 5 µL 2× Kappa SYBR Green I qPCR Mix, 0.2 µL forward and reverse primers (10 µM each), 1 µL of cDNA template, and the remaining volume was nuclease-free water using a CFX Connect™ Real-Time System (Bio-Rad, Berkeley, CA, USA). The thermocycling conditions of each qPCR consist of 95 °C for 45 s, followed by 40 cycles of 95 °C for 15 s, 50–65 °C for 15 s, and 70 °C for 30–60 s. Gene expressions were calculated using the 2^{−ΔΔCt} method [31]. Elongation factor 1 alpha (*EF1α*) and ribosomal protein L28 (*RPL28*) were used as housekeeping genes to normalize the gene expressions. RT-qPCR experiments consist of three biological and three technical replicates. The primers used in the current study are presented in Table 1.

Table 1. The primers used for RT-qPCR and dsRNA synthesis.

Primer Name	Forward Sequence	Reverse Sequence
JHBP	CCCATTAAACCATGCCACAGG	TGAAGCTTTTCCTGGTGTGTC
Vg	TGGTACGTGGTTATGCAGGA	TACTTCGACACTGGGGGTTTC
VgR	ATCTTTGTCCGGACCACACT	CGTCTGCACAATCTGTCTCG
CYP4M116	GACGCCAACTTTCCACTTCAAC	GCCCATCGCTGTTTCGCATA
CYP6AW1	GCCTTGAAACATCAGCCACAAC	GTCAATCCGTCGTGCTTACTCA
CYP339A1	TCTCGCTTCACCTCGTCCTG	CGAACGGCAGAACCATAGACTC
CYP9A307v2	AAAGGTTTCGTGGGCAGATTCTG	TCGTTTCAGGAAGTCTCGGTGAT
CYP4S55	GGTTCACGAGAGCATCTATTCA	CGAGAGCACCACCTCAACATC
CYP15C1	GCAGCAGGAGATAGATGAAGTCA	CACGGAGGATATGCGAAGAGTT
CYP321C40	GGAATGAGATACGCACGACTACA	CACCGCTTGCTTGCTGTACT
CYP6AB327	AAGGTGCTCTAGTGGAATCT	AATCCTGCGGCGAAGAATACAA
EF1 α	GAAGCCTGGTATGGTTGTCGT	GGGTGGGTTGTTCTTTGTG
RPL28	TCAGACGTGCTGAACACACA	GCCAGTCTTGGACAACCATT

2.6. Data and Life Table Analysis

Mortality data were analyzed using probit regression in PoloPlus software version 2.0 (LeOra Software Inc., Berkeley, CA, USA) to estimate the LC₁₀, LC₃₀, and LC₅₀ values of tetraniliprole, along with their corresponding 95% confidence intervals [19]. Life-history data of *T. absoluta* were analyzed based on the age-stage, two-sex life table theory using the TWOSEX-MSChart program (Ver. 07.06.2024) [26,32], which enables comprehensive evaluation of developmental, survival, and reproductive parameters across variable life stages and sexes. Means, variances, and standard errors of the biological and demographic parameters were estimated using a bootstrap resampling procedure with 100,000 iterations [33–35]. Statistical differences among treatment groups (LC₁₀, LC₃₀, and control) and between generations (F₀, F₁, and F₂) within each treatment group were determined using the paired bootstrap test at a significance level of $p < 0.05$. Survival rate, fecundity, life expectancy, and reproductive rate figures were made using SigmaPlot 12.0 (Systat Software Inc., San Jose, CA, USA).

2.7. Population Projection

The TIMING-MSChart program (Ver. 05.07.2024) [36] was used to analyze the population projection according to the standard method [37]. The simulation began with an initial population of 10 *T. absoluta* eggs for each of the control, LC₁₀, and LC₃₀ cohorts. Under the assumption of no biotic or abiotic suppression, the model projected population growth over 120 days for the F₁ and F₂ generations. The net reproductive rate (R_0) confidence interval was generated from 100,000 bootstrap iterations, with its 2.5th and 97.5th percentiles (representing the 2500th and 97,500th sorted values) defining the lower and upper bounds. These percentiles allowed the simulation of population growth to account for all inherent variability and uncertainty [38]. The outcomes of the log-based projections were then visualized using ‘ggplot2’ package of R (Ver. 4.1.3 Vienna, Austria).

3. Results

3.1. Toxicity of Tetraniliprole to *Tuta absoluta* Larvae

The LC₁₀, LC₃₀, and LC₅₀ of tetraniliprole against *T. absoluta* larvae were determined through probit regression analysis. The estimated values were 0.008 mg/L (LC₁₀), 0.018 mg/L (LC₃₀), and 0.029 mg/L (LC₅₀), with corresponding 95% confidence intervals (Table 2). These concentrations, along with a control (acetone), were subsequently used to evaluate their effects on the life table parameters of *T. absoluta* across two consecutive generations (F₁ and F₂).

Table 2. Toxicity of tetraniliprole against third-instar *Tuta absoluta* after 48 h exposure.

Treatments	Slope $\pm$ SE ^a	LC ₁₀ mg/L (95% CL) ^b	LC ₃₀ mg/L (95% CL) ^b	LC ₅₀ mg/L (95% CL) ^b	χ^2 (df) ^c	p-Value
Tetraniliprole	2.369 $\pm$ 0.216	0.008 (0.006–0.011)	0.018 (0.014–0.021)	0.029 (0.025–0.034)	7.035 (19)	0.994

^a Standard error; ^b 95% confidence intervals; ^c Chi-square value (χ^2) and degrees of freedom (df) calculated by PoloPlus 2.0.

3.2. The Sublethal Effects of Tetraniliprole on the Development of the Parental Generation (F₀)

The sublethal effects of tetraniliprole at LC₁₀ and LC₃₀ concentrations on the developmental biology of the parental generation (F₀) of *T. absoluta* are summarized in Table 3. Exposure to both concentrations significantly extended the larval and pupal developmental durations compared to the control group. Specifically, larval development was prolonged by 2.00 and 3.11 days at LC₁₀ and LC₃₀, respectively, while pupal development increased by 0.91 and 1.53 days. In contrast, adult longevity was significantly reduced in both males and females treated with tetraniliprole, indicating an adverse effect on adult survival. Moreover, a significant reduction in female fecundity was observed, with egg production decreasing by 67.64 and 121.72 eggs/female at LC₁₀ and LC₃₀, respectively, compared to untreated controls. Additionally, reproductive timing was also disrupted. Both the oviposition period and the adult preoviposition period (APOP) were significantly shortened in treated individuals, further demonstrating the negative impact of tetraniliprole on reproductive capacity and temporal dynamics of *T. absoluta*.

Table 3. Duration of various developmental stages and some reproductive parameters of parental generation (F₀) of *Tuta absoluta* treated with LC₁₀ and LC₃₀ of tetraniliprole.

Parameters	Control		Tetraniliprole LC ₁₀		Tetraniliprole LC ₃₀	
	n	Mean $\pm$ SE	n	Mean $\pm$ SE	n	Mean $\pm$ SE
Larva (days)	74	11.72 $\pm$ 0.14 ^c	69	13.72 $\pm$ 0.12 ^b	69	14.83 $\pm$ 0.18 ^a
Pupa (days)	72	7.21 $\pm$ 0.08 ^c	68	8.12 $\pm$ 0.08 ^b	69	8.74 $\pm$ 0.07 ^a
Female longevity (days)	31	23.06 $\pm$ 0.54 ^a	30	16.47 $\pm$ 0.88 ^b	27	13.89 $\pm$ 0.63 ^c
Male longevity (days)	41	21.12 $\pm$ 0.35 ^a	38	16.21 $\pm$ 0.36 ^b	42	13.64 $\pm$ 0.23 ^c
Fecundity (eggs/female)	31	192.87 $\pm$ 6.54 ^a	30	125.23 $\pm$ 5.11 ^b	27	71.15 $\pm$ 3.52 ^c
Oviposition days (days)	31	13.00 $\pm$ 0.38 ^a	30	8.73 $\pm$ 0.50 ^b	27	5.96 $\pm$ 0.44 ^c
Adult preoviposition period (days)	31	1.19 $\pm$ 0.07 ^b	30	2.17 $\pm$ 0.08 ^a	27	2.37 $\pm$ 0.09 ^a

Standard errors were estimated by using the bootstrap technique with 100,000 resamples. Differences were compared using the paired bootstrap test ($p < 0.05$). Means within a row followed by different lowercase letters indicate significant differences among the treatments.

3.3. The Sublethal Effects of Tetraniliprole on the Development of the Subsequent Generations (F₁ and F₂)

The sublethal effects of tetraniliprole on the development and longevity of *T. absoluta* in the F₁ and F₂ generations are detailed in Table 4. At LC₁₀, a significant reduction in the duration of egg, larval, and pupal stages was observed relative to the control, suggesting an acceleration of immature development. Conversely, LC₃₀ exposure significantly prolonged all three developmental stages across both generations, indicating a dose-dependent developmental delay. When comparing generations, only the egg and larval developmental periods were significantly shorter in LC₃₀-exposed individuals in the F₂ generation compared to F₁.

Table 4. Duration of various developmental stages of two subsequent *Tuta absoluta* generations (F₁ and F₂), whose parents (F₀) were treated with LC₁₀ and LC₃₀ of tetraniliprole.

Durations (Days)	Generations	Control		Tetraniliprole LC ₁₀		Tetraniliprole LC ₃₀	
		<i>n</i>	Mean ± SE	<i>n</i>	Mean ± SE	<i>n</i>	Mean ± SE
Egg	F ₁	75	4.41 ± 0.06 ^{bA}	72	4.13 ± 0.04 ^{cA}	70	5.53 ± 0.07 ^{aA}
	F ₂	75	4.39 ± 0.06 ^{bA}	71	4.14 ± 0.04 ^{cA}	76	5.33 ± 0.07 ^{aB}
Larva	F ₁	71	11.80 ± 0.16 ^{bA}	68	10.24 ± 0.16 ^{cA}	67	13.12 ± 0.14 ^{aA}
	F ₂	70	11.76 ± 0.17 ^{bA}	66	10.65 ± 0.19 ^{cA}	73	12.71 ± 0.14 ^{aB}
Pupa	F ₁	70	7.43 ± 0.10 ^{bA}	64	6.84 ± 0.10 ^{cA}	66	7.88 ± 0.15 ^{aA}
	F ₂	69	7.42 ± 0.10 ^{bA}	65	6.63 ± 0.09 ^{cA}	72	7.82 ± 0.06 ^{aA}
Total Preadult	F ₁	70	23.64 ± 0.19 ^{bA}	64	21.23 ± 0.18 ^{cA}	66	26.52 ± 0.23 ^{aA}
	F ₂	69	23.49 ± 0.19 ^{bA}	65	21.48 ± 0.20 ^{cA}	72	25.86 ± 0.17 ^{aB}
Female longevity	F ₁	27	23.19 ± 0.53 ^{bA}	28	25.79 ± 0.68 ^{aA}	29	19.24 ± 0.61 ^{cA}
	F ₂	30	23.80 ± 0.95 ^{aA}	29	25.52 ± 0.89 ^{aA}	30	20.37 ± 0.77 ^{bA}
Male longevity	F ₁	43	21.30 ± 0.31 ^{bA}	36	23.28 ± 0.36 ^{aA}	37	17.35 ± 0.26 ^{cB}
	F ₂	39	21.46 ± 0.30 ^{bA}	36	23.72 ± 0.20 ^{aA}	42	18.52 ± 0.22 ^{cA}
Total female longevity	F ₁	27	46.33 ± 0.65 ^{aA}	28	46.79 ± 0.77 ^{aA}	29	45.69 ± 0.60 ^{aA}
	F ₂	30	47.77 ± 1.06 ^{aA}	29	47.07 ± 1.03 ^{aA}	30	46.17 ± 0.78 ^{aA}
Total male longevity	F ₁	43	45.26 ± 0.41 ^{aA}	36	44.69 ± 0.42 ^{abA}	37	43.92 ± 0.43 ^{bA}
	F ₂	39	44.59 ± 0.42 ^{aA}	36	45.14 ± 0.33 ^{aA}	42	44.43 ± 0.26 ^{aA}

Standard errors were estimated by using the bootstrap technique with 100,000 resampling. Difference was compared using the paired bootstrap test ($p < 0.05$). Significantly different means within a row are denoted by different lowercase letters, while the means within a column followed by different uppercase letters indicate significant differences between two subsequent generations, F₁ and F₂.

Female longevity showed contrasting trends across concentrations and generations. In the F₁ generation, LC₁₀ exposure significantly increased female lifespan by 2.6 days, while LC₃₀ exposure reduced it by 3.95 days. However, in the F₂ generation, no statistically significant difference in female longevity was observed between the control and LC₁₀ treatment groups, but LC₃₀ reduced female lifespan from 23.80 ± 0.95 to 20.37 ± 0.77 days, confirming the persistent detrimental effects of higher sublethal doses. Male longevity increased significantly under LC₁₀ in both generations, but was consistently and significantly reduced at LC₃₀ exposure. Interestingly, male longevity was significantly higher in the F₂ than in the F₁ within the LC₃₀ treatment group. No significant variation in total female longevity was detected between treatment groups or across generations. However, total male longevity was significantly reduced under both LC₁₀ and LC₃₀ exposures in the F₁ generation, with no notable differences observed in the F₂ generation.

3.4. The Transgenerational Sublethal Effects of Tetraniliprole on the Progeny Generations (F₁ and F₂) of *Tuta absoluta*

The sublethal effects of tetraniliprole on the life table parameters of *T. absoluta* in the F₁ and F₂ generations are presented in Table 5. No significant differences in the net reproductive rate (R_0) were observed between the control and either of the sublethal treatments (LC₁₀ or LC₃₀), nor were intergenerational variations detected for this parameter, indicating a degree of reproductive stability under sublethal stress. However, both the intrinsic rate of increase (r) and the finite rate of increase (λ) exhibited concentration-dependent responses. Specifically, LC₁₀ exposure significantly elevated both parameters across generations, suggesting a potential hormetic effect. In contrast, exposure to LC₃₀ markedly suppressed both r and λ values in both generations. The mean generation time (T) was also notably affected by tetraniliprole. T was significantly shortened under

LC₁₀ (from 28.50 ± 0.32 to 26.63 ± 0.33 days in the F₁ generation, and from 29.74 ± 0.33 to 27.00 ± 0.39 days in the F₂), while LC₃₀ increased *T* by 3.96 and 2.65 days in F₁ and F₂, respectively.

Table 5. Reproduction and life table parameters of two subsequent (F₁ and F₂) generations of *Tuta absoluta*, whose parents (F₀) were treated with LC₁₀ and LC₃₀ of tetraniliprole.

Parameters	Generations	Control	Tetraniliprole LC ₁₀	Tetraniliprole LC ₃₀
		Mean $\pm$ SE	Mean $\pm$ SE	Mean $\pm$ SE
Net reproductive rate (<i>R</i> ₀) (offspring/individual)	F ₁	70.29 ± 10.94 ^{aA}	86.24 ± 13.20 ^{aA}	64.41 ± 9.34 ^{aA}
	F ₂	80.68 ± 11.93 ^{aA}	94.38 ± 13.67 ^{aA}	72.00 ± 10.53 ^{aA}
Intrinsic rate of increase (<i>r</i>) (day ^{−1})	F ₁	0.1492 ± 0.0061 ^{bA}	0.1674 ± 0.0064 ^{aA}	0.1272 ± 0.0047 ^{cA}
	F ₂	0.1476 ± 0.0055 ^{bA}	0.1684 ± 0.0061 ^{aA}	0.1320 ± 0.0049 ^{cA}
Finite rate of increase (λ) (day ^{−1})	F ₁	1.1609 ± 0.0070 ^{bA}	1.1822 ± 0.0076 ^{aA}	1.1356 ± 0.0054 ^{cA}
	F ₂	1.1591 ± 0.0063 ^{bA}	1.1835 ± 0.0072 ^{aA}	1.1412 ± 0.0056 ^{cA}
Mean generation time (<i>T</i>) (days)	F ₁	28.50 ± 0.32 ^{bB}	26.63 ± 0.33 ^{cA}	32.76 ± 0.31 ^{aA}
	F ₂	29.74 ± 0.33 ^{bA}	27.00 ± 0.39 ^{cA}	32.39 ± 0.35 ^{aA}
Fecundity (<i>F</i>) (eggs/female)	F ₁	195.26 ± 3.99 ^{bA}	221.75 ± 8.83 ^{aA}	155.48 ± 4.41 ^{cB}
	F ₂	201.70 ± 8.56 ^{bA}	231.07 ± 6.12 ^{aA}	182.40 ± 6.53 ^{bA}
Oviposition days (<i>O</i> _d) (days)	F ₁	12.96 ± 0.33 ^{aA}	12.93 ± 0.53 ^{aB}	10.10 ± 0.45 ^{bB}
	F ₂	12.17 ± 0.52 ^{bA}	14.83 ± 0.56 ^{aA}	13.00 ± 0.61 ^{bA}
Adult preoviposition period (APOP) (days)	F ₁	1.26 ± 0.09 ^{bA}	1.18 ± 0.07 ^{bA}	2.24 ± 0.08 ^{aA}
	F ₂	1.27 ± 0.08 ^{bA}	1.21 ± 0.08 ^{bA}	2.00 ± 0.09 ^{aA}
Total preoviposition period (TPOP) (days)	F ₁	24.41 ± 0.27 ^{bB}	22.18 ± 0.28 ^{cA}	28.69 ± 0.31 ^{aA}
	F ₂	25.23 ± 0.27 ^{bA}	22.76 ± 0.33 ^{cA}	27.80 ± 0.29 ^{aB}

Standard errors were estimated by using the bootstrap technique with 100,000 resampling. Difference was compared using the paired bootstrap test ($p < 0.05$). Significantly different means within a row are denoted by different lowercase letters, while the means within a column followed by different uppercase letters indicate significant differences between two subsequent generations, F₁ and F₂.

Fecundity responses were dose- and generation-dependent. LC₁₀ significantly enhanced fecundity in both F₁ and F₂ generations, while LC₃₀ significantly reduced fecundity in the F₁ generation, with no significant difference in the F₂. Notably, fecundity under LC₃₀ improved by 14.76% in F₂ compared to F₁. Regarding the oviposition period, no significant difference was recorded in LC₁₀-treated individuals in F₁. However, in F₂, oviposition was significantly extended (from 12.17 ± 0.52 to 14.83 ± 0.56 days). An opposite trend was observed for LC₃₀-exposed insects, where oviposition was reduced relative to the control. Nonetheless, both LC₁₀ and LC₃₀ treatments resulted in a notable increase in oviposition period in the F₂ generation compared to F₁, highlighting a generational effect. The adult preoviposition period (APOP) was not considerably affected by LC₁₀, but significantly extended under LC₃₀ in both generations. A similar pattern was observed for the total preoviposition period (TPOP), which was significantly increased under LC₃₀ but reduced under LC₁₀.

3.5. Age-Stage Specific Survival Rate, Fecundity, and Life Expectancy of Tetraniliprole Exposed *Tuta absoluta*

The age-specific survival rate (l_x), age-specific fecundity (m_x), and the age-specific maternity ($l_x m_x$) of *T. absoluta* in the F₁ and F₂ generations following tetraniliprole exposure are illustrated in Figure 1. The m_x curves exhibited marked differences in fecundity across generations and treatment levels. At LC₁₀, maximum fecundity (0.4–0.6 offspring/female/day) occurred around day 25 in both F₁ and F₂ generations. In contrast, at LC₃₀, peak fecundity

(0.2–0.4) was delayed until approximately day 30, indicating a concentration-dependent effect of tetraniliprole on reproductive timing and output. The trends observed in the maternity function ($l_x m_x$) mirrored those of m_x , further highlighting the generational impact of sublethal exposure. However, no significant deviations in the age-specific survival rate (l_x) were observed across treated and control groups in either generation.

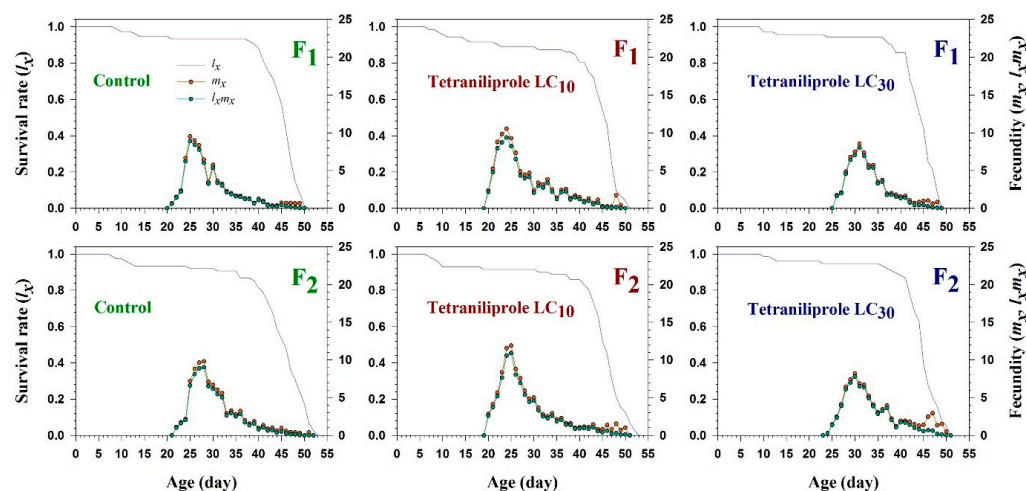


Figure 1. Age-specific survival rate (l_x), age-specific fecundity (m_x), and age-specific maternity ($l_x m_x$) of F₁ and F₂ generations of *Tuta absoluta* originating from F₀ individuals exposed to tetraniliprole (LC₁₀ and LC₃₀).

The age-stage-specific survival rate (s_{xj}), representing the probability that an individual egg survives to age x and stage j , showed overlapping trends between treatments and control during immature stages (Figure 2). However, s_{xj} was notably reduced in adult males and females of the F₂ generation at both LC₁₀ and LC₃₀. Conversely, larval s_{xj} values were increased under both concentrations, suggesting a stage-specific response to tetraniliprole exposure. The age-stage-specific life expectancy (e_{xj}), indicating the expected remaining lifespan of an individual at age x and stage j , also varied with treatment and generation (Figure 3). Female life expectancy under LC₁₀ was 34 days in the F₁, declining to 27 days at LC₃₀. In F₂, females lived an average of 35 days at LC₁₀, while life expectancy decreased to 31 days at LC₃₀. These values were slightly lower than the control groups, where life expectancies were 33 and 34 days for F₁ and F₂, respectively.

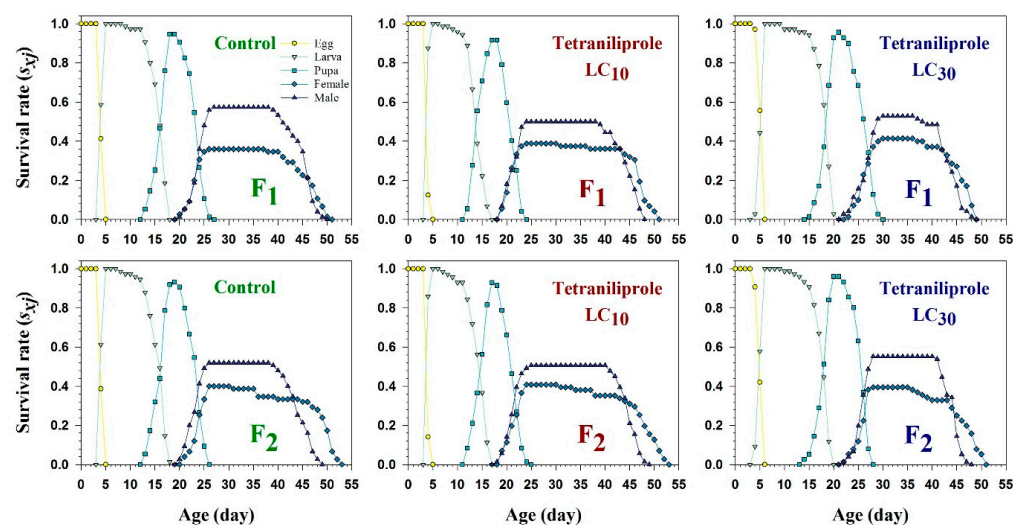


Figure 2. Age-specific survival rate (s_{xj}) of F₁ and F₂ generations of *Tuta absoluta* originating from F₀ individuals exposed to tetraniliprole (LC₁₀ and LC₃₀).

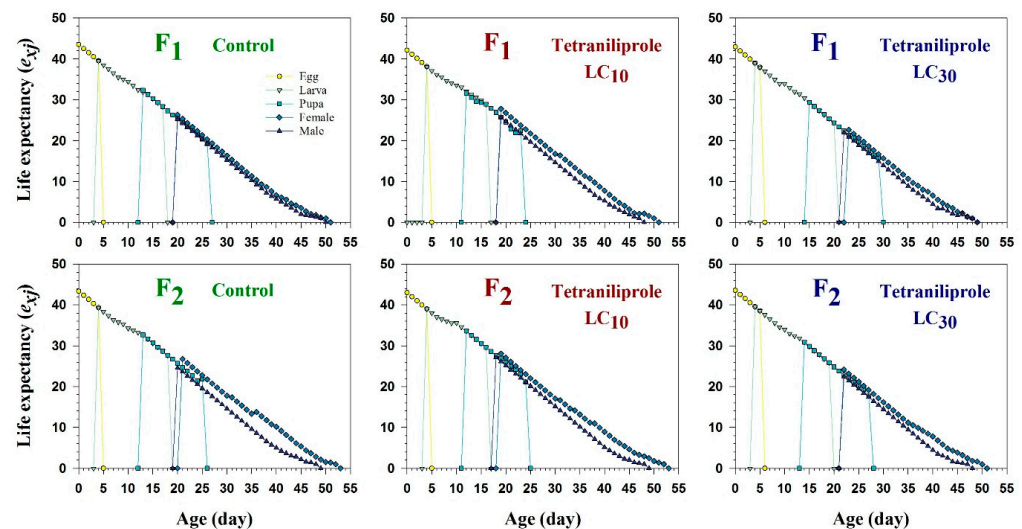


Figure 3. Age-specific life expectancy (e_{xj}) of F₁ and F₂ generations of *Tuta absoluta* originating from F₀ individuals exposed to tetraniliprole (LC₁₀ and LC₃₀).

Age-stage-specific reproductive values (v_{xj}), representing the future reproductive potential of individuals at each age and stage, were significantly reduced in LC₃₀-treated females in both generations compared to controls and LC₁₀ treatments (Figure 4). This reduction indicates a transgenerational suppression of reproductive capacity at higher sublethal concentrations.

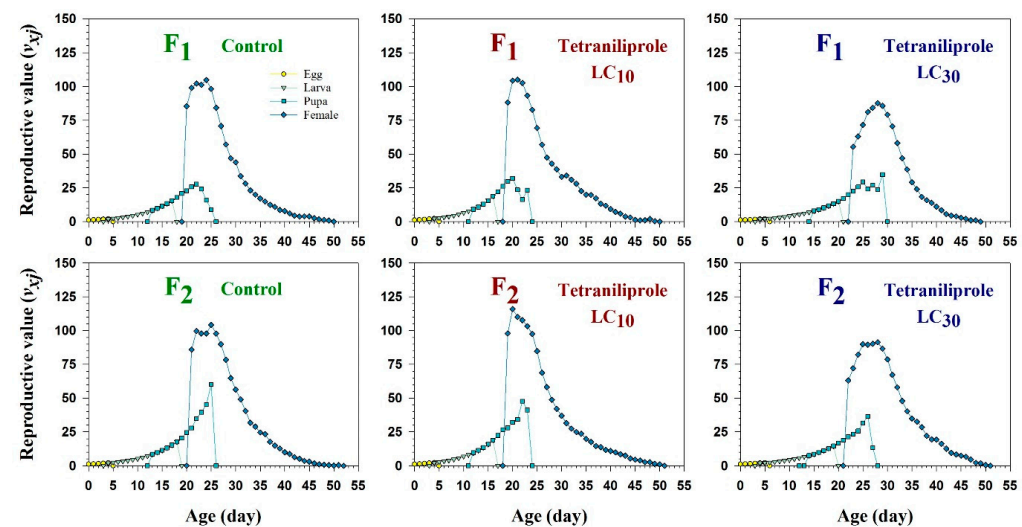


Figure 4. Age-specific reproductive rate (v_{xj}) of F₁ and F₂ generations of *Tuta absoluta* originating from F₀ individuals exposed to tetraniliprole (LC₁₀ and LC₃₀).

3.6. Population Projection

The population growth of *T. absoluta* over 120 days (F₁ and F₂ generations) for the tetraniliprole treatments (LC₁₀, LC₃₀) and the control group, including confidence intervals, is shown in Figure 5. Population sizes were greatest in the F₁ and F₂ generations after parental exposure to the LC₁₀ dose of tetraniliprole, implying a hormetic effect that enhanced population growth. Conversely, population projections for the F₁ and F₂ generations following parental exposure to LC₃₀ were lower than those of the control, suggesting a suppressive effect at this concentration (Figure 5). This study reveals the concentration-dependent influence of tetraniliprole on *T. absoluta*'s population dynamics across multiple generations.

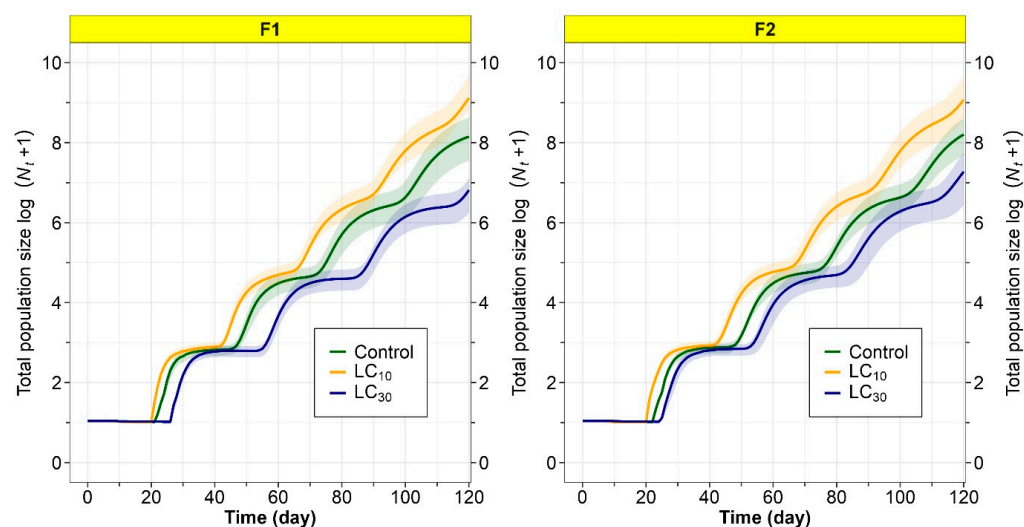


Figure 5. Total population size log ($N_t + 1$) of F₁ and F₂ generations *Tuta absoluta* originated from F₀ individuals exposed to the LC₁₀ and LC₃₀ of tetraniliprole.

3.7. Transgenerational Effects of Tetraniliprole on Developmental and Resistance Genes

Following the exposure of the parental generation (F₀) to sublethal and low-lethal concentrations of tetraniliprole, we analyzed its transgenerational effects on the relative mRNA expression levels of genes linked to development, reproduction, and resistance. These effects were examined in the directly exposed F₀ generation as well as in the unexposed progeny generations (F₁ and F₂) of *T. absoluta* (Figures 6 and 7). Results showed that the expression levels of *Vg*, *VgR*, and *JHBP* were significantly (*Vg*, $F_{2,17} = 38.59$, $p < 0.001$; *VgR*, $F_{2,17} = 27.09$, $p < 0.001$; *JHBP*, $F_{2,17} = 19.94$, $p < 0.001$) reduced in *T. absoluta* directly exposed to the LC₁₀ (0.46-, 0.52-, and 0.62-fold) and LC₃₀ (0.38-, 0.43-, and 0.41-fold) of tetraniliprole compared to the control (Figure 6a). In the F₁ generation, the *Vg* and *VgR* were significantly upregulated by 1.62- and 1.44-fold at LC₁₀ (*Vg*, $F_{2,17} = 15.55$, $p < 0.001$ and *VgR*, $F_{2,17} = 14.02$, $p < 0.001$), while no effects were noted for LC₃₀ concentration (Figure 6b). In contrast, the expression level of *JHBP* was significantly downregulated by 0.71-fold at LC₃₀ (*JHBP*, $F_{2,17} = 13.02$, $p < 0.001$), while no effects were observed at LC₁₀ compared to the control. The expression levels of these genes were also upregulated by 1.60-, 2.51-, and 1.56-fold in the LC₁₀-treated individuals (*Vg*, $F_{2,17} = 18.92$, $p < 0.001$; *VgR*, $F_{2,17} = 49.51$, $p < 0.001$; *JHBP*, $F_{2,17} = 17.06$, $p < 0.001$), while no effects were found at the LC₃₀-treated group compared to control (Figure 6c).

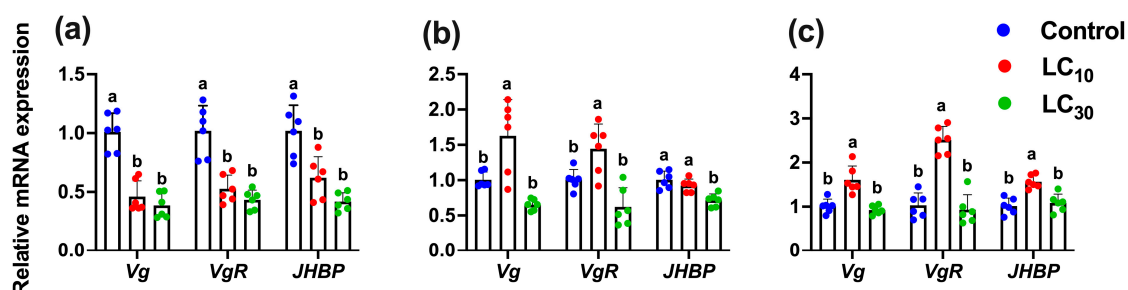


Figure 6. The relative mRNA expression level of development and reproduction-related genes (*Vg*, *VgR*, and *JHBP*) in the parental F₀ (a) and the progeny F₁ (b) and F₂ (c) generations of *Tuta absoluta* after F₀ treatment with the LC₁₀ and LC₃₀ of tetraniliprole. The expression level is expressed as the mean ($\pm$ SE) of the three biological replicates. Letters above the bars represent significant differences at $p < 0.05$ level using one-way analysis of variance with Tukey's post hoc test (IBM, SPSS Statistics, Armonk, NY, USA, version 29).

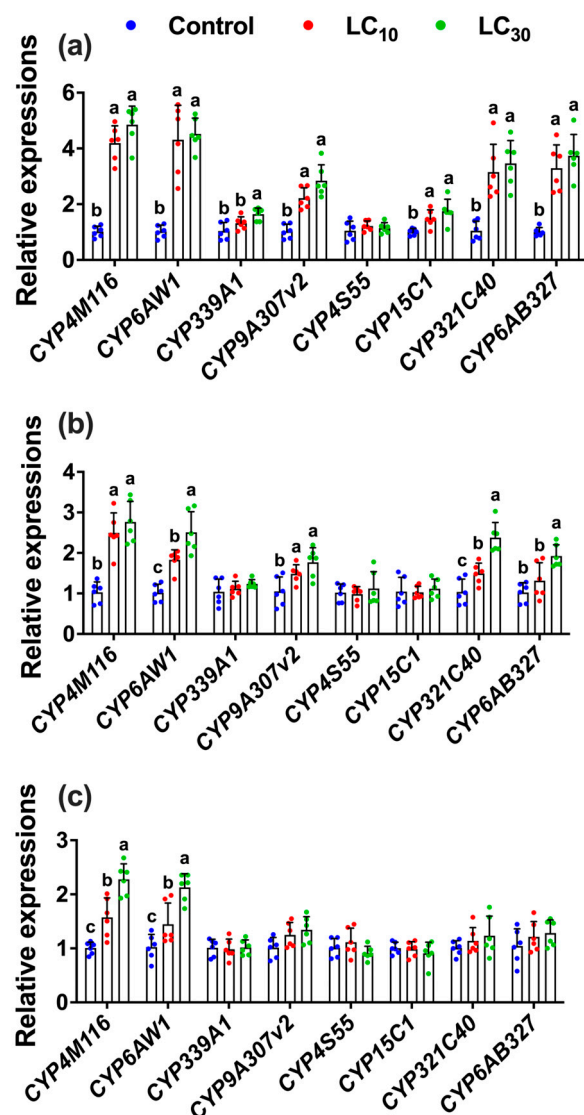


Figure 7. Expressions of P450 genes in the parental F₀ (a) and the progeny F₁ (b) and F₂ (c) generations of *Tuta absoluta* after F₀ treatment to the LC₁₀ and LC₃₀ of tetraniliprole. The expression level is expressed as the mean ($\pm$ SE) of the three biological replicates. Letters above the bars represent significant differences at $p < 0.05$ level using one-way analysis of variance with Tukey's post hoc test (IBM, SPSS Statistics, Armonk, NY, USA, version 29).

Further, the expression levels of resistance-related cytochrome P450 genes such as *CYP4M116* ($F_{2,17} = 87.38$, $p < 0.001$), *CYP6AW1* ($F_{2,17} = 23.13$, $p < 0.001$), *CYP321C40* ($F_{2,17} = 17.48$, $p < 0.001$), *CYP6AB327* ($F_{2,17} = 29.35$, $p < 0.001$), *CYP9A307v2* ($F_{2,17} = 28.83$, $p < 0.001$), and *CYP15C1* ($F_{2,17} = 8.57$, $p = 0.003$) were all significantly upregulated with fold increases ranging from 1.64- to 4.85-fold in the directly exposed parental generation (F₀) to the LC₁₀ and LC₃₀ of tetraniliprole, while *CYP339A1* was upregulated only at LC₃₀ as compared to control (Figure 7a). In the F₁ generation, the expressions of *CYP4M116* ($F_{2,17} = 27.82$, $p < 0.001$), *CYP6AW1* ($F_{2,17} = 27.57$, $p < 0.001$), *CYP321C40* ($F_{2,17} = 27.62$, $p < 0.001$), *CYP6AB327* ($F_{2,17} = 11.40$, $p < 0.001$), and *CYP9A307v2* ($F_{2,17} = 7.65$, $p = 0.005$) were upregulated with fold expressions ranging from 1.48 to 2.76 at the LC₁₀ and LC₃₀ of tetraniliprole as compared to control (Figure 7b). However, only two P450 genes, such as *CYP4M116* ($F_{2,17} = 32.63$, $p < 0.001$) and *CYP6AW1* ($F_{2,17} = 20.63$, $p < 0.001$), were upregulated in the F₂ generation with expression ranges from 1.44- to 2.27-fold following parental exposure to the sublethal and low lethal concentrations of tetraniliprole

as compared to control (Figure 7c). These results demonstrate that tetraniliprole upregulates resistance-related genes in *T. absoluta*, suggesting enhanced insecticide breakdown and a potential for resistance evolution following sublethal or low-lethal exposure.

4. Discussion

This study provides valuable insights into the lethal and sublethal effects of tetraniliprole on *T. absoluta*, a globally important pest of tomato crops. The estimated LC₁₀, LC₃₀, and LC₅₀ values confirm the high toxicity of tetraniliprole to the larval stages of *T. absoluta*, consistent with its known mode of action as a ryanodine receptor modulator in arthropods [39]. These findings support the potential inclusion of tetraniliprole in integrated pest management (IPM) programs targeting *T. absoluta*.

Sublethal (LC₁₀) and low lethal (LC₃₀) exposures significantly impacted developmental and reproductive traits in both the directly exposed parental generation (F₀) and their offspring (F₁ and F₂). In the F₀ generation, longer larval and pupal stages under sublethal treatments suggest developmental delays caused by physiological stress, likely related to disrupted calcium balance via ryanodine receptor activation [40]. Additionally, earlier research reported that sublethal concentrations of various insecticides, including diamides, caused extended developmental periods in lepidopteran pests [41]. Furthermore, reduced adult lifespan and fecundity in F₀ indicate a fitness cost among survivors, consistent with previous studies on arthropods (including Lepidopterans) exposed to diamides and other insecticides [17,18,42].

In subsequent generations, responses varied based on both concentration and generation. At LC₁₀, a pattern of faster development and higher fecundity indicates a hormetic effect, where low-concentration stress can stimulate physiological processes [43,44]. Conversely, exposure to LC₃₀ led to delayed development, decreased fecundity, shorter adult lifespan, and lower reproductive value (v_{xj}), suggesting transgenerational stress effects or possible epigenetic regulation [45].

Life table parameters clearly reflected these effects. At LC₁₀, both the intrinsic rate of increase (r) and the finite rate of increase (λ) were raised, while at LC₃₀, these rates decreased significantly. These patterns are especially important for pest management, as they indicate that sublethal insecticide residues at low concentrations could unintentionally boost population growth, whereas higher sublethal levels may inhibit it [46]. The mean generation time (T) was shorter under LC₁₀, encouraging faster generational turnover, but longer under LC₃₀, which could slow population growth.

Age-stage-specific parameters further supported these findings. Delayed peaks in fecundity, reduced life expectancy (e_{xj}), and lower reproductive values (v_{xj}) at LC₃₀ highlight disrupted reproductive strategies [32]. Interestingly, increased oviposition periods and population sizes under LC₁₀ in F₁ suggest heightened reproductive effort in response to mild sublethal stress. Sex-specific effects were also prominent. LC₃₀ exposure caused a decline in male longevity, potentially impairing mating success and sperm competition [47]. Conversely, increased male longevity at LC₁₀ may indicate compensatory mechanisms or decreased mating effort under stress conditions. Overall, these results show that while tetraniliprole is very effective at lethal concentrations, its sublethal effects are complex and can either suppress or promote *T. absoluta* populations depending on the concentration and generation.

Vg and VgR genes act as key molecular indicators of female reproductive capacity in insects, often reflecting fecundity status under environmental and chemical stressors [48]. While many studies have reported a downregulation of these genes in response to insecticidal pressure, this is frequently seen as a sign of impaired reproduction or endocrine disruption [24,25]. Our study, however, shows a different pattern. Specifically, we observed

a significant upregulation of *Vg* and *VgR* expression in insects exposed to the LC₁₀ concentration of tetraniliprole, indicating a hormetic response. Hormesis, which is a stimulatory effect at low doses of an otherwise inhibitory agent, may be an adaptive strategy where the organism temporarily boosts reproductive output as a response to mild chemical stress. This reproductive boost was even more noticeable in the F₂ generation at the LC₃₀ level, where *Vg* and *VgR* expression exceeded the levels seen in both F₀ and F₁. These findings suggest a transgenerational acclimation effect, possibly driven by epigenetic changes or altered endocrine signaling pathways. In addition to reproductive genes, cytochrome P450 monooxygenases (CYPs) are central to insecticide detoxification and have long been linked to resistance development [30,49]. In our study, *CYP4M116* expression was significantly upregulated in F₀ after tetraniliprole exposure, reflecting a strong metabolic response in the first generation. However, a decrease in expression levels in F₁ and F₂, although still above control levels, may indicate feedback inhibition, reduced selection pressure, or physiological costs across generations. These patterns highlight the dynamic nature of gene-environment interactions that shape resistance phenotypes over time.

In contrast, *CYP6AB327* and *CYP6AW1* showed sustained upregulation across LC₁₀ and LC₃₀ treatments and generations, indicating a more consistent and potentially heritable metabolic resistance mechanism. The involvement of these genes aligns with their known roles in detoxifying various insecticides, including spinosad, diamides, and neonicotinoids [50,51]. However, the absence of significant expression in other P450 genes such as *CYP4S55*, *CYP9A307v2*, and *CYP15C1* highlights that detoxification pathways are gene-specific and selective, likely influenced by the chemical structure of the insecticide, dosage, and exposure duration.

These findings agree with an increasing amount of evidence suggesting that resistance can develop from the activation of common detoxification genes due to the widespread use of chemical insecticides [1,50]. This overlap in metabolic pathways presents a significant risk to sustainable pest management, as it can weaken rotation strategies if cross-resistance genes are not accurately identified and monitored. Overall, our results lay the groundwork for understanding the complex transgenerational effects of tetraniliprole on *T. absoluta* and their impact on population management. Future research should investigate these dynamics under continuous exposure across multiple generations to better reflect field conditions. Such studies would help determine whether the observed hormetic response persists, diminishes, or increases over time, and how including generational mortality in population growth models might affect the long-term dynamics of pest populations under ongoing insecticide use.

5. Conclusions

In conclusion, tetraniliprole shows dual concentration-dependent transgenerational effects on *T. absoluta*, causing hormesis at LC₁₀ but suppression at LC₃₀. These sublethal effects, driven by changes in gene expression, emphasize a significant risk of population resurgence and should be considered in resistance management strategies.

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