Harnessing Hormesis: Exploring Insecticide Dose-Response Dynamics for Sustainable Pest Management

Abstract

Hormesis, a biological phenomenon in which hazardous substances become less damaging or less effective at greater concentrations while still having therapeutic effects at lower quantities, is important for managing pests. Hormesis, which was first discovered in the 1940s, significantly affects the best way to utilize pesticides. The mechanisms of hormesis, such as behavioural modifications, metabolic activation, detoxification processes, stress reactions, target site saturation, and physiological reactions, are examined in this review. Comprehending these mechanisms is crucial in formulating efficacious and enduring pest management tactics. Utilizing hormetic effects can lower pollution levels in the environment, slow the emergence of resistance, and improve the general effectiveness of pesticides. The review underscores the critical importance of incorporating dose and environmental factors into effective pest management strategies. It emphasizes the necessity of hormesis-based integrated pest management (IPM) programs that strike a balance between efficient pest control and negligible negative effects on the environment and human health. In the end, agroecosystems can benefit from improved pest management strategies that are more sustainable and successful by comprehending and utilizing the principles of hormesis. This can also lessen the need for high-dose chemical treatments.

Keywords: Hormesis, Insecticide Efficacy, Integrated Pest Management, Environmental Toxicology, Agroecosystem

1. Introduction

Hormesis, a biological phenomenon where low doses of a harmful substance can have beneficial effects, was first proposed by Southam and Ehrlich in 1943 after observing yeast growth when exposed to harmful chemicals (Southam and Ehrlich, 1943). Since then, it has been documented across various biological systems, especially in toxicology and pest control (Calabrese and Blain, 2011; Calabrese et al., 2007). This biphasic dose-response relationship, characterized by stimulation at low doses and inhibition at higher doses, makes hormesis a complex but significant phenomenon (Kendig et al., 2010). Understanding hormesis is crucial for optimizing pest management strategies. Traditional pest management techniques often involve high pesticide dosages for maximum effect, which can lead to pest resistance, environmental contamination, and non-target effects (Popp et al., 2013; Damalas and Eleftherohorinos, 2011). Leveraging the beneficial effects of low doses through hormesis can lead to more sustainable, effective, and environmentally responsible pest control practices (Guedes et al., 2016).

The mechanisms of hormesis are intricate, involving various physiological and biochemical responses that contribute to its effects. These include enhanced stress resistance, improved detoxification processes, and better metabolic functions (Calabrese et al., 2007; Mattson, 2008; Lushchak, 2011). In pest management, hormesis can paradoxically increase pest survival and reproduction at low pesticide doses, which, when strategically managed, can enhance pest control outcomes (Cutler, 2013). Recent research has shown that low doses of insecticides can increase the effectiveness of biological control agents, helping to reduce pest populations without negatively affecting beneficial organisms (Desneux et al., 2007; Guedes et al., 2016). Furthermore, understanding the dose-response relationship is vital for developing integrated pest management (IPM) programs that minimize negative environmental and human health impacts (Aktar et al., 2009). This review explores the mechanisms of hormesis and its implications for pest management, aiming to provide a comprehensive overview of how this phenomenon can be leveraged to create more sustainable pest control strategies. The insights gained could inform the development of innovative pest management approaches that balance efficacy with environmental safety.

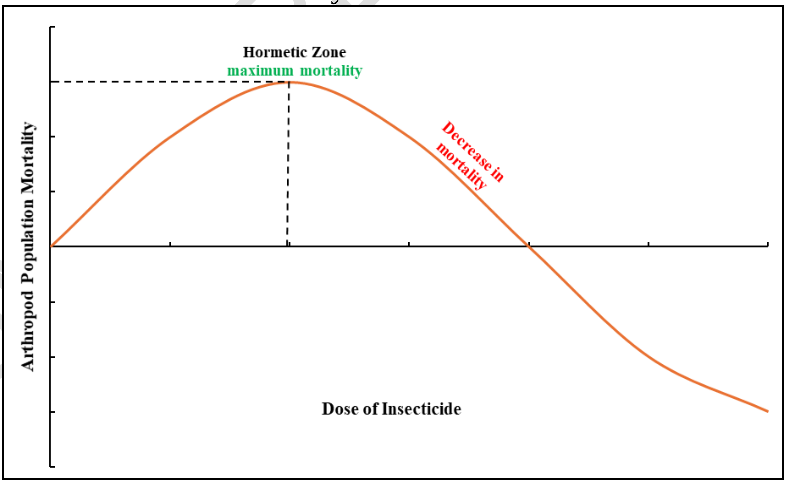

Figure 1: Biphasic Dose-Response Curve Illustrating Hormesis in Insecticide Application

The Figure 1 demonstrates the concept of hormesis in insecticide application, showing that at low to moderate doses, the mortality rate of an arthropod population increases with the dose, reaching a peak at the "maximum mortality" point within the hormetic zone. Beyond this optimal dose range, further increases in insecticide dose paradoxically led to a decrease in mortality. This decrease can be attributed to biological mechanisms such as detoxification, behavioral adaptations, or stress responses in the arthropods that mitigate the insecticide's effects. Understanding this hormetic response is essential for integrated pest management (IPM) as it highlights the importance of determining the optimal insecticide dosage that maximizes pest control while minimizing resistance development and environmental impact. The biphasic dose-response curve depicted here aligns with the findings of Calabrese and Baldwin (2002), who illustrated similar hormetic effects in their study on toxicology and pharmacology, emphasizing the significance of the hormetic zone where low doses of a toxicant can stimulate beneficial responses while higher doses are inhibitory.

2. Mechanisms of Hormesis

The counterintuitive increase in efficacy at lower doses is caused by a variety of mechanisms that give rise to hormesis. These mechanisms encompass alterations in behavior, metabolic stimulation, detoxification processes, stress reactions, saturation of target sites, and physiological reactions. To effectively manage pests and take advantage of hormesis, it is imperative to comprehend these mechanisms.

2.1. Behavioural Changes:

Hormesis in insects is often influenced by behavioral changes in response to pesticide doses. At low concentrations, insects may not detect the pesticide, leading to increased contact and higher fatality rates, while at higher concentrations, they may avoid the toxin, reducing exposure. Desneux et al. (2007) found that sublethal doses of thiamethoxam increased foraging activity in *Bemisia tabaci*, leading to greater pesticide uptake and increased mortality. Goulson (2013) reviewed the impacts of neonicotinoids on pollinators, noting that sublethal exposure often altered behaviors, increasing susceptibility. Cresswell (2011) observed that sublethal doses of imidacloprid in honeybees (*Apis mellifera*) increased foraging, enhancing pesticide exposure. Sandrock et al. (2014) demonstrated that sublethal pyrethroid exposure impaired foraging efficiency and increased mortality in *Bombus terrestris*. Similarly, Williamson et al. (2013) found that spinosad induced hyperactivity in *Drosophila melanogaster*, leading to higher exposure and mortality.

2.2. Metabolic Activation:

For some pesticides, metabolic activation within the insect's body is crucial for toxicity. Increased dosages can overwhelm or inhibit the insect's detoxification mechanisms, reducing the activation process, while lower doses may allow for more efficient activation, increasing mortality. Liu et al. (2015) showed that the metabolic pathways in *Plutella xylostella* were more effective at lower concentrations, enhancing the toxicity of pesticides like chlorpyrifos. Bass et al. (2014) found that the metabolic activation of carbamates in *Myzus persicae* increased insecticide toxicity at lower doses. Silva et al. (2012) highlighted the significance of metabolic activation in pesticide efficacy in *Tetranychus urticae*, emphasizing its role in pest management. Other studies support these findings, such as Devine et al. (1996), who found that metabolic activation of neonicotinoids in *Nilaparvata lugens* was more efficient at lower doses, leading to higher mortality. Bonmatin et al. (2015) also demonstrated that metabolic pathways in various insects were upregulated at lower doses of neonicotinoids, enhancing their toxicity.

2.3. Detoxification Mechanisms:

Insects use enzymes, like cytochrome P450 monooxygenases (CYPs), carboxylesterases (COEs), glutathione S-transferases (GSTs), ATP-binding cassette (ABC) transporters, UDP-glucosyltransferases (UGTs), to remove toxic chemicals from their bodies. Higher pesticide doses can induce the overexpression of these detoxifying enzymes, potentially improving the insect's ability to withstand exposure. In contrast, lower doses may not trigger detoxification, leading to higher mortality. Desneux et al. (2007) and Ricupero et al. (2020) demonstrated that detoxifying enzymes significantly affect the effectiveness of insecticides like methoprene at varying doses. Li et al. (2007) further emphasized the role of these enzymes in pesticide resistance and hormesis in *Spodoptera litura*. Ahmad et al. (2007) found that detoxification enzyme activity in *Spodoptera exigua* increased at higher doses of lambda-cyhalothrin, reducing its efficacy. Pavlidi et al. (2015) showed that glutathione S-transferase overexpression in *Tetranychus urticae* reduced susceptibility to abamectin at higher doses. Ranson and Lissenden (2016) observed that increased enzyme activity in *Anopheles gambiae* at higher permethrin doses led to decreased mortality.

2.4. Stress Responses:

High pesticide dosages can induce stress reactions in insects, triggering defense mechanisms that are not activated at lower concentrations, leading to a decrease in mortality. Guedes and Cutler (2014) showed that organophosphate-induced stress in *Bemisia tabaci* played a crucial role in hormesis. Opit et al. (2012) similarly demonstrated how stress reactions influenced mortality in *Rhyzopertha dominica* under varying pesticide doses. Khan et al. (2013) observed that lower doses of phosphine in *Tribolium castaneum* did not activate stress responses, resulting in higher mortality. Hoffmann and Willi (2008) reported that in *Drosophila melanogaster*, stress responses were more pronounced at higher insecticide doses, which reduced insecticide efficacy. Cai et al. (2017) showed that in *Helicoverpa armigera*, higher doses of insecticides triggered increased stress protein expression, which contributed to reduced mortality. These findings support the understanding that stress responses are integral to the effectiveness of pesticide treatments and can influence pest management strategies.

2.5. Target Site Saturation:

Higher pesticide dosages can saturate target sites, such as enzymes or receptors, in the insect's body, preventing additional pesticide molecules from causing harm and leading to a plateau or reduction in mortality. Devine and Furlong (2007) found that *Anopheles gambiae* experienced target site saturation at higher pyrethroid doses, decreasing mortality. Sparks et al. (2012) observed this phenomenon in *Helicoverpa zea*. Soderlund and Bloomquist (1989) showed that permethrin's efficacy was impacted by target site saturation. These results are corroborated by additional research: Hemingway et al. (2004) noted reduced mortality in *Culex quinquefasciatus* at higher organophosphate doses, Scott (1990) found reduced efficacy of pyrethroids in *Musca domestica* at higher doses, and Feyereisen et al. (2015) demonstrated similar effects in *Drosophila melanogaster* at elevated insecticide doses.

2.6. Physiological Responses:

Physiological reactions to lower amounts of pesticides can leave insects more vulnerable to the insecticide's harmful effects, while higher concentrations may induce immediate but less deadly disturbances. Desneux et al. (2007) provided evidence that physiological alterations at reduced insecticide dosages increased overall toxicity in *Bemisia tabaci*. Khan et al. (2013) discussed the impact of sublethal doses on physiological responses in *Tribolium castaneum*, showing that these responses can affect the efficacy of insecticides at different doses. Bahlai et al. (2010) found that physiological responses in *Apis mellifera* to lower doses of various insecticides led to increased sensitivity and higher mortality. Thompson et al. (2005) demonstrated that sublethal doses of insecticides in *Helicoverpa armigera* altered physiological responses, increasing the overall effectiveness of the insecticides. Gentz et al. (2010) discussed how physiological changes in *Drosophila suzukii* at lower doses of spinosad led to higher mortality.

3. Understanding the Concept of Hormesis

The integration of hormesis into pest management strategies represents a promising approach to creating more effective, environmentally friendly, and sustainable pest control methods. By focusing on the advantageous effects of low pesticide doses, it is possible to enhance pest management efficacy while minimizing adverse impacts on ecosystems and reducing the risk of resistance development. Understanding hormesis is crucial for several reasons:

3.1. Optimizing Pesticide Use:

Using large amounts of insecticides to get optimal effectiveness is a common practice in traditional pest management techniques. On the other hand, excessive dosages may cause harm to non-target species, contaminate the environment, and cause pest resistance. Pest management can be modified to use smaller dosages of insecticides efficiently, minimizing these adverse effects, by understanding hormesis. According to research by Calabrese and Baldwin (2003), hormesis has the potential to change environmental science and toxicology by proving its beneficial effects at low concentrations. Luckey (2019) emphasized the potential for hormesis to revolutionize pest management by reducing the amount of chemicals needed while maintaining effectiveness.

3.2. Reducing Environmental Impact:

Pesticides applied at high doses harm non-target creatures, soil, and water, and hence contribute to environmental contamination. Hormesis-based tactics reduce pollution of the environment by using lower amounts of pesticides. Reducing pesticide dosages has been shown by Anderson and Lydy (2002) to lessen environmental toxicity, which is good for ecosystems and biodiversity.

3.3. Enhancing Sustainability:

Maintaining a balance between efficient pest treatment and minimal impact on the environment and human health is the goal of sustainable pest management. Hormesis, by leveraging its low-dose effects, provides a framework for developing sustainable pest management techniques. By promoting reduced dependency on chemical inputs and enhancing long-term sustainability, hormesis plays a crucial role in integrated pest management (IPM) programs, as highlighted by studies such as those by Morse and Buhler (1997) and Gilliom (2007).

3.4. Mitigating Resistance Development:

Insecticides tend to become less effective over time as pests often develop resistance to high dosages of these chemicals. By using lower dosages that may not strongly trigger resistance mechanisms, hormesis can help in delaying the development of resistance. Studies by Ffrench-Constant et al. (2004) and Gould (1998) provide evidence supporting the idea that lower doses can reduce the selection pressure for resistance, thereby extending the effective lifespan of insecticides.

3.5. Improving Human and Animal Health:

High pesticide dosages can pose significant health risks to both humans and animals due to exposure and bioaccumulation. These risks can be mitigated by adopting pest management strategies informed by hormesis. Carson (1962) and Aktar et al. (2009) provide strong support for the idea that reducing pesticide doses can lead to safer agricultural and urban environments, highlighting the health benefits of minimizing exposure to harmful chemicals.

4. Classification of Insecticide Groups Showing and Not Showing Hormesis

Understanding the hormetic responses of different insecticide groups is crucial for optimizing pest management strategies. Hormesis refers to the phenomenon where low doses of a toxic substance can stimulate beneficial effects, while higher doses may be harmful. This concept is particularly relevant in pest management, where sublethal doses of insecticides can sometimes enhance their efficacy by triggering hormetic effects. Table 1 summarizes the classification of various insecticide groups based on their hormetic responses.

Table 1: Presence or Absence of Hormesis in Various Insecticide Groups

Insecticide Group	Shows Hormesis	Does Not Show Hormesis	Examples
Anthranilic Diamides	✓		Chlorantraniliprole (Lahm et al., 2007; Cordova et al., 2006)
Benzoylureas	✓		Diflubenzuron (Graf, 1993)
Carbamates		✓	Carbaryl (Gaines, 1969)
Diamides	✓		Flubendiamide (Tohnishi et al., 2005)
Insect Growth Regulators (IGRs)	✓		Methoprene (Henrick et al., 1973)
Neonicotinoids	✓		Imidacloprid (Nauen et al., 1998)
Organochlorines		✓	Dieldrin (Walker, 2008)

Organophosphates	✓		Chlorpyrifos (Zhao et al., 1996)
Oxadiazines	✓		Indoxacarb (Wing et al., 2010)
Phenylpyrazoles		✓	Fipronil (Gunasekara et al., 2007)
Pyrroles		✓	Chlorfenapyr (Black et al., 1994)
Pyrethroids	✓		Permethrin (Bloomquist, 1993)
Spinosyns	✓		Spinosad (Sparks et al., 1998)
Tetramic Acid Derivatives		✓	Spirotetramat (Brück et al., 2009)

4.1. Insecticide Groups Not Showing Hormesis

While many insecticides exhibit hormesis, where sublethal doses increase efficacy or alter insect behavior in beneficial ways, others do not show such effects. This classification is critical for understanding how different insecticide groups influence pest management and resistance dynamics. Insecticides that do not display hormesis generally follow a linear dose-response model, where the effect increases proportionally with the dose, without the biphasic response seen in hormetic substances. These insecticides typically act through mechanisms that do not induce hormetic effects, such as causing direct and linear physiological damage or through mechanisms that saturate target sites at higher doses.

4.2. Evidence Contradicting the Occurrence of Hormesis in Various Insecticide Groups

4.2.1. Carbamates

Fukuto (1990) highlighted the toxicology of carbamate insecticides, emphasizing their mechanism of action through acetylcholinesterase inhibition and noting the absence of hormetic effects, with a consistently toxic response observed across various studies. Similarly, Casida and Durkin (2013) investigated the effects of carbamates, including carbaryl and methomyl, and reported no evidence of hormesis, as these compounds demonstrated a linear dose-response relationship. Furthermore, Hemingway and Karunaratne (1998) examined resistance mechanisms in mosquitoes and concluded that carbamates, such as propoxur, do not induce hormetic effects but instead elicit a typical toxicological response.

4.2.2. Phenylpyrazoles

Gunasekara et al. (2007) examined the environmental fate and toxicology of fipronil, a phenylpyrazole insecticide, and reported no evidence of hormetic effects, highlighting its straightforward toxic response in both target and non-target organisms. Similarly, Tingle et al. (2003) studied the effects of fipronil and other phenylpyrazoles on various invertebrates and found no signs of hormesis, observing instead a typical dose-dependent toxic response. Additionally, Hainzl and Casida (1996) investigated the mode of action of fipronil and concluded that it does not induce hormetic effects, as the insecticide consistently caused mortality without any low-dose stimulation effects in multiple insect species.

4.2.3. Organochlorines

Narahashi et al. (1998) studied the neurotoxic effects of organochlorines such as DDT and observed no evidence of hormesis, reporting a consistent toxicological response across various doses. Similarly, Ecobichon (2001) reviewed the toxicity of organochlorine pesticides, including aldrin and dieldrin, and concluded that these compounds do not induce hormetic effects, instead exhibiting a linear dose-response curve leading to toxicity. The ATSDR (2018) further discussed organochlorines like chlordane and heptachlor, indicating that these substances do not exhibit hormesis but cause adverse effects at all exposure levels. Additionally, Brown (1992) reviewed occupational studies involving chlordane exposure and found no evidence of hormesis, linking the pesticide to various toxic effects.

4.2.4. Pyrroles

Abdelhamid et al. (2022) investigated the toxicological effects of new pyrrole derivatives on *Spodoptera littoralis* and reported no evidence of hormetic responses, demonstrating that these compounds, including chlorfenapyr, exhibit a consistent toxic effect without low-dose stimulation. Similarly, Kavallieratos et al. (2011) studied the efficacy of chlorfenapyr in controlling stored-product insect pests and observed that abiotic and biotic factors influence its effectiveness while maintaining a consistent toxic response with no hormetic effects under varying conditions. Additionally, Black et al. (1994) examined the action of pyrrole insecticides and concluded that these compounds do not induce hormesis, consistently causing mortality without low-dose stimulation in insect populations.

4.2.5. Tetramic Acid Derivatives

Alam et al. (2020) studied the effects of spiromesifen, a tetramic acid derivative, on *Musca domestica* and found no evidence of hormetic responses, demonstrating a consistent toxic effect without low-dose stimulation. Similarly, Bielza et al. (2019) investigated resistance to spiromesifen and spirotetramat in *Bemisia tabaci* field populations in Spain and reported no signs of hormesis, observing a linear dose-response relationship without low-dose stimulation. Additionally, Brück et al. (2009) reviewed the performance of spiromesifen in agricultural settings and concluded that tetramic acid derivatives like spiromesifen do not exhibit hormesis, instead producing a predictable toxic response.

4.3. Insecticide Groups Showing Hormesis

Unlike traditional insecticides that often exhibit linear dose-response relationships, several insecticide groups have been observed to exhibit hormetic effects. These effects are characterized by enhanced physiological responses, increased activity, or improved survival at sublethal doses, which can potentially optimize pest control strategies.

4.4. Evidence Demonstrating Hormesis Induced by Insecticide Groups

4.4.1. Benzoylureas

Xia et al. (2024) investigated the sublethal and transgenerational effects of lufenuron, a benzoylurea insecticide, on *Panonychus citri* and reported evidence of hormetic effects, with low doses enhancing certain biological traits across generations. Similarly, Hou et al. (2024) studied the transgenerational hormesis and sublethal effects of various insecticides, including diflubenzuron, on *Spodoptera frugiperda* and its endoparasitoid *Cotesia marginiventris*, finding that low doses of diflubenzuron induced hormetic effects, leading to improved survival and development across generations. Additionally, Teixeira et al. (2024) examined the embryotoxic effects of diflubenzuron on zebrafish (*Danio rerio*) and observed hormetic effects, with low doses stimulating certain developmental processes.

4.4.2. Diamides

Wang et al. (2022) investigated the hormetic effects of chlorantraniliprole, a diamide insecticide, on the egg parasitoid *Trichogramma chilonis*, used for managing rice lepidopterans, and found that low doses enhanced biological functions, including increased parasitism rates and longevity. Similarly, Li et al. (2023) examined the sublethal effects of broflanilide, a novel meta-diamide pesticide, on *Spodoptera litura*, reporting hormetic effects, with low doses leading to increased survival and reproductive rates in treated populations. Additionally, Zhang et al. (2015) studied the lethal and sublethal effects of cyantraniliprole on *Bactrocera dorsalis* and observed hormesis, as low doses stimulated increased survival and reproductive rates in the treated population.

4.4.3. Insect Growth Regulators (IGRs)

Hussain et al. (2024) studied the sublethal impacts of Buprofezin and Pyriproxyfen, both insect growth regulators (IGRs), on the cotton mealybug *Phenacoccus solenopsis*, and reported evidence of transgenerational hormesis, with low doses enhancing survival, growth, and reproductive rates across generations. Similarly, Santos et al. (2018) investigated the non-targeted insecticidal stress of IGRs on the Neotropical brown stink bug *Euschistus heros* and observed hormetic effects, as low doses improved sexual fitness and overall reproductive performance.

4.4.4. Neonicotinoids

Ullah et al. (2020) investigated the transgenerational hormesis effects of thiamethoxam, a neonicotinoid insecticide, on Aphis gossypii and found that low doses enhanced survival and reproduction across generations while altering gene expression associated with these traits. Similarly, Ding et al. (2018) studied the sublethal and hormetic effects of clothianidin on the black cutworm (*Agrotis ipsilon*), reporting that low doses induced hormetic effects, including increased survival, reproduction, and enhanced physiological responses. Additionally, Qu et al. (2015) examined the sublethal and hormesis effects of imidacloprid on the soybean aphid (*Aphis glycines*) and observed that low doses enhanced survival, reproduction, and development in the treated populations.

4.4.5. Organophosphates

Deng et al. (2016) studied the hormetic effects of chlorpyrifos, an organophosphate insecticide, on insecticide-resistant and -susceptible populations of *Plutella xylostella* (diamondback moth) under varying temperatures and found that low doses enhanced survival and reproduction, particularly under high-temperature conditions. Similarly, Dewer et al. (2016) investigated the behavioral and metabolic effects of sublethal doses of chlorpyrifos on the Egyptian cotton leafworm (*Spodoptera littoralis*), observing hormetic effects such as increased metabolic activity and altered behavior. Additionally, Silva et al. (2024) examined the impact of temperature on the hormetic response of *Myzus persicae* (green peach aphid) after sublethal exposure to organophosphate insecticides and found that low doses induced hormetic effects, with temperature influencing the extent of the response.

4.4.6. Oxadiazines

Rajab et al. (2022) studied the sublethal effects of indoxacarb, an oxadiazine insecticide, on the life history traits of *Blattella germanica* (German cockroach) and found that low doses induced hormetic effects, including increased survival, reproductive rates, and enhanced development in the treated populations. Similarly, Wang et al. (2023) examined the sublethal effects of an indoxacarb enantiomer on the diamondback moth (*Plutella xylostella*) and its predator *Chrysoperla sinica*, and found that low doses induced hormetic effects, such as increased survival and enhanced physiological responses in both the pest and the predator.

4.4.7. Pyrethroids

Qu et al. (2017) investigated the sublethal and hormetic effects of beta-cypermethrin, a pyrethroid insecticide, on the soybean aphid (*Aphis glycines*) and found that low doses induced hormetic effects, enhancing biological traits such as reproductive potential, survival rates, and overall life table parameters. Similarly, Rigby et al. (2021) studied the impact of sublethal permethrin exposure on both susceptible and resistant genotypes of the urban disease vector *Aedes aegypti* and found that low doses induced hormetic effects, including increased survival and altered physiological responses, which varied depending on the genotype. Additionally, Malbert-Colas et al. (2020) examined the effects of low concentrations of deltamethrin on the pest moth *Spodoptera littoralis* and found that the hormetic effects were dependent on developmental stages and sexes, with low doses stimulating increased survival and physiological responses in specific groups.

4.4.8. Spinosyns

Biondi et al. (2012) investigated the non-target impact of spinosyns, including spinosad, on beneficial arthropods and found that low doses induced hormetic effects, such as increased physiological activity and enhanced survival rates, in various beneficial arthropod species. Similarly, D'Ávila et al. (2018) studied the effects of spinosad on the aphid parasitoid *Aphidius colemani* and found that low doses induced hormetic effects, leading to increased survival, parasitism rates, and reproductive output in the parasitoid population. Additionally, Deans & Hutchison (2022) examined the hormetic and transgenerational effects of spinosad on *Drosophila suzukii* (spotted-wing drosophila) and found that low doses induced hormetic effects, enhancing survival and reproductive performance, with some effects persisting across generations.

5. Why do certain Insecticides Show Hormesis?

Hormesis, characterized by beneficial effects at low doses of a toxicant, varies among different insecticide groups due to their distinct modes of action. Understanding why specific insecticides exhibit hormetic effects is crucial for optimizing pest management strategies. Hormesis often results from the interaction between the insecticide's biochemical target and the physiological responses it triggers at sublethal doses.

5.1. Mechanisms of Hormesis Induced by Different Insecticide Groups

5.1.1. Neonicotinoids

i) **Activation of Nicotinic Acetylcholine Receptors (nAChRs):** Neonicotinoids, such as imidacloprid and thiamethoxam, primarily target the nicotinic acetylcholine receptors (nAChRs) in the nervous system of insects. These receptors play a crucial role in transmitting nerve impulses. When exposed to low doses of neonicotinoids, these receptors can be partially activated, leading to a mild increase in neuronal activity. This low-level stimulation can trigger a stress response in the insect, leading to changes in behavior and physiology. For example, Qu et al. (2017) observed that sublethal doses of beta-cypermethrin, a related pyrethroid, led to enhanced survival and reproductive potential in *Aphis glycines*, a mechanism that can be similarly observed with neonicotinoids.

ii) **Enhanced Behavior and Physiological Functions:** At low doses, neonicotinoids may enhance certain behavioral and physiological functions in insects, such as feeding, movement, and reproduction. This enhancement is part of the hormetic response, where the organism's biological systems are stimulated to adapt to the low-level stress induced by the insecticide. This response can make the insects more active and increase their reproductive output. However, this increased activity and physiological function can also make them more vulnerable to subsequent insecticide exposures or environmental stresses. Ullah et al. (2020) demonstrated that thiamethoxam at sublethal doses led to transgenerational effects, with alterations in gene expression that enhanced the survival and reproduction of *Aphis gossypii*.

iii) **Detoxification and Metabolic Activation:** Low doses of neonicotinoids can also stimulate the activity of detoxification enzymes in insects. These enzymes, such as cytochrome P450s, are responsible for breaking down toxic substances. The mild stress induced by low-dose exposure can upregulate these detoxification pathways, temporarily enhancing the insect's ability to survive in the presence of the insecticide. However, prolonged exposure can lead to an overburdened detoxification system, eventually resulting in increased mortality. Ding et al. (2018) found that low doses of clothianidin, a neonicotinoid, induced a hormetic response in the black cutworm (*Agrotis ipsilon*), enhancing physiological activity and potentially leading to greater mortality under continued exposure.

5.1.2. Pyrethroids

i) **Affect Sodium Channels in Nerve Cells:** Pyrethroids, such as permethrin and deltamethrin, target sodium channels in the nerve cells of insects. These channels are essential for the initiation and propagation of nerve impulses. At low doses, pyrethroids cause a prolonged opening of these sodium channels, leading to increased nerve firing and overstimulation of the nervous system. This overstimulation can result in heightened activity, increased movement, and stress responses in insects, which may enhance their chances of survival in the short term.

For example, Qu et al. (2017) demonstrated that low doses of beta-cypermethrin increased physiological activity and stress responses in *Aphis glycines*, leading to enhanced survival and reproduction.

ii) **Sublethal Doses Can Alter Behavior:** At sublethal doses, pyrethroids can significantly alter insect behavior, such as increasing locomotor activity, making insects more likely to come into contact with lethal doses of the insecticide or other environmental hazards. This behavioral change is part of the hormetic response, where low doses of a stressor induce a beneficial effect that increases the chances of encountering a subsequent lethal exposure. Rigby et al. (2021) found that sublethal permethrin exposure increased the activity and stress responses in both susceptible and resistant genotypes of *Aedes aegypti*, thereby altering their interactions with the environment and potentially increasing their susceptibility to further exposure.

iii) **Enhancement of Stress Responses:** Low doses of pyrethroids can also enhance stress responses in insects, which may involve upregulation of detoxification enzymes or increased metabolic activity. This enhanced response can temporarily improve the insect's resilience but can also lead to greater mortality if the stress is prolonged or if the insect encounters a subsequent higher dose of the insecticide. Malbert-Colas et al. (2020) observed that low concentrations of deltamethrin induced hormetic effects in *Spodoptera littoralis*, with the effects varying depending on the developmental stage and sex of the insect.

5.1.3. Organophosphates

i) **Inhibit Acetylcholinesterase:** Organophosphates, such as chlorpyrifos and malathion, inhibit the enzyme acetylcholinesterase (AChE), which is crucial for breaking down acetylcholine in the synaptic cleft of nerve cells. At low doses, this inhibition leads to an accumulation of acetylcholine, resulting in enhanced cholinergic signaling and overstimulation of the nervous system. This overstimulation can induce stress responses in insects, making them more susceptible to further exposures. For instance, Deng et al. (2016) demonstrated that low doses of chlorpyrifos induced hormetic effects in *Plutella xylostella*, leading to enhanced survival and reproduction, especially under high-temperature conditions.

ii) **Low Doses May Upregulate Detoxification Enzymes:** At sublethal doses, organophosphates can trigger the upregulation of detoxification enzymes such as cytochrome P450s, glutathione S-transferases, and esterases in insects. This upregulation is a part of the hormetic response, where the organism's metabolic processes are stimulated to cope with the toxicant. In *Helicoverpa armigera*, for example, this response can initially improve survival and resistance, but it may also lead to increased susceptibility if the stress persists or if the insect encounters a higher dose. Dewer et al. (2016) observed that sublethal doses of chlorpyrifos enhanced metabolic activity in *Spodoptera littoralis*, indicating a similar mechanism likely at play in other insects like *Helicoverpa armigera*.

iii) **Induction of Hormetic Responses:** Low doses of organophosphates can induce hormetic responses by stimulating adaptive mechanisms in insects. These responses may include increased activity, enhanced feeding, and improved reproductive success. However, these initial benefits can make insects more vulnerable to further environmental stressors or higher doses of the insecticide. Silva et al. (2024) demonstrated that sublethal exposure to organophosphates increased stress responses and susceptibility in *Myzus persicae*, especially when combined with environmental stress factors such as temperature variations.

5.1.4. Insect Growth Regulators (IGRs)

i) **Interfere with Insect Development and Hormonal Pathways:** Insect Growth Regulators (IGRs) disrupt normal insect development by interfering with hormonal pathways that regulate molting and metamorphosis. At low doses, these disruptions can paradoxically enhance growth and developmental processes, leading to a hormetic effect. For example, Santos et al. (2018) found that low doses of insecticides, including IGRs, could enhance reproductive fitness in non-target species like *Euschistus heros*, indicating the potential for IGRs to induce hormetic effects through similar mechanisms.

ii) **Transgenerational Effects with Hormesis in Subsequent Generations:** IGRs can induce transgenerational hormetic effects, where the offspring of treated insects exhibit enhanced growth or reproductive success. This has been observed in pest species such as *Phenacoccus solenopsis*, where low doses of IGRs like buprofezin and pyriproxyfen led to hormesis that persisted across generations. Hussain et al. (2024) demonstrated that sublethal exposure to these IGRs resulted in increased survival and reproduction in subsequent generations, highlighting the long-term implications of hormesis in pest populations.

5.1.5. Spinosyns

i) **Target Nicotinic Acetylcholine Receptors and GABA Receptors:** Spinosyns, such as spinosad, primarily target nicotinic acetylcholine receptors (nAChRs) and gamma-aminobutyric acid (GABA) receptors in insects. At low doses, the activation of these receptors leads to increased neuronal activity, causing overstimulation of the nervous system. This overstimulation can trigger stress responses in insects, making them more susceptible to subsequent exposures. Biondi et al. (2012) reported that spinosyns could induce various physiological effects, including hormesis, in beneficial arthropods, which suggests that similar mechanisms may occur in pest species.

ii) **Enhanced Physiological Activity at Low Doses:** At low doses, spinosyns can enhance physiological activity in insects, such as increased locomotion, feeding, or reproduction. This heightened activity can make insects more likely to encounter lethal exposures or exacerbate stress responses, ultimately leading to higher mortality. D'Ávila et al. (2018) found that sublethal doses of spinosad led to increased parasitism and reproductive output in the aphid parasitoid *Aphidius colemani*, highlighting the hormetic effects of spinosyns in non-target species, which may also apply to pests.

iii) **Induction of Hormetic and Transgenerational Effects:** Spinosyns can also induce hormetic effects that persist across generations. Deans & Hutchison (2022) demonstrated that low doses of spinosad induced hormetic responses in *Drosophila suzukii* (spotted-wing drosophila), leading to increased survival and reproductive performance that were passed on to subsequent generations, highlighting the potential long-term impacts of low-dose exposure.

5.1.6. Diamides

i) **Affect Ryanodine Receptors:** Diamides, such as chlorantraniliprole and cyantraniliprole, target ryanodine receptors in insect muscle cells. These receptors regulate the release of calcium ions, which are crucial for muscle contraction. At low doses, diamides cause a controlled release of calcium, leading to increased muscle contraction and activity. This heightened activity can stimulate physiological processes and make insects more susceptible to environmental stressors or subsequent insecticide exposures. For example, Wang et al. (2022) found that low doses of chlorantraniliprole induced hormetic effects in a key egg parasitoid, enhancing its effectiveness in controlling rice lepidopteran pests.

ii) **Enhance Biological Functions:** At sublethal doses, diamides can enhance certain biological functions in insects, such as feeding, reproduction, and growth. These enhancements are part of the hormetic response, where low levels of stress from the insecticide stimulate beneficial physiological changes. Li et al. (2023) observed that low doses of broflanilide, a novel meta-diamide, led to enhanced physiological activity and survival in *Spodoptera litura*, indicating a hormetic effect that could influence pest resilience and management strategies.

iii) **Induction of Stress Responses:** The activation of ryanodine receptors by low doses of diamides can also induce stress responses, leading to increased metabolic activity and detoxification efforts by the insect. This can initially improve survival but may eventually lead to greater susceptibility to further exposures. Zhang et al. (2015) found that low doses of cyantraniliprole led to enhanced physiological responses in *Bactrocera dorsalis*, resulting in increased mortality, demonstrating the potential hormetic effects of this diamide.

5.1.7. Benzoylureas

i) **Disrupt Chitin Synthesis:** Benzoylureas, such as diflubenzuron, inhibit chitin synthesis, which is crucial for the formation of the insect exoskeleton. This disruption leads to incomplete molting and eventual death in insects. However, at low doses, these insecticides can paradoxically stimulate growth and development, a phenomenon observed in species like *Spodoptera littoralis*. For instance, Xia et al. (2024) documented that sublethal doses of lufenuron, a benzoylurea, enhanced certain biological traits in *Panonychus citri*, indicating a hormetic response.

ii) **Transgenerational Effects with Hormesis in Subsequent Generations:** Benzoylureas can induce transgenerational effects, where hormesis is observed not only in the directly exposed generation but also in subsequent generations. This effect has been noted in species like *Ostrinia nubilalis* (European corn borer), where exposure to low doses of benzoylureas led to enhanced survival and reproductive success across multiple generations. Hou et al. (2024) reported similar transgenerational hormesis effects in *Spodoptera frugiperda* when exposed to sublethal doses of insecticides, suggesting that benzoylureas could have long-lasting impacts on pest populations.

iii) **Stimulate Growth and Development:** Low doses of benzoylureas can paradoxically stimulate growth and development in insects, leading to enhanced physiological functions. This hormetic response can make insects more resilient to environmental stressors and potentially more difficult to manage. Teixeira et al. (2024) found that sublethal doses of diflubenzuron led to increased developmental rates and survival in zebrafish embryos, which suggests that similar effects could be observed in pest insects, contributing to the resilience of pest populations.

5.1.8. Oxadiazines

i) **Block Sodium Channels:** Oxadiazines, such as indoxacarb, work by blocking sodium channels in the nervous system of insects. This action disrupts nerve impulse transmission, leading to paralysis and eventually death. However, at low doses, the partial blockage of sodium channels can paradoxically stimulate increased activity in insects, making them more susceptible to environmental stressors or subsequent insecticide exposures. Wang et al. (2023) observed that sublethal doses of indoxacarb stimulated increased activity and physiological responses in *Plutella xylostella*, indicating a hormetic effect that could enhance the effectiveness of pest control strategies.

ii) **Enhanced Physiological Activity at Low Doses:** At sublethal doses, oxadiazines can enhance certain physiological activities in insects, such as feeding, reproduction, and locomotion. This enhanced activity, while initially appearing beneficial to the insect, can actually lead to increased mortality as the insect becomes more vulnerable to additional stressors or higher doses of the insecticide. Rajab et al. (2022) demonstrated that low doses of indoxacarb led to increased susceptibility and altered life history traits in *Blattella germanica*, suggesting that hormetic effects could similarly affect other pest species like *Helicoverpa armigera*.

iii) **Induction of Stress Responses:** The activation of sodium channels at low doses can also induce stress responses in insects, leading to increased metabolic activity and detoxification efforts. These stress responses may initially help the insect survive, but they can also make it more susceptible to further exposures. Guedes et al. (2019) found that low doses of indoxacarb induced stress responses in *Tuta absoluta*, increasing mortality rates and demonstrating the potential for hormetic effects to enhance pest management strategies.

The diverse mechanisms underlying hormesis in insecticides reflect their unique interactions with insect physiology and biochemistry. By targeting specific receptors or enzymatic pathways, these insecticides can induce hormetic effects that enhance insect susceptibility or stress responses at low doses. Understanding these mechanisms not only aids in optimizing pest management practices but also highlights the potential for more targeted and effective use of insecticides. Future research should continue to explore these interactions to refine pest control strategies and improve their sustainability.

6. Conclusion

The presence of hormesis in insecticides highlights the need to incorporate these effects into pest control strategies for enhanced efficacy. Sublethal doses can trigger beneficial physiological responses, optimizing pest management practices for better control. A deeper understanding of hormesis, including its influence on insect behavior, resistance development, and physiological responses, can guide the creation of more effective and sustainable pest management approaches. This knowledge enables the design of strategies that not only control pest populations more efficiently but also reduce the environmental impact of pest control measures. Careful consideration of dose levels and environmental conditions is vital, allowing for fine-tuned approaches that maximize effectiveness while minimizing unintended consequences. Pest management informed by hormesis can lead to resilient agroecosystems, improved crop yields, and long-term sustainability. Ultimately, advancing our understanding of hormesis will help develop pest control solutions that are both effective and environmentally responsible, benefiting agricultural productivity and ecosystem health.

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