

Studying the Phenomenon of Hormesis and Its Effect on Insects

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ABSTRACT

Hormesis is a well-known adaptive mechanism that shows the stimulating effect of low concentrations of chemicals on living organisms. By this adaptive mechanism, mild stressors can enhance the host's protective capacity, while the same factors are lethal or harmful at excessive levels. In agricultural ecosystems, insects face many stressors such as heat, chemicals, and nutrient deficiencies, often at low levels. Currently, the hormetic effects of insects are well known and this phenomenon can be used to manage insects, structure, and ecological function in agricultural ecosystems. Insects are ubiquitous and exist in almost all living organisms, both terrestrial and freshwater. Ecosystems in agricultural environments are willingly or unwillingly exposed to a set of synthetic pesticides and other chemical and non-chemical stressors. Therefore, many biological and non-biological processes in the pest control that an insect is exposed to in the field change in terms of space and time. Studying the phenomenon of hormesis and paying attention to it in management programs is of great importance. In the studies of this phenomenon, it should be noted that to evaluate the effects of hormesis caused by insecticides, it is important to conduct a field study and experiment in the field to generalize it to the environment and ecosystem. Due to the importance of this phenomenon, few studies have been done regarding toxicology in the field of insects. It is suggested that the studies should be more carefully examined for morphological, physiological, molecular, behavioral, and demographic markers for hormesis or coping with it.

Keywords: Insects, Manage insects, Hormesis, Agricultural ecosystems.

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INTRODUCTION

Humans use different methods to control and dispose of plant pests to prevent the destruction and destruction of their agricultural products, which is obtained by spending a lot of effort and time, and also due to the population growth and the limitations in the production of various food products. Among these methods, one of the most common is the use of pesticides. The definition of pesticide provided by the US Environmental Protection Agency is that a pesticide is a substance or mixture of substances that is used to prevent, destroy, eliminate, or reduce any pest [1, 2].

The management of pests (insects) in the last 70 years has been mainly via the use of chemical

pesticides. Therefore, insect populations in forestry and agriculture are potentially exposed to large numbers of pesticides that may happen through digestive and respiratory contact [3-5]. The effect of insecticides depends on various factors, however the dose is the main determinant of the effect of insecticides. The dose of pesticide that the insect is exposed to varies greatly in different places and times. For example, growers try to spray pesticide evenly over their plants, but even a small wind can cause drift, resulting in variable amounts of the pesticide solution being sprayed onto plants across the field.

Pesticide evaporation, which is especially important on dry and hot days in terms of insecticide effectiveness, can significantly reduce

the amount of pesticide remaining on the target. Even within a plant, spray penetration through the canopy can differ significantly. Also, the amount of pesticide absorption will be different in the upper and lower levels of the plant. Temperature, humidity, acidity, soil, light absorption by the plant, and chemical and microbial degradation on the soil or foliage are the main processes that reduce and change the solution used toxicity. For example, the photodegradation rate of an insecticide will differ with light intensity [6, 7]. It is also possible that the systemic insecticides that are used on the soil or crops are decomposed in the plant under the influence of mechanisms and the toxicity of the insecticide is reduced. In addition, systemic insecticide concentrations can vary over time in the same plant as well as in new and old foliage [8, 9]. Therefore, many of the biotic and abiotic processes in pest control that an insect is exposed to in the field are subject to change spatially and temporally. Although the response relationships study has traditionally been accounted for by non-threshold or threshold linear models, the response model is a biphasic model determined by stimulation at low dose and inhibition at high dose and is at present widely used as a general biological phenomenon model [3-5].

As a result, although hormesis is an important phenomenon in pest management, however, contrary to the potential consequences of hormesis stimuli in the management of pests and the opportunities that models can provide in primary research, this phenomenon has received relatively little attention from Toxicologists. Considering the importance of the phenomenon of hormesis, this article investigates the hormetic effects of various factors in insects according to previous research.

Concepts of hormesis in insects

The stimulating effect of low concentrations of toxic chemicals on living organisms is called hormesis [10]. The hormesis concept has evolved significantly over the years, and several terms have been utilized to describe homorhematic dose-response. Hormesis is derived from the Greek root meaning desire and quick movement. It is usually used in biological responses to low doses of toxins and other stressors [11, 12].

In the literature related to insects, three terms Hormoligosis, Hormesis, and Pesticide-mediated

homeostatic modulation are mainly used. Hormesis is used in the case of toxins and stimulants when their effects in low and high doses are the opposite of each other [3-5]. In other words, hormesis refers to a process in which a cell, organism, or group of living organisms shows a biphasic (dual) response to processed amounts of a substance under specific conditions (chemical, olfactory stimulus, or metabolic stress).

Usually, contact with low doses produces stimulating or beneficial effects and high doses produce inhibitory or toxic effects, and this phenomenon often occurs in toxicological observations [13-15]. This phenomenon was first observed in studies related to growth regulators including herbicides or even drugs [16]. Then it was observed and studied the chemicals secreted from living plant organs or decaying plant remains from the surface of the plant to the biochemical levels in the cells. This phenomenon has been observed in countless unicellular and multicellular organisms and is used for many biological actions, such as the growth of lifespan, cognitive function, multiple molecular and metabolic processes, and immune response [17]. Today, the phenomenon of hormesis has been proven for many factors such as mercury, arsenic, insecticides, and radiation, and it can be said that all living organisms, including bacteria, rodents, birds, and worms, use this vital mechanism to survive. In research, it was shown that low amounts of cadmium enhanced the reproductive capacity of snails, but high doses were lethal [18]. Or that the element selenium is a micronutrient and is essential for human health (it is involved in the proper functioning of 30 types of proteins), but if it is consumed in large amounts, it is toxic and can cause death. Hormetic impacts are not restricted to chemical stressors including heavy metals and pesticides and may appear following mild radiation-induced temperature stress [19].

The terms Hormoligant and Hormoligosis were coined by Lucky at the First International Conference on Antibiotics in Agriculture [20]. Lackey described hormesis as a condition in which minute amounts of any stressor (social, psychological, physical, or chemical) are irritating to the organism under various conditions, while larger amounts of the stressor can be adverse to the same organism. Here the

norm of high-dose inhibition and low-dose stimulation is revealed. Lackey's definition introduces hormesis utilization to conditions where the organism is stressed but no stimulation is reported until a few amount of a second stressor is introduced into the system. Hormoligosis can be optimized if a small amount, but not too small, of an individual's developmental stages to deal with subsequent stresses. Distinguishing between these potential interactive impacts is essential because the degree of stimulation can be approximately predicted in a mixture by knowing the concentration-response relationships of the individual stresses. Since all stressful factors may cause hormesis, therefore, hormesis can be introduced as a type of mixed hormesis [3-5].

Cohen [21] proposed the homeostatic modulation concept by pesticides. He argued that the term hormesis is not utilized in conditions where stimulatory impacts are reported in a pest arthropod that is neither controlled nor targeted by a pesticide. He specified acaricides (stressors that target ticks) from pesticides (chemicals that impact both types of arthropods) and insecticides (toxic chemicals, particularly insects). Examples are given as cases in which tick reproduction stimulation is observed following exposure to insecticides such as carbaryl, DDT, insecticidal pyrethroids, or imidacloprid. These compounds are not considered acaricides in terms of pattern of use. And they are not predestinate to control tick pests. But insects and ticks often live in the same environment, and in some cases where the above compounds are utilized to manage pest insects, an increase in tick populations has been observed. He believes that the stimulatory impacts reported with pesticides that are non-toxic at high doses to arthropods (such as the reproduction stimulation of the two-spotted tartan mite) cannot be assigned to hormesis and has presented the term modulation of pesticide-mediated homeostatic. The broader term includes stimulatory and hormesis impacts of pesticides on pests of non-target.

It seems that the term hormesis, instead of the terms homeostatic and hormesis modulation by pesticide, is at least sufficient to illustrate the stimulatory responses that have been encountered in the toxicology of insects. Modulation of pesticide-mediated homeostatic

response does not suggest a different mechanistic basis than hormesis. It is a semantically based concept and biologically inseparable from hormesis. Hormoligosis is also a term of strong historical significance in insects and toxicology is a term utilized by several authors when explaining insecticide-induced irritation in insects. By explanation, it may be separated from hormesis that any organism, cell, or insect must experience sub-optimal conditions before any experienced biological stimulation by an insecticide low dose or any stressor. But it is a case of mixed hormesis [3-5].

The importance of studying hormesis in insects

Emphasis on lethality as an endpoint has historically dominated trials, as sublethal impacts have often been overlooked. This trend has changed with the important recognition of pesticide-induced hormesis, but with the relatively passive involvement of science, following a speculative perspective rooted mainly in the management of agricultural pest and crop yield. In the management of agricultural pests, the direct effects of pesticides on pest species are now directed to the natural enemies of pollinators and pest species [22].

Toxicological studies of insect pests and useful insects have traditionally focused more on lethal effects and high doses, i.e., LD50/LC50 data, as toxicological researches in other disciplines do. In addition, the significance of low-dose insecticide exposure and its lethal effects has long been understood. These are generally introduced in the harmful effects context of low doses on insects. Fertility, longevity, behavior, and similar endpoints, further response-stimulation of biological processes of insecticide-induced through mechanisms of hormetic, have received far less attention. Biological disciplines have devoted much effort to the investigation of insect biochemistry, physiology, molecular biology, toxicology, behavior, genetics, and reproduction, and this work provides an excellent foundation for early dose-response research. The many insect species genomes have been fully or partially mapped [23] and the several function of insect genes is known. Therefore, there are many opportunities to research the basic function of hormesis utilizing insects as model organisms [3-5].

Following the application of an insecticide, there is sometimes an increase in the population of insects or mites at a rate greater than that observed without its use. This may be reported in the primary insect targeted with an insecticide (named pest resurgence) or in a secondary insect species that are initially less economically important (known as "secondary pest outbreaks") [24]. For example, a study showed that low-lethal doses of limonene (LD20) increased the lifespan of adult Mediterranean flies when deprived of protein. When females were exposed to sub-lethal doses of limonene, it had a positive effect on increasing fertility [25].

Evidence for hormesis in insects

Sun [26] reported that high amounts of rotenone spraying were harmful to female aphids, but female aphids treated with low amounts of the poison had more reproduction than control aphids. Subsequently, dieldrin lethal doses were reported to enhance the *Drosophila* lifespan [27] and to increase housefly weight and fertility [28]. Other early studies on the housefly showed that reproduction was stimulated when the pest was exposed to lethal concentrations of different insecticides [29, 30].

Kuenen [31] found that when weevils were fed wheat contaminated with lethal concentrations of DEET, they produced about 20% more offspring than unexposed weevils [31]. It has also been reported in other research that DEDT stimulates egg-laying in beneficial insects (predators) [32]. A study on insect hormesis, when exposed to lethal concentrations of 14 various insecticides, increased the weight of house crickets, was done by Lackey [33]. This was one of the first studies to introduce a low-dose stimulation mechanism.

Chelliah *et al.* [34] reveal that topical utilization of insecticides increases the reproductive output and longevity of the citrus brown shield weevil, but this response varies related to the active ingredient and dose. In another research, stimulation of reproduction and growth caused by insecticides was reported in some aphid species. Qu *et al.* [35] observed in their research that poplar leaf-eating larvae survived organophosphorus and carbamate insecticide treatments. They became heavier pupae and consisted of more total protein and calcium than untreated larvae. In the early 1990s and

subsequent years, the hormesis study was described by biological stimulation in insects (bees, thrips, collembolan beetles, woodlice, and several species of flies, beetles, and butterflies). Cohen [21] presented a report on the stimulatory effects of pesticides on ticks. In many studies, biological stimulation from low insecticide doses is not reported as hormesis. This underscores that the concept of hormesis is not understood by all insect toxicologists who may be now working on this problem [3-5]. Hormesis has been documented in insects in many taxonomic orders that occur in the groups of gradual metamorphosis, incomplete metamorphosis, and complete metamorphosis, indicating that hormesis is a common phenomenon in insects [3-5].

In a study, it has been seen that insects exposed to stressors are affected as adults, pupae, larvae, or eggs, and usually, the stimulating effects are transmitted throughout the life stage [36]. However intergenerational impacts over time have been less investigated. The effect of using different concentrations of chlorpyrifos on *Platella xylostella* (DEM) resistant and sensitive species was investigated by Deng *et al.* [37]. These insecticide doses used significantly stimulated the growth and fertility of the species. They increased sensitivity and resistance at 25 °C. They also increased the activity of acetylcholinesterase and glutathione S-transferases at 25° C. Many various insecticide active ingredients can produce hormesis effects, which again shows this phenomenon generality. However, some studies to date have studied the insecticide neurotoxins.

The nature and occurrence of hormesis, for instance, growth regulators of parasites, insects, or pathogens occurring in agricultural systems, has been little studied [3-5]. Some research demonstrated some form of reproductive stimulation, however, some studies have determined effects on other parameters including weight and some behavioral and physiological measures. Few have mentioned molecular, hormonal, or biochemical changes in insect hormesis phenomenon [3-5]. In another different research, Lalouette *et al.* [38] investigated the impacts of lethal doses of residual activity, deltamethrin, and persistence in the environment, on the sexual behavior and environmental olfactory system of the cotton

leaf-eating insect. The results show the hormetic effect of a deltamethrin sublethal dose on the response of males to sex pheromone. In another study, Caribbean fruit fly pupae were exposed to anoxia because, during pupation, they are often exposed to heavy tropical rainfall in the soil and face anoxic stress.

The results showed that the lipid levels were the highest in all stages of pupal when they were exposed to previous anoxia. Therefore, prior anoxia contributes to the performance of the organism and shifts sources toward lipid storage by the development of pupal-adult, also enhancing insect growth and fecundity [39]. Stress-induced alters in youth hormones, genes, and vitellogenin in the TIS/TOR signaling pathway, which is directly related to regulating reproduction, development, and growth.

In the research of Rix and Cutler [40], the effects of phenotypic stimuli after exposure to stress and their biochemical or molecular responses were investigated. Stimulation of reproduction, development and growth, survival and longevity, tolerance to temperature, starvation, chemicals, and drought, was in response to stressors such as oxidative stress, pesticides, temperature, crowding, radiation, and starvation. Stimulation of reproduction was often observed around the control treatment and treatments lower than 25%. In many cases, molecular and biochemical responses were directly related to phenotypic responses.

Stimulant concentrations

Meta-analyses show that hormetic stimulation usually peaks at no growth inhibitory concentrations (NOEC). However, in insect studies, irritation is sometimes stated at concentrations much higher than the NOEC. Stimulation above levels of control is not uncommon after exposure to concentrations in the range of LC₂₅. Also, stimulation has been observed in 50LC coils. The relative concentrations that irritate insects are exactly variable and sometimes appear to deviate from the quantitative characteristics normally observed in hormonal responses. Mainly in several cases, it is reported that irritation is caused by insecticide with concentrations much higher than the ineffective concentration. Examination of response variances among treated groups (eg insects exposed to LC₂₅

concentration of insecticide) and control groups in this research indicates that individuals within treated groups and across groups respond homogeneously. So the findings are not altered by the few who have unusually high reproductive output.

It is essential to remember that in a situation field, though reproduction may be stimulated in some insects by exposure to an insecticide concentration of LC₂₅, 25% of the population will be killed by this concentration (susceptible groups), which probably neutralizes the stimulating effects on the population as a factor. Overall, however, the apparent stimulatory effects of the insecticide at concentrations well above the NOEC level are a significant deviation from the defined hormonal dose-response and deserve further investigation [3-5].

The nature of the stressor

Hormesis is recognized as an adaptive mechanism using which mild stressors can enhance the capacity of host protection, while those at extreme levels are lethal or harmful [41]. Insects in agricultural ecosystems struggle with many stressors such as heat, chemicals, and nutrient deficiencies, which are often faced at low levels. It is now well known that exposure to mitigation stress induces stimulatory effects in insects, with application for ecological structure, insect management, and function in agricultural ecosystems. Entomological agroecologists concerned with hormesis need to examine hypotheses that have implications for species interactions, community structure, and function [42].

Where the chemical's molecular structure is very similar, the capability of these various chemicals to persuade hormesis may be different [43]. It is also sometimes reported that insecticides have no stimulatory effects at low doses (not needed around the NOEC). For instance, Chelliah *et al.* [34] reported that while stimulation of reproductive in *Nilaparva lugens* at LC₅₀ and LC₂₅ doses of Decamethrin (a synthetic pyrethroid insecticide), and Methyl parathion (an organophosphate insecticide), respectively, when the pest was exposed to Perthane (a chlorinated hydrocarbon) no irritation was found at multiple similar concentrations under the LC₅₀. Neubauer *et al.* [44] reported great hormetic impacts in aphids exposed to aldicarb

lethal concentrations, but not in Dimethoate or Ethiofencarb. Similarly, the LC30 concentration of endosulfan resulted in decreased growth time for *Heliocoverpa armigera*. However, the same amount of Spinosad, chlorpyrifos, cypermethrin, and asphalt had harmful effects on insect growth. Therefore, the dose-response curves change with the action mode or chemical structure. Unlike neurotoxins, Ho Ramsis has been less studied in insects exposed to pest growth regulators at low doses with insect pathogens [3-5].

Hormesis in populations of insecticide-resistant

Insecticide resistance remains a main issue for pest management (vector control and insect) [45]. Experiments show that hormesis can be a further mechanism that contributes to the phenomenon of pest resurgence. Such resurgence can not only lead to enhanced crop damage but can also cause additional pesticide spraying, potentially exacerbating the effect on non-target insects and the expansion of environmental pollution and insecticide resistance. This problem may be particularly relevant in populations of insecticide-resistant pests, where the effects of insecticides expose insects to the hormic response curve zone. It increases the resistant population's reproduction and increases the resistance alleles frequency. Therefore, insecticide-induced hormesis may be momentous for pesticide resistance evolution and the resistance management programs design, but this has not been well studied [46]. In a study, the effect of Nitenpyram, a neonicotinoid insecticide, was studied for six generations on *Nilaparvata lagens* (BPH), a migratory pest of rice in subtropical, tropical, and temperate regions, at LC20 concentration. It not only enhanced biological fitness (in terms of estimated population size and life table parameters), but also prepared the insect for greater tolerance/resistance to the insecticides nitenpyram, cycloxaprid, and imidacloprid [47].

Beneficial insects and hormesis

Management and mass breeding of useful insects is a multi-billion dollar industry. The potential beneficial consequences of hormesis for human health are well documented, and we may use hormetic principles during insect mass rearing to improve the longevity, immunity, or

reproductive output of insects. Guedes *et al.* [48] reveal that exposure to a permethrin low dose increased the reproductive output of the useful insect predator *Podisus distinctus* and reduced the reproductive time. Similar results were observed in the case of the predatory insect *Suppurus cincticeps* [49]. The parasitoid bee *Encarsia Formosa* showed the hormesis phenomenon when exposed to LC10 concentration of Spirotetramat, which accelerated the location of the host (*Bemisia tahaci* Gennadius) and increased the efficiency of the bee [50]. In another study, Cutler and Rix [51] stated that bees showed a positive and hormetic reaction to low doses of some chemical stressors. Long-term studies should be conducted to characterize whether these types of hormesis-based results can translate into economic affairs during the mass rearing of useful insects.

CONCLUSION

Insects are ubiquitous and exist in almost all living organisms, both terrestrial and freshwater. Ecosystems in agricultural environments are willingly or unwillingly exposed to a set of synthetic pesticides and other chemical and non-chemical stressors. Therefore, many biological and non-biological processes in the pest control that an insect is exposed to in the field change in terms of space and time. Studying the phenomenon of hormesis and paying attention to it in management programs is of great importance. In the studies of this phenomenon, it should be noted that to evaluate the effects of hormesis caused by insecticides, it is important to conduct a field study and experiment in the field to generalize it to the environment and ecosystem. Due to the importance of this phenomenon, few studies have been done regarding toxicology in the field of insects. It is suggested that the studies should be more carefully examined for physiological, molecular, behavioral, morphological, and demographic markers for hormesis or coping with it.

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