



INSECT GUT MICROBIOTA AND PESTICIDE DEGRADATION IN RESPONSE TO INNATE METABOLITES- A REVIEW

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ABSTRACT

Insects host a diverse microbiota in their gut, encompassing bacteria, fungi, viruses, and archaea, influencing their physiology, nutrition, and overall health. The composition of these microbial communities varies with factors like insect species, diet, and the environment. Insect gut microbiota serve pivotal roles such as aiding digestion, synthesizing essential nutrients, safeguarding against pathogens, and detoxifying toxins, including insecticides. A particularly promising facet of their function lies in influencing the metabolism of insecticides. These gut microbiotas can either augment or diminish insecticide toxicity through mechanisms like enzymatic breakdown, sequestration, target site alteration, or modulation of the insect's immune response. Understanding these interactions is paramount for devising sustainable pest management strategies. This review explores into insect gut microbiota, their impact on insecticide susceptibility, and the potential use of microbial metabolites in ecofriendly pest control. We explore pesticide degradation mechanisms, the consequences of microbiota disruption on susceptibility, and the role of microbiota-produced metabolites in shaping pesticide efficacy. Ultimately, we highlight the potential of microbiota manipulation as a strategy to enhance insecticide effectiveness and combat pesticide resistance in pest management.

Key words: Insect gut, microbiota, *Drosophila*, *Bactrocera*, pesticides, degradation, primary and secondary symbionts, enzymes, metabolites, physiology, insecticides, microorganisms, xenobiotics

Insects are hosts to various microorganisms which inhabit their gut and play a significant role in their physiology and health (Cheng et al., 2017). The gut microbiota aids in nutrient acquisition, digestion, and synthesis of essential compounds (Jing et al., 2020). Insecticides are chemicals designed to target insect pests and disrupt their physiological processes leading to their death (Khan and Ahmad 2019). However, there is evidence that the gut microbiota can metabolize and degrade some insecticides, leading to reduced efficacy and increased resistance (Mahas et al., 2023; Siddiqui et al., 2022). Additionally, exposure to insecticides can also disrupt the gut microbiota, leading to altered metabolites and potential health impacts (Jaffar et al., 2022). This review will explore the interaction between insect gut microbiota, insecticides, and innate metabolites and their influence on insect physiology and management. Pesticides are the most widely used tools for controlling insect pest populations in agriculture and public health. However, their extensive

use has led to widespread environmental contamination, with potential negative effects on human health and biodiversity (Khan et al., 2023). Furthermore, the emergence of pesticide-resistant pest populations poses a major challenge for pest management (Li et al., 2021). Insects have a complex gut microbiota, which can play a significant role in the metabolism of xenobiotic compounds, cytochrome; monooxygenases (P540; P450s) including pesticides, phytochemicals and environmental hazardous substances (Chaitra and Kalia 2020; Lu et al., 2021). The gut microbiota can break down and detoxify pesticides, as well as produce innate metabolites that can further influence pesticide metabolism and efficacy (Muñoz-Benavent et al., 2021; Schmidt and Engel 2021). Hence, understanding the interactions between insect gut microbiota and pesticides can provide insights into novel strategies for pest management that are both effective and environmentally sustainable (Giambò et al., 2021). Recent advances in molecular and sequencing

technologies have greatly expanded our understanding of the diversity and function of insect gut microbiota. Moreover, the discovery of novel metabolites produced by these microbial communities has opened up new avenues for the development of biologically-based pest management tools (Huang et al., 2019). Insect gut microbiota plays a crucial role in the metabolism of xenobiotic compounds, including pesticides. The disruption of gut microbiota due to pesticide exposure can lead to altered metabolism and bioavailability of these compounds, potentially affecting insecticide efficacy and resistance. Additionally, the gut microbiota produces innate metabolites that can further influence pesticide degradation and susceptibility.

Insects can host a wide variety of symbiotic relationships with microorganisms, including both primary and secondary symbionts. The location of these symbionts within the insect's body can vary depending on the species of insect and the specific symbiotic relationship (Martin et al., 2023). Here's a general overview of primary and secondary symbionts are typically found in insects.

Primary Symbionts (PS)

PS are typically essential for the insect's survival and often have a long coevolutionary history with their host. They are usually located within specialized cells or tissues of the insect, such as bacteriocytes (specialized host cells for harboring bacteria) or mycetocytes. Moreover, commonly found in the digestive system, specifically the midgut or hindgut, where they aid in the digestion of complex nutrients or provide essential nutrients that are lacking in the insect's diet. Aphids, for example, have PS called *Buchnera aphidicola* located

in specialized cells called bacteriocytes within their bodies (Martin et al., 2023).

Secondary Symbionts (SS)

SS are not as tightly integrated into the insect's physiology as primary symbionts and are often facultative, meaning their presence is not essential for the insect's survival. They can be found in various locations within the insect's body, and their distribution can vary. SS can inhabit the insect's gut, reproductive organs, or other tissues. Some SS are found within specialized cells similar to bacteriocytes, while others may be more loosely associated with the insect's cells or circulatory system. The location of SS can also vary between different insect species and even within populations of the same species. Symbiotic relationships can vary widely among different insect species. The presence and location of symbionts depend on factors such as the insect's diet, life history, and environmental conditions. Furthermore, ongoing research continues to discover new and captivating understandings into the complexity of insect-microbe interactions (Li et al., 2023).

Role of primary and secondary endosymbionts in pesticide degradation

The use of pesticides in agriculture has played a pivotal role in increasing crop yields and protecting crops from pests and diseases. However, the widespread application of pesticides has raised concerns about their environmental impact, including their persistence in soil and water ecosystems. In recent years, researchers have been exploring novel and sustainable approaches to mitigate the negative effects of pesticides. One promising avenue of research involves the utilization of primary and secondary endosymbionts in pesticide

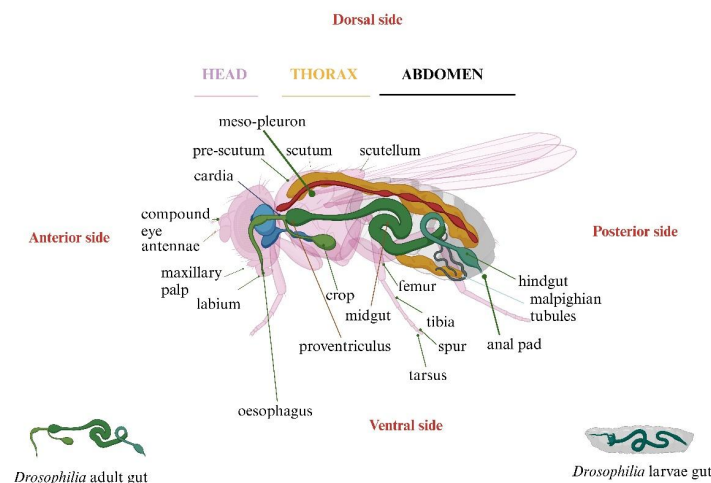


Fig. 1. Insect gut a schematic diagram of model *Drosophila*

degradation. These microscopic organisms, often found within the bodies of insects, have shown remarkable capabilities in breaking down and detoxifying various pesticides some are listed as. *Burkholderia gladioli* (in darkling beetle), *Snodgrassella alvi* (in honey bee), *Sulcia muelleri* and *Pantoea agglomerans* (in leafhopper), *Hamiltonella defensa* and *Buchnera aphidicola* (in aphids), *Wolbachia* spp. and *Asaia* spp. (in mosquitoes), *Wigglesworthia glossinidia*, and *Sodalis glossinidius* (in Tsetse fly), This comprehensive review explores the roles of primary and secondary endosymbionts in pesticide degradation and their potential applications in sustainable pest management strategies (Liu and Guo 2019; Martin et al., 2023).

Primary endosymbionts (PE): PE are micro-organisms that have co-evolved with their host insects over millions of years. They reside primarily in specialized cells or organs of their insect hosts and often have a mutualistic relationship with them. These endosymbionts are crucial for the survival and reproduction of the host insects (McCutcheon et al., 2019). Role in Pesticide Degradation: PE have been found to possess various enzymatic pathways that can metabolize and detoxify pesticides. These enzymes can break down specific chemical compounds found in pesticides, rendering them less toxic to the host insect. In some cases, PE can even confer resistance to certain pesticides. Examples: a). *Buchnera aphidicola*: Found in aphids, *Buchnera* has been shown to play a role in detoxifying organophosphate and carbamate insecticides. b). *Wolbachia*: Although primarily known for its reproductive manipulation effects, *Wolbachia* can also influence pesticide susceptibility in certain insects (Martin et al., 2023; Štarhová Serbina et al., 2022).

Secondary endosymbionts (SE): SE are typically not as tightly integrated into their host's biology as SE. They may be present in only certain populations of a host species or under specific environmental conditions. Role in pesticide degradation: SE often exhibit more diverse metabolic capabilities compared to PE. Some SE possess enzymes that can break down a wider range of pesticide compounds, making them potential candidates for bioremediation purposes. Examples: a). *Hamiltonella defensa*: Found in aphids, *H. defensa* has been associated with increased resistance to parasitoid wasps and certain pesticides. b). *Serratia symbiotica*: This secondary endosymbiont has been linked to increased tolerance to various environmental stresses, including pesticides, in aphids (Csorba et al., 2022; Martin et al., 2023).

Applications in pest management or as biological control: Utilizing primary and secondary endosymbionts that can metabolize pesticides could enhance the natural pest control mechanisms. This approach could reduce the need for chemical pesticides and minimize their environmental impact. Bioremediation: Linking the pesticide-degrading capabilities of endosymbionts for bioremediation purposes offers a sustainable approach for cleaning up pesticide-contaminated environments. Genetic Engineering: Researchers are exploring ways to transfer pesticide-degrading genes from endosymbionts into crop plants or beneficial insects to confer pesticide resistance (Gomes et al., 2023).

Removal with antibiotics and degradation in insects

PS are often intimately associated with their insect hosts and play critical roles in their biology. Eliminating PS in insects like aphids can have significant consequences for the insect's fitness and survival e.g., Aphids and *Buchnera aphidicola* and camellia spiny whitefly, *Aleurocanthus camelliae*. Several studies have conducted experiments to eliminate PS using antibiotics. For instance, when aphids are treated with antibiotics targeting *Buchnera aphidicola*, the primary symbiont, it disrupts the essential nutritional mutualism. Aphids deprived of *Buchnera* may exhibit reduced reproduction, slowed development, and increased susceptibility to environmental stressors. In some cases, for degradation of PS can be selectively degraded or eliminated by the host's immune system. For example, aphids possess a specialized mechanism called the bacteriocyte-infiltrating conoid, which allows them to selectively eliminate *Buchnera* when necessary. This occurs during the production of specialized dispersal forms (alates) that do not require the symbiont-dependent traits needed for regular reproduction (Tan et al., 2023).

SS often have more variable relationships with their hosts and can be facultative. Eliminating SS may have less severe consequences for the insect's survival compared to primary symbionts e.g., whiteflies and rickettsia. SS can be eliminated with antibiotics as well. For instance, whiteflies can harbor SSSs like Rickettsia. When treated with antibiotics targeting Rickettsia, researchers have observed altered reproductive ratios and various fitness effects in whiteflies. However, these effects are generally less critical for the insect's survival compared to primary symbionts. The degradation of secondary symbionts may occur through evolutionary processes. Some insect populations may naturally lose SS over time, leading to changes in host-symbiont

interactions. This can be due to the selective advantage of carrying or losing the SS in different environments or under changing ecological conditions. Eliminating or degrading symbionts can vary depending on the specific insect-symbiont system, the antibiotic used, and the environmental context. In several cases, the relationship between insects and their symbionts for example in whitefly an intricate and dynamic, and complete elimination of symbionts can have far-reaching consequences for both the insect and the surrounding ecosystem. Further researchers needed to investigate these relationships to better understand their ecological and evolutionary implications (Tan et al., 2023).

Transient symbionts (TS) play a distinct role in insects compared to primary or secondary symbionts. While primary and secondary symbionts are typically long-term and often vertically transmitted, transient symbionts have a shorter association with their host, and their transmission is usually horizontal. Here's an overview of the role of TS in insects, along with examples:

Role of TS

In the environmental adaptation TS can help insects adapt to changing environmental conditions. Insects often encounter various microorganisms in their environment, and some of these TS can provide short-term benefits that enhance the insect's fitness (Frago et al., 2020). These benefits may include improved tolerance to specific stressors, such as heat, toxins, or pathogens. For the nutritional supplementation in some transient symbionts can assist insects in obtaining essential nutrients or metabolizing non-standard food sources. It can be particularly beneficial when the insect's primary diet lacks certain nutrients. TS can contribute to the insect's ability to exploit diverse food resources. Protection in the pathogen defense of insects may acquire TS that produce antimicrobial compounds or compete with harmful pathogens for resources. These transient symbionts can help protect the insect from infections by pathogens and parasites. In the reproduction and Fitness TS can influence various aspects of insect reproduction and fitness. They may impact mating behavior, fecundity, or the quality of offspring produced by the insect host. In many cases, TS can alter the sex ratio of the insect's offspring, affecting population dynamics. Some examples of TS in Insects are *Wolbachia* is a well-known example of a transient symbiont in insects. It is a bacterium that infects a wide range of insect species and is known for its ability to

manipulate host reproduction (Miller 2013). *Wolbachia* can induce cytoplasmic incompatibility, where infected males are unable to successfully reproduce with uninfected females or females infected with a different strain of *Wolbachia*. This reproductive manipulation can lead to the rapid spread of *Wolbachia* within insect populations. *Spiroplasma* is another TS found in various insect species. It can influence host reproductive patterns, alter insect development, and confer resistance to certain pathogens. For example, *Spiroplasma* in *Drosophila* fruit flies can affect the fly's ability to resist parasitoid wasp infections. *Arsenophonus* is a TS that has been identified in several insect groups. It is known for its potential role in providing resistance to parasitoid wasp attacks in aphids and other insects. *Arsenophonus* may contribute to the defense mechanisms of its insect host against parasitic wasps (Blow and Douglas 2019; Nováková et al., 2015).

Mechanisms of pesticide degradation by gut microbiota

Insecticides are widely used in agricultural production to control pests and increase crop yields (He et al., 2022; Jaffar et al., 2023; Li et al., 2022c). However, their extensive use has resulted in environmental contamination, which poses significant risks to human health and the environment. The gut microbiota of insects plays a crucial role in the degradation of pesticides, as they possess enzymes capable of breaking down these chemicals. Understanding the mechanisms involved in pesticide degradation through insect gut microbiota is therefore important for developing sustainable pest management strategies (Jang and Kikuchi 2020). Several studies have demonstrated the involvement of gut microbiota in pesticide degradation (Gomes et al., 2020; Li et al., 2022b), the gut microbiota of fall armyworm *Spodoptera frugiperda*, cotton bollworm *Helicoverpa armigera* were shown to degrade the insecticide (chlorpyrifos) have been identified in several bacterial strains that were capable of degrading synthetic pesticides and promotes sex pheromones, including *Bacillus* (Gui et al., 2023; Singh et al., 2022), *Enterobacter*, *Lactobacillus plantarum*, *Enterobacter cloacae*, *Photobacterium luminescens*, *Wolbachia*, and *Pseudomonas* species. Further investigation revealed that the gut microbiota produced several enzymes involved in pesticide degradation, such as esterase and cytochrome P450. Similarly, in many comprehensive studies (Bai et al., 2019; Cheng et al., 2017; Siddiqui et al., 2022; Zhu et al., 2023), the gut microbiota of silkworms *Bombyx mori*, cotton leaf worm *Spodoptera littoralis*, cotton aphid *Aphis gossypii* Glover, Colorado

potato beetle *Leptinotarsa decemlineata* (Say), diamondback moth *Plutella xylostella*, parasitic wasp *Eretmocerus mundus* (Mercet), bedbug *Cimex lectularius* (Linnaeus), fruit fly *Bactrocera dorsalis*, honey bee *Apis mellifera*, was shown to degrade the insecticide chlorantraniliprole. The study identified several bacterial strains, such as *Enterobacter cloacae* (*E. cloacae*), *Enterococcus* and *Lactobacillus*, that were capable of degrading chlorantraniliprole. Further analysis revealed that the gut microbiota produced several enzymes involved in pesticide degradation, such as carboxylesterase and glutathione S-transferase. Several other studies have explored the role of gut microbiota in the degradation of herbicides. In a study by (Wang et al., 2018), the gut microbiota of honey bees was shown to degrade the herbicide glyphosate. These studies identified several bacterial strains, including *Lactobacillus* and *Bifidobacterium*, that were capable of degrading glyphosate. Further analysis revealed that the gut microbiota produced several enzymes involved in pesticide degradation, such as amino-methyl-phosphonic acid (AMPA) lyase and glycine oxidase. In addition to the gut microbiota, innate metabolites produced by insects have also been shown to play a role in pesticide degradation. In a study (Cohn et al., 2022), the larvae of the black soldier fly were shown to produce metabolites that were capable of degrading the insecticide imidacloprid. Moreover, identified several metabolites, including 6-chloronicotinic acid and nicotinic acid, that were involved in the degradation of imidacloprid. Further analysis revealed that the metabolites were produced by the gut microbiota of the black soldier fly. The mechanisms involved in pesticide degradation in insect

gut microbiota are complex and involve the production of several enzymes and metabolites. However, several features, such as diet, environmental factors, and host genetics, can influence the composition and activity of gut microbiota, which can affect pesticide degradation. For example, a study (Engel and Moran 2013), showed that the composition of gut microbiota in honey bees was affected via exposure to the herbicide glyphosate. The exposure resulted in a significant reduction in the abundance of several bacterial strains capable of degrading glyphosate (Motta et al., 2022). In the gut microbiota of insects plays a crucial role in the degradation of synthetic pesticides, and several studies have identified the bacterial strains and enzymes involved in pesticide degradation. In addition, innate metabolites produced through insects have also been shown to play a role in pesticide degradation (Jang and Kikuchi 2020; Yun et al., 2014). However, the composition and activity of gut microbiota can be influenced by several factors, which can affect pesticide degradation. Understanding the mechanisms involved in pesticide degradation, insect gut microbiota is important for developing sustainable pest management strategies that minimize environmental contamination and reduce the risk to human health (French et al., 2021; Siddiqui et al., 2022).

Impact of microbiota disruption on insecticide susceptibility

Insects are the most abundant and diverse group of faunas on the earth, and they play an indispensable role in ecosystems (Holtof et al., 2019). However, they can also be significant pests in agriculture, causing billions of dollars in crop damage annually

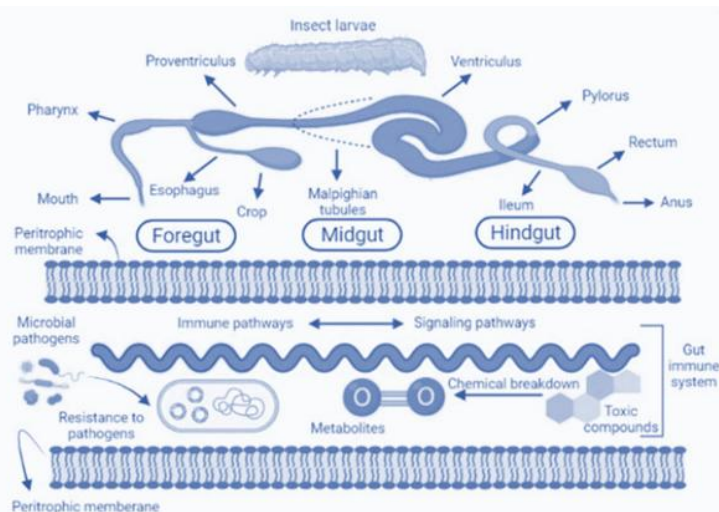


Fig. 2. Insect gut microbiota resistance to pesticides. A graphical representation.

(Scudder, 2017). Insecticides are commonly used to control insect pests, but the overuse of these chemicals can lead to resistance development, environmental contamination, and negative effects on non-target organisms (Naqqash et al., 2016). Insect gut microbiota have been identified as an essential factor in the detoxification of pesticides, and their disruption can lead to increased insecticide susceptibility (Gao et al., 2022; HS and KKalia, 2022). Recent investigate has shown that gut microbiota enzymes can detoxify various classes of insecticides, including organophosphates, pyrethroids, and neonicotinoids. The gut microbiota of insects can degrade these pesticides through various mechanisms, including hydrolysis, oxidation, and reduction (Jaffar et al., 2022; Sogorb and Vilanova, 2002). For example, the gut microbiota of the diamondback moth, *Plutella xylostella*, can degrade the pyrethroid insecticide deltamethrin through the production of detoxification enzymes such as esterases and cytochrome P450s (Li et al., 2022a; Zhang et al., 2013). The gut microbiota of insects has been shown to play an important role in various biological processes, including digestion, immunity, and reproduction. New studies have also indicated that the gut microbiota can have a significant impact on insecticide susceptibility and resistance. In this review, we will discuss the impact of microbiota on insecticide susceptibility in *Bactrocera dorsalis*, one of the most economically important pests of fruits and vegetables. Several research have explored that the gut microbiota can influence insecticide susceptibility in *B. dorsalis*. For example, it has been shown that antibiotic, and synthetic pesticides treatment can alter the gut microbiota composition, leading to increased resistance to insecticides such as chlorpyrifos and fipronil. This effect is thought to be due to the disruption of the gut microbiota's role in metabolizing and detoxifying insecticides, leading to higher levels of toxic metabolites in the insect's body (Huang et al., 2013; Koc et al., 2022; Li et al., 2007). Moreover, research has shown that the gut microbiota can also affect the expression of insecticide resistance genes in *B. dorsalis*. Studies have found that certain gut bacteria can induce the expression of insecticide resistance genes, leading to decreased exposure to insecticides. On the other hand, some gut bacteria have been shown to inhibit the expression of these genes, leading to increased susceptibility to insecticides (Xia et al., 2018; Yang and Cong 2021).

Manipulating the gut microbiota of *B. dorsalis* has the potential to improve pest management strategies by increasing susceptibility to insecticides. Approaches

such as using selective insecticides, biocontrol programs and antibiotics to selectively decrease the growth of certain gut bacteria or using bacteriophages to target specific bacteria could be explored as potential pest management tools. The gut microbiota of *B. dorsalis* plays a significant role in insecticide tolerance, and further research on the mechanisms involved could lead to novel pest management strategies (Bai et al., 2019; Zhang et al., 2022a). Disrupting the gut microbiota through antibiotics or other means has been shown to increase insecticide susceptibility in many insect species. For instance, a study found that the administration of antibiotics to the gut bacteria of mosquito *Culex quinquefasciatus* and *Anopheles arabiensis* increased its susceptibility to the streptomycin, erythromycin and insecticide permethrin (Barnard et al., 2019; Seal and Chatterjee 2019; Yang et al., 2021). Another study demonstrated that the disruption of gut microbiota through antibiotic treatment increased the susceptibility of the cotton bollworm, *Helicoverpa armigera*, to the Bt-resistant, endosulfan, carbamates and organophosphate insecticide chlorpyrifos (Myint Khaing et al., 2018; Torres-Vila et al., 2002). The impact of microbiota disruption on insecticide susceptibility has also been studied in the context of insecticide resistance. Research has shown that the gut microbiota of resistant insects can play a role in the detoxification of pesticides, and that disrupting this microbiota can increase insecticide susceptibility in resistant populations (Sato et al., 2021). For example, a study found that disrupting the gut microbiota treatment increased the susceptibility of a resistant strain of the tobacco budworm, *Heliothis virescens*, to the chlorantraniliprole, organophosphate, canavanine, an arginine antimetabolite, *Bt Vip3Aa*, and l-2-amino-4- butyric acid (Blanco et al., 2009; Pickett et al., 2017; Zilnik and Burrack 2021).

It is imperative note that the relationship between gut microbiota and insecticide susceptibility is complex and can vary depending on the insect species, the type of insecticide, and other factors. For example, some studies have shown that disrupting gut microbiota can increase insecticide susceptibility, while others have shown no effect or even a decrease in susceptibility. Additionally, the composition of gut microbiota can differ between insect populations, which can affect pesticide detoxification and susceptibility. Further research is needed to better understand the mechanisms underlying the relationship between gut microbiota and insecticide susceptibility, as well as to develop effective and sustainable pest management strategies that take into account the role of gut microbiota.

Innate metabolites produced by gut microbiota and their influence on pesticide metabolism

In recent years, there has been growing interest in the role of gut microbiota in the metabolism of insecticides. It is now widely recognized that the microbiota inhabiting the gut of insects can play a key role in the detoxification of insecticides (Jaffar et al., 2022), thus affecting their efficacy and ultimately impacting pest management strategies. The gut microbiota can directly degrade insecticides or produce metabolites that aid in their detoxification. The latter mechanism is particularly intriguing, as it suggests that gut microbiota may serve as a reservoir of metabolites with potential applications in pesticide metabolism (Siddiqui et al., 2022). We explore the role of innate metabolites produced by gut microbiota and their influence on pesticide metabolism. The gut microbiota in insect digestive system is a complex ecosystem consisting of a diverse array of microorganisms, including archaea, bacteria, protozoa, fungi, and viruses (Muñoz-Benavent et al., 2021). These microorganisms can interact with each other and with their host in a variety of ways, influencing various physiological processes, including digestion, immune function, and metabolism (Wang et al., 2020). Recent studies have shown that gut microbiota can also play significant role in the metabolism of insecticides. For example, the gut microbiota of some insects can degrade pyrethroid insecticides, such as permethrin, by producing esterase that hydrolyze the ester bonds in these insecticides (Cruse et al., 2023; Gómez-Govea et al., 2022). Other gut microbes can produce carboxylesterases that can also degrade pyrethroids and indoxacarb (Ramya et al., 2016). In addition to direct degradation of insecticides, gut microbiota can also produce metabolites that indirectly aid in the detoxification of insecticides (Sogorb and Vilanova 2002). For example, gut microbiota can produce enzymes such as cytochrome P450s, which can modify the insecticidal potential, making them more easily excreted by the host (Lu et al., 2021). Additionally, gut microbiota can produce metabolites that act as antagonists of insecticide target sites, reducing their efficacy. For example, some gut microbes can produce γ -aminobutyric acid (GABA), which can bind to and inhibit the GABA receptor, the target of some insecticides such as fipronil (Nauen et al., 2022; Rashmi et al., 2018; Zhou et al., 2018).

The gut microbiota can also modulate the expression of insecticide resistance genes in their host. For e.g., some gut microbes can induce the expression of

detoxification genes in the host, leading to increased resistance to insecticides. On the other hand, some gut microbes can also suppress the expression of resistance genes, leading to increased susceptibility to insecticides (Amezian et al., 2021; Marcombe et al., 2009).

Advanced research has shown that the gut microbiota of insects can produce a variety of innate metabolites that have potential applications in pesticide metabolism (Engel and Moran 2013). As an instance, gut microbes have ability to produce short-chain fatty acids (SCFAs), such as acetate, propionate, and butyrate, which have been shown to enhance the detoxification of insecticides in the host. SCFAs have also been shown to induce the expression of genes involved in detoxification pathways in honey bees and other insects (Thakur et al., 2023; Wang et al., 2018), further enhancing their efficacy as detoxification agents. Another class of innate metabolites produced by gut microbiota is indole derivatives, which have been shown to enhance the activity of detoxification enzymes such as cytochrome P450s. Indole derivatives have also been shown to modulate the expression of genes involved in insecticide resistance, leading to increased susceptibility to insecticides (Schmidt and Engel 2021; Zhang et al., 2022b). Furthermore, gut microbiota can produce other metabolites, such as phenolics, alkaloids, and terpenoids, which have been shown to play a role in insecticide metabolism (Zhao et al., 2022). Phenolics, for example, have been shown to enhance the activity of detoxification enzymes such as glutathione S-transferases, which are involved in the detoxification of organophosphate insecticides (Vaish et al., 2020). Alkaloids and terpenoids have also been shown to enhance the activity of detoxification enzymes and modulate the expression of genes involved in insecticide resistance (Muñoz et al., 2020).

Potential applications of gut microbiota manipulation in pest management

Insect gut microbiota plays a necessary role in nutrient acquisition, digestion, and metabolism. The gut microbiota comprises bacteria, fungi, viruses, and archaea, which coexist in a symbiotic relationship with their insect host. Microbes in the gut produce essential vitamins and amino acids, digest complex polysaccharides, and degrade xenobiotics. Recent studies have also revealed the gut microbiota's role in regulating immune responses and behavior, making it an essential factor in insect physiology. The gut microbiota of insects has been shown to play important roles in many aspects of their biology, including digestion,

immunity, and behavior. In recent years, researchers have begun to investigate the potential of manipulating the gut microbiota to improve pest management strategies (Jang and Kikuchi 2020; Yun et al., 2014). Manipulation of the gut microbiota can be achieved through a variety of methods, including the use of probiotics, prebiotics, and antibiotics. This review will discuss the advantages and current research on potential applications of gut microbiota in pest management. Management of the gut microbiota has several potential advantages in pest control. Firstly, it could provide a more targeted and sustainable approach to pest control compared to traditional chemical insecticides, which can have negative impacts on non-target organisms and the environment. Secondly, it could help to overcome issues of insecticide resistance by targeting multiple aspects of insect biology. Finally, manipulation of the gut microbiota could also have broader applications in agricultural production, such as improving nutrient utilization and stress tolerance in crops (Schmidt and Engel 2021). Developing methods for employed the gut microbiota research has focused on insects to improve pest management. One approach is the use of probiotics, which involves the application of beneficial bacteria to the insect gut to enhance their health and reduce susceptibility to pests. For example, *Lactobacillus*, *Saccharomyces*, *Streptococcus*, *Bacillus* and *Lactobacillus plantarum* has been shown to improve the survival of honeybees infected with the parasite *Nosema ceranae*, which causes significant losses in bee populations (Bloemendaal et al., 2021; Engel and Moran 2013; Guarner et al., 2012). Prebiotics, which are substances that promote the growth of beneficial gut bacteria, have also been investigated for their potential in pest management. In a study on the tomato fruit

borer *Helicoverpa armigera*, probiotic supplementation increased the abundance of beneficial gut bacteria and reduced larval growth and survival (Paramasiva et al., 2014; Tian et al., 2023).

An antibiotic treatment has also been explored for their potential in pest management. Various studies on the diamondback moth *Plutella xylostella* found that the antibiotic levofloxacin, rifampicin, streptomycin sulfate, ciprofloxacin, and metronidazole reduced the abundance of gut bacteria and increased susceptibility to the insecticide chlorpyrifos and *Bacillus thuringiensis*. Manipulation of the gut microbiota has the potential to provide a more sustainable and targeted approach to pest management, with potential applications in both agricultural production and public health (Lin et al., 2015; Xia et al., 2018). Nevertheless, further research is needed to develop effective and practical methods for manipulating the gut microbiota of insects, and to understand the broader impacts of these interventions on insect and environmental health.

Insecticides and their interaction with gut microbiota

Insecticides target specific physiological processes in insects, leading to their abnormality or mortality. However, some insecticides can be metabolized and degraded by the gut microbiota, leading to reduced efficacy and increased resistance (Siddiqui et al., 2022). An example, pyrethroid insecticides are metabolized by gut bacteria, leading to reduced toxicity in certain insects. Similarly, organophosphate insecticides are degraded by gut bacteria, leading to increased resistance in many species of insects. This phenomenon highlights the importance of considering the role of the gut microbiota in insecticide resistance management.

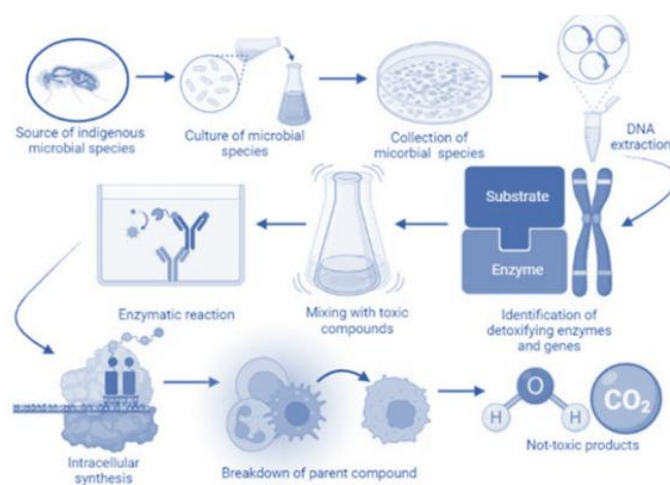


Fig. 3. Isolation techniques from insect gut microbial community and their roles in degradation (Jaffar et al., 2022)

Gut microbiota disruption and their influence on innate metabolites

Exposure to insecticides can also disrupt the gut microbiota, leading to altered metabolites and potential health impacts (Jaffar et al., 2022). Disruption of the gut microbiota can lead to increased susceptibility to pathogens, reduced nutrient acquisition, and transformed behavior. Furthermore, changed metabolites produced by the gut microbiota can also impact insect physiology and behavior (Gómez-Govea et al., 2022). For example, some bacteria in the gut produce short-chain fatty acids, which can regulate host metabolism and immune responses. Therefore, disruption of gut microbiota can lead to a significant impact on insect physiology and strength in insects (Engel and Moran 2013; Muñoz-Benavent et al., 2021).

The insect gut microbiota has a significant impact on the host's susceptibility to insecticides. Gut microbiota composition can alter the expression of host genes involved in detoxification pathways and insecticide targets. This paper aimed to review the literature on the impact of microbiota disruption on insecticide susceptibility in and its potential applications in pest management. The use of insecticides has been the primary control method, but insecticide resistance has emerged as a significant challenge (Jaffar and Lu 2022). Recent studies have shown that gut microbiota composition plays a crucial role in the susceptibility of insects to insecticides. For example, the gut microbiota of *B. dorsalis* is dominated by Proteobacteria and Firmicutes, which have been shown to play a role in the metabolism of insecticides (Wang et al., 2011). Alternative study found that the depletion of gut microbiota through antibiotic treatment increased the susceptibility of *B. dorsalis* to the insecticide chlorpyrifos (Zhang et al., 2022a). The authors suggested that the depletion of gut microbiota reduces the expression of genes involved in the detoxification of insecticides, leading to increased susceptibility. Gut microbiota of invasive ants associated with gut bacteria nesting preference (Huang et al., 2020) and *B. dorsalis* can also confer resistance to insecticides and oviposition aversion (Li et al., 2020). The investigators identified bacterium, trimethylpyrazine (TMP), tetramethylpyrazine (TTMP), and *Klebsiella oxytoca*, that metabolizes the pheromone in midgut insecticide chlorpyrifos, thereby reducing its toxicity to *B. dorsalis* and degradation also effected (Guentzel 1996; Koc et al., 2022; Ren et al., 2021). Manipulating gut microbiota to enhance insecticide susceptibility or to reduce insecticide resistance offers several advantages. First, it

provides an alternative to chemical insecticides, which are increasingly ineffective due to the development of resistance. Second, it offers a targeted approach that does not affect non-target organisms, reducing the environmental impact of pest control measures. Finally, it could potentially be used in combination with other control methods, such as biological control, to enhance their efficacy. However, there are also potential disadvantages to deploying gut microbiota. One concern is the potential for unintended consequences, such as the spread of antibiotic resistance genes or the unintended killing of beneficial microorganisms (Lillehoj et al., 2018; Lin et al., 2021; Muñoz-Benavent et al., 2021). Additionally, it is unclear how stable and effective gut microbiota manipulation methods are in the field, as laboratory studies may not accurately reflect real-world conditions.

CONCLUSIONS

In conclusion, gut microbiota composition plays a central role in the susceptibility of insects to insecticides, including *B. dorsalis* (Liu et al., 2022). Eliminating of gut microbiota to enhance insecticide susceptibility or reduce insecticide resistance offers several advantages, including a targeted approach that does not affect non-target organisms and the potential for use in combination with other control methods (Francis and Aneesh 2022; Meng et al., 2019). However, potential disadvantages include unintended consequences and uncertainty regarding the efficacy of gut microbiota manipulation methods in the field. Future research should focus on developing safe and effective gut microbiota manipulation methods that can be applied in the field to enhance pest management efforts. The gut microbiota plays a critical role in insect physiology and health. Exposure to insecticides can disrupt the gut microbiota and alter metabolites, leading to potential health impacts. Additionally, some insecticides can be metabolized and degraded by the gut microbiota, leading to reduced efficacy and increased resistance. Therefore, it is essential to consider the role of the gut microbiota in insecticide resistance management and insect physiology. Future research should focus on understanding the interactions between the gut microbiota, insecticides, and innate metabolites to improve our understanding of insect physiology and management.

AUTHOR CONTRIBUTION STATEMENT

SJ performed, conceived and designed review research. SJ revised and conceived the overall study.

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CONFLICT OF INTEREST

No conflict of interest.

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