Entomological Research

WILEY

INVITED REVIEW OPEN ACCESS

Global Perspective of Insecticide Resistance in Bed Bugs and Management Options

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Received: 13 February 2025 | **Revised:** 13 February 2025 | **Accepted:** 18 March 2025

Funding: The author received no specific funding for this work.

Keywords: *Cimex hemipterus* | *Cimex lectularius* | pest management | resistance mechanisms

ABSTRACT

The global resurgence of bed bugs (*Cimex lectularius* L. and *Cimex hemipterus* [F.]) over the past 25 years has presented significant challenges to the pest management industry, with insecticide resistance as a leading cause of control failures. This review provides a synthesis of bed bug insecticide resistance research from 2018 to the present, highlighting insecticide resistance profiles, resistance mechanisms, and management strategies. Resistance to pyrethroids, neonicotinoids, organophosphates, carbamates, and other insecticides is widespread, with documented cases of metabolic resistance (cytochrome P450s, esterases, glutathione S-transferase and ABC transporters), target site insensitivity (point mutations in voltage-gated sodium channel genes [*kdr*], paralogous acetylcholinesterase gene (*p-Ace*), and GABA receptor gene [*rdl*]), penetration resistance (cuticular thickening), and symbiont-mediated resistance. This paper also reviews the effective management options against insecticide-resistant bed bugs, including insecticide mixtures and synergists, entomopathogenic fungi (*Beauveria bassiana*), and physical methods such as heat treatment, desiccant dust, and fumigation. Additionally, novel approaches, such as RNA interference and bed bug baits, provide new directions but require further research. Lastly, socio-economic disparities affect bed bug management, especially in lower-income communities.

1 | Introduction

Bed bugs are an important group of indoor blood-feeding insect pests. Due to their hematophagous habits and synanthropic nature, bed bug bites can lead to various physical, psychological, and social impacts that depend on an individual's sensitivity and the severity of the infestation. These impacts include skin reactions such as itchy welts, allergic responses (Lavaud and Dutau 2020; Yu et al. 2024), and secondary infections from excessive scratching (Sheele et al. 2019); sleep disturbances and insomnia (Fung et al. 2021) caused by persistent itching, psychological issues like stress, anxiety, and delusional parasitosis (Ashcroft et al. 2015; Peron et al. 2018), social stigma and isolation (Peron et al. 2018), and, anemia (Izri et al. 2020; Sheele et al. 2021). Thomas et al. (2024) analyzed 71,925 general practice consultations related to bed bug infestations in France from 2019 to 2020, estimating an annual incidence rate of 109 per 100,000 inhabitants. 39% of patients experienced moderate-to-severe impacts on daily life. Factors associated with significant repercussions included visible bed bugs, skin lesions from scratching, lesions on the head and neck, and psychological distress. Home infested with bed bugs also showed increased levels of respirable allergens such as histamine (DeVries et al. 2018; Gaire et al. 2022; Gordon et al. 2023; Principato et al. 2023) and tropomyosin (Gordon and DeVries 2024).

In addition, when pest management professionals frequently use the same ineffective insecticides (such as pyrethroids) to treat bed bugs, those homes are often left with elevated levels of insecticide residues. This leads to the accumulation of insecticides within indoor environments while the bed bug issues remain. This situation is compounded by homeowners attempting to address subpar bed bug control by self-administering over-the-counter, ineffective products. For example, total release foggers (TRF) release significant amounts of pyrethroids into indoor spaces (Nakagawa et al. 2017; DeVries et al. 2019). The long-term effects of pyrethroid exposure on humans have been linked to their impact on the cardiovascular system, which increases the risk of overall mortality in the general adult population (Bao et al. 2019). This health concern further compounds the already staggering financial burden of healthcare. Recent studies also suggest that pyrethroid exposure may be associated with an increased risk of depression (Li et al. 2023) and sleep problems in adult male adolescents (Zhou et al. 2023). Sleep deprivation could lead to a reduction in work productivity and an increase in work-related accidents.

Although bed bugs are not known to transmit any pathogens beyond laboratory experiments, this is a debatable notion (Pietri 2020). Recently, Meraj et al. (2024) demonstrated that bed bugs have various immune defense mechanisms, including the expression of antimicrobial peptides such as prolixicin, which could inhibit the establishment and replication of pathogens and their transmission.

Over the last 25 years, the pest management industry has seen a drastic increase in demand for bed bug control due to the global resurgence of bed bugs (Doggett and Lee 2023). A recent survey on pest management professionals in the United States revealed that there has been a steady increase in the number of pest management companies offering bed bug control services—from 71% in 2017 to 86% in 2024. Fifty-five percent of the survey respondents also thought there would be an increase in the number of bed bug jobs in the next 12 months (PCT 2025). In 2020, approximately $1 billion was spent on bed bug management in the United States alone (Lee et al. 2018; Doggett and Lee 2023). Besides being an important urban insect pest, bed bugs also infest poultry farms (Foley 2021).

Globally, bed bug infestations in the human environment are caused by two species: the common bed bug (*Cimex lectularius* L.) and the tropical bed bug (*Cimex hemipterus* [F.]). *C. lectularius* is mainly found in the temperate and subtropical regions, while *C. hemipterus* is predominantly found in the tropics (Lee et al. 2023). Both species are synanthropic and can coexist sympatrically in Africa, Australia, Florida, Hawaii, and Taiwan. In some situations, both species may also be found in the same building or structure, e.g., in Kwazulu, South Africa (Newberry et al. 1987).

Recent advances in building design and indoor climate control systems have made the indoor environment increasingly uniform worldwide (Lee et al. 2023). This could explain the reason why, in recent years, tropical bed bug infestations have increasingly been found in temperate regions, for example, in France (Bèrenger and Pluot-Sigwalt 2017; Chebbah et al. 2021), Iran (Hosseini-Chegeni et al. 2019), Italy (Masini et al. 2020), Russia (Gapon 2016; Prisniy 2020; Golub et al. 2020; Martynov et al. 2020), Spain (Pradera and Ruiz 2020), Central Europe (Balvin et al. 2021), Norway (Hage et al. 2022), Japan (Komatsu et al. 2016, 2018) and South Korea (Cho et al. 2023). Similarly, the common bed bug infestations were also found in the tropics (Cambronero-Heinrichs et al. 2020; de Lima et al. 2021), although at a much lesser frequency.

Many hypotheses have been proposed regarding the resurgence of bed bugs. These include insecticide resistance, changes in pest management practices, globalization, and increased travel and trade in infested furniture (Doggett et al. 2018). Among these hypotheses, insecticide resistance is the leading cause of the resurgence (Dang et al. 2017).

Several review papers and book chapters on bed bugs have been published over the last decade, including on control strategies (Doggett et al. 2012; Kells 2018; Lee et al. 2018; Doggett and Lee 2023), monitoring (Vaidyanathan and Feldlaufer 2013; Cooper and Wang 2018; Crawley and Borden 2021), and insecticide resistance (Dang et al. 2017; Romero 2018). This paper provides the global perspective of insecticide resistance in bed bugs in recent years (from 2018 to the present) and the challenges associated with insecticide resistance. It also reviews some practical management options available to manage insecticide-resistant bed bugs.

2 | Chemical Control of Bed Bugs

Chemical treatment remains the most popular method to control bed bugs due to their ease of application (Lee et al. 2018). Because of bed bugs' pierce-sucking mouthparts and attraction to CO_2, body heat, and other body-related compounds, the only available system to deliver the insecticides to bed bugs has been limited to a dermal-contact approach. Unless there are changes in the development of oral delivery systems for blood-sucking insects in the future, it is unlikely to have a feasible toxic bait formulation for bed bugs. Since the introduction of DDT in the 1940s, pest management professionals have used more than 12 classes of insecticides to manage bed bug infestations (Lee et al. 2018; Doggett and Lee 2023). In recent years, organophosphates, pyrethroids, neonicotinoids, pyrethroid-neonicotinoid mixture, phenyl pyrazoles, pyrroles, meta-diamides, insect growth regulators, diatomaceous earth, silica dust, botanical insecticides in different formulations have been evaluated or used to control bed bugs. The insecticide formulations include liquid spray, pressurized aerosol, total release foggers, insecticide-impregnated fabric/bednets, insecticide dust, repellent, and fumigant (Table 1). While some are effective (for example, pressurized aerosol when applied as direct spray, and fumigant), others are ineffective against insecticide-resistant bed bugs. Residual activity depends on the formulation. All (except fumigant) do not have ovicidal activity. Insecticide resistance has become a major challenge to the pest management professionals.

3 | Insecticide Resistance

Since the first report of DDT resistance in *C. lectularius* (Johnson and Hill 1948), both bed bug species have become resistant to most of the major classes of insecticides used in their control, including the pyrethroids, organophosphates, carbamates, chlorinated hydrocarbons, and neonicotinoids (Dang et al. 2017).

TABLE 1 | Chemical control options, their activity, and effectiveness against insecticide-resistant bed bugs.

Formulation	Residual activity	Ovicidal activity	Effectiveness on resistant bed bugs, and limitation	References
Liquid spray	Moderate	No	Poor as residual treatment	Leong et al. (2020); Potter et al. (2012); Wang et al. (2015, 2016)
Pressurized aerosol	Short to moderate	No	Effective when applied as direct spray	Goddard (2013); Akhtar and Isman (2016); Wang et al. (2016)
Insecticide-impregnated fabric/bednets	Long	No	Poor	Doggett et al. (2011); Jones et al. (2013); Leong et al. (2023); Hayes and Schal (2022)
Total release foggers	Short	No	Not effective, poor in penetration into bed bug hiding areas.	Jones and Bryant (2012); DeVries et al. (2019)
Insecticide dust	Long	No	Good, but could be affected by bed bugs with penetration resistance.	Lilly, Latham, et al. (2016); Lilly, Webb, et al. (2016); Singh et al. (2016); Kong et al. (2024)
Repellent (DEET)	Moderate	No	Conflicting results	Vassena et al. (2019); Hayes and Schal (2024)
Fumigant (sulfuryl fluoride)	None	Yes	Effective, but only licensed fumigators are authorized to treat	You et al. (2014); Gillenwaters and Scheffrahn (2019); Todd et al. (2021)

Between 2018 and 2024, there have been numerous reports on insecticide resistance on *C. lectularius* and *C. hemipterus* from around the world, especially towards carbamates, neonicotinoids, organophosphates, phenylpyrazoles, pyrethroids and pyrethroid-neonicotinoid mixture (Table 2). Resistance mechanisms documented include penetration resistance, metabolic resistance (namely cytochrome P450 monooxygenases [P450s], esterase, and ATP-binding cassette transporters [ABC transporters]), target site insensitivity (*kdr*), and symbiont-mediated resistance (Table 3).

Penetration resistance reduces insecticide penetration into the insect due to a thickened cuticle or overexpression of cuticular proteins (Lilly, Latham, et al. 2016; Lilly, Webb, et al. 2016; Soh and Veera Singham 2021). An investigation on *C. lectularius* revealed a positive correlation between cuticular thickness and pyrethroid resistance level (Lilly, Webb, et al. 2016), while fenitrothion and imidacloprid resistance in field *C. hemipterus* strains were potentially associated with an increased cuticular thickness (Soh and Veera Singham 2021).

Metabolic resistance mechanisms in bed bugs involve major enzyme groups such as P450s, esterases, and ABC transporters. Overexpression of P450 genes (e.g., *CYP397A1*, *CYP398A1*, *CYP6A2*, *CYP6DN1*, *CYP6DM2*, *CYP400A1*) in insecticide-resistant *C. lectularius* significantly enhanced P450 activities and conferred pyrethroid resistance (Adelman et al. 2011; Mamidala et al. 2012; Zhu et al. 2013; Vander Pan et al. 2020). For esterases, overexpression of carboxylesterase genes (e.g., *CE3959* and *CE21331*) induced pyrethroid resistance in *C. lectularius* (Adelman et al. 2011; Zhu et al. 2013). The role of esterases in conferring resistance to organophosphates and carbamates in *C. hemipterus* (Karunaratne et al. 2007) and neonicotinoids in *C. lectularius* (Romero and Anderson 2016) was revealed using biochemical assays. ABC transporters facilitate the removal of toxins across the membrane. Due to overexpression of ABC transporter encoding genes (e.g., *Abc 8* and *Abc9*), this novel mechanism mediated pyrethroid resistance in *C. lectularius* (Mamidala et al. 2012; Zhu et al. 2013).

Point mutations in the voltage-gated sodium channel (VGSC) cause target site insensitivity (known as *kdr*) to pyrethroid action (Dang et al. 2017; Romero 2018). Various mutations conferring *kdr*-resistance to pyrethroids have been identified in *C. lectularius*, e.g., V419L, L925I, and I936F (Dang, Toi, Lilly, Bu, et al. 2015; Yoon et al. 2008; Vander Pan et al. 2020; Lewis et al. 2022; Ghavami et al. 2021; Cho et al. 2024; Porras-Villamil et al. 2025; Yu et al. 2025) and in *C. hemipterus*, particularly M918I and L1014F. Other mutations also have been found in *C. hemipterus* (e.g., A468T, L899V, D953G, V1016E, L1014F, and L1017F/S). However, their roles in conferring resistance are not substantiated (Dang, Toi, Lilly, Lee, et al. 2015; Ghavami et al. 2021; Punchihewa et al. 2019; Dang et al. 2021; Soh and Veera Singham 2021; Cho et al. 2023; Porras-Villamil et al. 2025). When both M918I and L1014F mutations were present in *C. hemipterus*, the resistant bed bugs showed a significantly higher knockdown time when tested against pyrethroids, exhibiting super-*kdr* characteristics (Dang, Toi, Lilly, Lee, et al. 2015; Dang et al. 2021; Soh and Veera Singham 2021; Zhao et al. 2020; Cho et al. 2023). Insensitive GABA receptor (*rdl*) due to A302S mutation confers resistance to fipronil and cyclodiene insecticides (González-Morales et al. 2021). A novel mutation, F348Y, on the paralogous acetylcholinesterase gene (*p-Ace*), was recently identified to confer organophosphate and carbamate resistance in *C. lectularius* and *C. hemipterus* (Komagata et al. 2021).

Besides, bacterial symbionts also affected insecticide susceptibility in *C. hemipterus*. Soh and Veera Singham (2022) used rifampicin antibiotic treatment to disrupt the microbiota and its impact on susceptibility to deltamethrin (pyrethroid), fenitrothion (organophosphate), and imidacloprid (neonicotinoid) was evaluated. Rifampicin-treated bed bugs exhibited increased

TABLE 2 | Reports on insecticide resistance profiles in *C. lectularius* and *C. hemipterus* from around the world between 2018 and 2024.

Species	Country	Class(s)	Insecticide[a]	Test method[b]	Mortality (%)/Resistance ratio	Reference
C. lectularius	Brazil	Carbamate	Bendiocarb (S)	SC on FP	46.6% mortality (label rate)	Pessoa et al. (2021)
	France	Carbamate	Bendiocarb (TG)	SC on FP	0–14.2% mortality (at 3 mg/cm^2)	Candy et al. (2018)
	Argentina	Carbamate	Propoxur (TG)	TP	High resistance (164– >1070X)	Cáceres et al. (2019)
	Brazil	Carbamate	propoxur (S)	SC on FP	100% mortality (label rate)	Pessoa et al. (2021)
	USA	Neonicotinoid	Acetamiprid (TG)	TP	1.0 >288X	Yu et al. (2023)
	USA	Neonicotinoid	Imidacloprid (TG)	TP	1.2–76.9X	Yu et al. (2023)
	Argentina	Neonicotinoid	Imidacloprid (TG)	TP	High resistance (24–196X)	Cáceres et al. (2019)
	Italy	Neonicotinoid	Imidacloprid (TG)	TP	High resistance (757X)	Cáceres et al. (2023)
	Brazil	Neonicotinoid	Thiamethoxam (S)	SC on FP	16.6% mortality (label rate)	Pessoa et al. (2021)
	Argentina	Organophosphate	Azametiphos (TG)	TP	High resistance (21–823X)	Cáceres et al. (2019)
	Iran	Organophosphate	Diazinon (TG)	SC on FP	Resistant	Berenji et al. (2019)
	Iran	Organophosphate	Malathion (TG)	SC on FP	Resistant	Berenji et al. (2019)
	Brazil	Phenylpyrazole	Fipronil (S)	SC on FP	6.6% mortality (label rate)	Pessoa et al. (2021)
	USA	Phenylpyrazole	Fipronil (TG)	TP	1.4– >492X	González-Morales et al. (2021)
	Brazil	Pyrethrin	Pyrethrin (S)	SC on FP	0% mortality (label rate)	Pessoa et al. (2021)
	Brazil	Pyrethroid	Alphacypermethrin (S)	SC on FP	6.6% mortality (label rate)	Pessoa et al. (2021)
	Brazil	Pyrethroid	bifenthrin (S)	SC on FP	80% mortality (label rate)	Pessoa et al. (2021)
	Argentina	Pyrethroid	Deltamethrin (TG)	TP	7000– >40,000X	Cáceres et al. (2019)
	Brazil	Pyrethroid	Deltamethrin (TG)	SC on FP	0% mortality (0.132 mg/cm^2)	Pessoa et al. (2021)
	Germany	Pyrethroid	Deltamethrin (TG)	SC on FP	4.3–20.7X	Vander Pan et al. (2019)
	USA	Pyrethroid	deltamethrin (TG)	TP	291,626X	Gaire et al. (2020)
	Italy	Pyrethroid	Deltamethrin (TG)	TP	Very high resistance (>40,000X)	Cáceres et al. (2023)
	USA	Pyrethroid	Deltamethrin (TG)	TP	1.0 – >160X	Yu et al. (2023)
	Iran	Pyrethroid	Lambdacyhalothrin (TG)	SC on FP	Resistant	Berenji et al. (2019)
	Multi countries	Pyrethroid	Permethrin (ML)	SC on FB	2–78% (4-d exposure)	Leong et al. (2023)
	Brazil	Pyrethroid + chitin synthesis inhibitor	Alphacypermethrin + flufenoxuron (S)	SC on FP	3.3% mortality (label rate)	Pessoa et al. (2021)
	Brazil	Pyrethroid + neonicotinoid	Betacyfluthrin + imidacloprid (S)	SC on FP	3.3% mortality (label rate)	Pessoa et al. (2021)
	USA	Pyrethroid + Neonicotinoid	Betacyfluthrin + imidacloprid (S)	SC on FP	25–133X	Yu et al. (2023)
		Pyrethroid + Neonicotinoid	Lambdacyhalothrin + thiamethoxam (S)	SC on FP	200–1450X	Yu et al. (2023)
		Pyrethroid + Neonicotinoid	Bifenthrin + acetamiprid (S)	SC on FP	200–2550X	Yu et al. (2023)

(Continues)

TABLE 2 | (Continued)

Species	Country	Class(s)	Insecticide[a]	Test method[b]	Mortality (%)/Resistance ratio	Reference
C. hemipterus	Nigeria	Carbamate	Bendiocarb (TG)	SC on FP	46.6% (0.1% bendiocarb) at 72-h	Oboh et al. (2022)
	Malaysia	Carbamate	Propoxur (TG)	SC on FP	Moderate resistance	Zahran and Ab Majid (2019)
	Indonesia	Carbamate	Propoxur (TG)	SC on FP	10% (at 0.1% propoxur)	Soviana et al. (2019)
	Sri Lanka	Carbamate	Propoxur (TG)	SC on FP	Potentially resistant	Punchihewa et al. (2019)
	Sri Lanka	Chlorinated hydrocarbon	DDT (TG)	SC on FP	Resistant	Punchihewa et al. (2019)
	Malaysia	Chlorinated hydrocarbon	DDT (TG)	SC on FP	>29X	Dang et al. (2021)
	Nigeria	Chlorinated hydrocarbon	DDT (TG)	SC on FP	14.8% (4% DDT) at 72-h	Oboh et al. (2022)
	Malaysia	Neonicotinoid	Imidacloprid (TG)	SC on PD	43.3–73.3% (at 192 mg/m^2)	Soh and Veera Singham (2021)
	Ghana	Organophosphate	Chlorpyrifos-ethyl (S)	SC on FP	100% mortality (24-h exposure)	Deku et al. (2021)
	Ghana	Organophosphate	Chlorpyrifos (S)	SC on FP	97% mortality (24-h exposure)	Deku et al. (2021)
	Tanzania	Organophosphate	Dichlorvos (TG)	SC on FP	No resistance	Baraka et al. (2020)
	Ghana	Organophosphate	Dichlorvos (S)	SC on FP	100% mortality (24-h exposure)	Deku et al. (2021)
	Malaysia	Organophosphate	Fenitrothion (S)	SC on PD	1.2–14.6X	Leong et al. (2020)
	Malaysia	Organophosphate	Fenitrothion (TG)	SC on PD	0–100% (at 192 mg/m^2)	Soh and Veera Singham (2021)
	Indonesia	Organophosphate	Malathion (TG)	SC on FP	87.5% (at 5% malathion)	Soviana et al. (2019)
	Sri Lanka	Organophosphate	Malathion (TG)	SC on FP	Resistant	Punchihewa et al. (2019)
	Malaysia	Organophosphate	Malathion (TG)	SC on FP	14.3– >96.6X	Dang et al. (2021)
	Nigeria	Organophosphate	Malathion (TG)	SC on FP	53.3% (5% malathion at 72-h	Oboh et al. (2022)
	Iran	Organophosphate	Phoxim (TG)	SC on FP	20X	Babagolzadeh et al. (2023)
	Iran	Organophosphate	Propetamphos (TG)	SC on FP	60X	Babagolzadeh et al. (2023)
	Ghana	Pyrethroid	Alphacypermethrin	SC on FP	17% mortality (24-h exposure)	Deku et al. (2021)
	Indonesia	Pyrethroid	Deltamethrin (TG)	SC on FP	21.4% (at 0.05% deltamethrin)	Soviana et al. (2019)
	Malaysia	Pyrethroid	Deltamethrin (TG)	SC on FP	3–20% mortality (at 0.05% deltamethrin)	Zahran and Ab Majid (2019)
	Malaysia	Pyrethroid	Deltamethrin (TG)	SC on FP	>224X	Dang et al. (2021)
	Malaysia	Pyrethroid	Deltamethrin (TG)	SC on PD	3.3–20% (at 556 mg/m^2)	Soh and Veera Singham (2021)
	Iran	Pyrethroid	Deltamethrin (TG)	SC on FP	5.5X	Tiotour et al. (2022)
	Iran	Pyrethroid	Deltamethrin (TG)	SC on FP	22X	Babagolzadeh et al. (2023)
	Malaysia	Pyrethroid	Lambdacyhalothrin (TG)	SC on FP	>205X	Dang et al. (2021)
	Tanzania	Pyrethroid	Permethrin (TG)	SC on FP	High resistance	Baraka et al. (2020)
	Iran	Pyrethroid	Permethrin (TG)	SC on FP	5.35–7.58X	Ghavami et al. (2021)
	Malaysia	Pyrethroid	Permethrin (TG)	SC on FP	>137X	Dang et al. (2021)
	Multi countries	Pyrethroid	Permethrin (ML)	SC on FB	2–100% (4-d exposure)	Leong et al. (2023)

(Continues)

TABLE 2 | (Continued)

Species	Country	Class(s)	Insecticide[a]	Test method[b]	Mortality (%)/Resistance ratio	Reference
	Nigeria	Pyrethroid	Permethrin (TG)	SC on FP	18.9% mortality (0.75% permethrin) at 72-h	Oboh et al. (2022)
	Malaysia	Pyrethroid	Phenothrin (S)	SC on PD	303– >365.5X)	Leong et al. (2020)
	Malaysia	Pyrethroid	Tetramethin + cyphenothrin (S)	SC on PD	388.3– >605X	Leong et al. (2020)
	Ghana	Pyrethroid+ neonicotinoid	Alphacypermethrin+ Acetamiprid (S)	SC on FP	20% mortality (24-h exposure)	Deku et al. (2021)
	Malaysia	Pyrethroid+ neonicotinoid	Betacyfluthrin + Imidacloprid (S)	SC on PD	7.3–16.7X	Leong et al. (2020)
	Malaysia	Pyrethroid + neonicotinoid	Betacyfluthrin + Imidacloprid (S)	SC on FP	>233X (at 118 mg/m^2)	Dang et al. (2023)
		Pyrethroid + Neonicotinoid	Betacyfluthrin + Imidacloprid (S)	SC on PD	6.5–128.2X (at 118 mg/m^2)	Dang et al. (2023)
	Malaysia	Pyrethroid+ neonicotinoid	Lambdacyhalothrin+ Thiamethoxam (S)	SC on PD	1.4–4.7X	Leong et al. (2020)
		Pyrethroid + Neonicotinoid	Lambdacyhalothrin + Thiamethoxam (S)	SC on FP	>210X (at 204 mg/m^2)	Dang et al. (2023)
		Pyrethroid + Neonicotinoid	Lambdacyhalothrin + Thiamethoxam (S)	SC on PD	1.8–8.3X (at 204 mg/m^2)	Dang et al. (2023)

[a]ML = Mattress liner, TG = technical grade, S = spray formulation.
[b]FB = fabric, FP = filter paper, PD = Petri dish, TP = topical bioassay, SC = surface contact.

susceptibility to fenitrothion and imidacloprid but not deltamethrin; metagenomic 16S rRNA sequencing revealed changes in microbiota composition. Reintroducing microbiota from untreated bugs restored insecticide tolerance, confirming symbiont involvement in insecticide resistance.

At this stage, some resistance mechanisms are not well-researched in bed bugs. Mutation at nicotinic acetylcholine receptor (*nAChR*) that confers neonicotinoid resistance has not been reported, despite many cases of neonicotinoid resistance have been reported. In other hemipterans, *nAChR* mutations such as V65I, V104I, and R81T were reported in neonicotinoid-resistant aphids (Hirata et al. 2017; Zhang et al. 2024). Another resistance mechanism that is least known in bed bugs is behavioral resistance. An avoidance behavioral response towards pyrethroid had been documented in the past. Insecticide-susceptible and insecticide-resistant *C. lectularius* may either avoid resting on deltamethrin-treated filter paper or increase their movement upon direct contact with sublethal doses of deltamethrin (Romero et al. 2009). However, whether this behavior is unique to insecticide-resistant bed bugs is unknown.

4 | Management Options Against Insecticide-Resistant bed Bugs

Widespread insecticide resistance has rendered many chemical control options ineffective. Table 4 provides a list of effective control options for managing resistant bed bugs under the influence of different resistance mechanisms.

4.1 | Pyrethroid-Neonicotinoid Mixture

One approach to overcoming pyrethroid resistance in bed bugs is the combination of a pyrethroid with a neonicotinoid, i.e., using a mixture of insecticides with two different modes of action. Earlier studies have shown that pyrethroid-neonicotinoid mixtures have demonstrated excellent performance against bed bugs (Potter et al. 2012; Wang et al. 2015, 2016). More recent research, however, has documented that both *C. lectularius* and *C. hemipterus* could develop resistance to these mixture formulations (Leong et al. 2020; Dang et al. 2023; Yu et al. 2023; Yu et al. 2025) due to the involvement of cytochrome P450 that could confer resistance to both pyrethroid and neonicotinoid classes. One way to overcome this is to add piperonyl butoxide (PBO) to the mixture. PBO is a general inhibitor of the P450 enzyme.

Sun et al. (2016) demonstrated that flies with 2 VGSC point mutations (M918T + L1014F) were more susceptible than those with only one point mutation when treated with multi-halogenated benzyl pyrethroids, such as transfluthrin and tefluthrin. The results were contrary when they were treated with deltamethrin and permethrin. This was because multi-fluorinated pyrethroids such as transfluthrin have a distinct subtype mode of action of type I pyrethroid (Egunjobi et al. (2024). This may explain why a commercial bed bug mixture formulation that contained multi-fluorinated pyrethroid + neonicotinoid + PBO (metofluthrin, clothianidin, and PBO) is highly effective against pyrethroid-resistant bed bugs, despite the insects possessing both VGSC mutations and cytochrome P450 resistance mechanisms (Chow-Yang Lee, unpublished data).

TABLE 3 | Insecticide resistance mechanisms in *C. lectularius* and *C. hemipterus*.

Species	Resistance mechanisms	References
C. lectularius	Reduced penetration	Lilly, Latham, et al. (2016); Lilly, Webb, et al. (2016)
	Metabolic resistance	
	Cytochrome P450	Gonzalez-Morales and Romero (2018); Cáceres et al. (2019); Cho et al. (2020); Gaire et al. (2020); Vander Pan et al. (2020); González-Morales et al. (2021); Cáceres et al. (2023); Yu et al. (2025)
	Esterase (eg. carboxylesterase)	Gonzalez-Morales and Romero (2018); Gaire et al. (2020); González-Morales et al. (2021); Cáceres et al. (2023); Yu et al. (2025)
	Glutathione S-transferase (GST)	Gonzalez-Morales and Romero (2018); Yu et al. (2025)
	Target site insensitivity	
	VGSC (eg. V419L, L925I, I936F)	Balvin and Booth (2018); Holleman et al. (2019); Gaire et al. (2020); Samiei et al. (2020); Vander Pan et al. (2020); Akhoundi et al. (2021); Ghavami et al. (2021); Lewis et al. (2022); Cho et al. (2024); Porras-Villamil et al. (2025); Yu et al. (2025)
	p-Ace (F348Y)	Komagata et al. (2021)
	Insensitive GABA receptor (*rdl* mutation - A302S)	Gonzalez-Morales et al. (2021)
	nAChR	Not known[a]
	Endosymbiont	Not known[a]
	ATP-transporter	Mamidala et al. (2012); Zhu et al. (2013)
	Behavioral resistance	Not known[a]
C. hemipterus	Reduced penetration	Soh and Veera Singham (2021)
	Metabolic resistance	
	Cytochrome P450	Dang et al. (2021)
	Esterase	Punchihewa et al. (2019); Dang et al. (2021)
	Glutathione S-transferase (GST)	Dang et al. (2021)
	Target site insensitivity	
	VGSC (eg. M918I, D953G, L1014F)	Punchihewa et al. (2019); Dang et al. (2021); Lewis et al. (2020); Zhao et al. (2020); Soh and Veera Singham (2021); Tiotour et al. (2022); Cho et al. (2023); Cho et al. (2024); Porras-Villamil et al. (2025)
	p-Ace	Not known[a]
	Insensitive GABA receptor (*rdl* mutation)	Not known[a]
	nAChR	Not known[a]
	Endosymbiont	Soh and Veera Singham (2022)
	ATP-transporter	Not known[a]
	Behavioral resistance	Not known[a]

[a]Not information is available at this stage.

4.2 | Botanical Insecticides

Natural products containing essential oils such as neem, cedar, clove, peppermint, geranium, and lemongrass are becoming increasingly popular for bed bug control. In the U.S., many of these formulations are exempted from EPA registration under Section 25(b) of FIFRA (Federal Insecticide, Fungicide, and Rodenticide Act), as they contain active and inert ingredients considered to pose minimum risk. Consequently, these products do not require an EPA registration number and are not subject to

TABLE 4 | Effective control options and their suitability for bed bugs with different resistance mechanisms.

Control option	Resistance mechanisms: Suitable for	Resistance mechanisms: Not suitable for	Advantage(s)	Limitation(s)	References
Pyrethroid-neonicotinoid mixture spray	Target site insensitivity (*kdr*), esterase, GST	Cytochrome P450	Easy to apply and require less amount of time, residual activity	Resistance issue, especially those due to cytochrome P450, which is very common	Lee et al. (2018); Leong et al. (2020); Dang et al. (2023); Yu et al. (2023)
Pyrethroid-neonicotinoid- PBO mixture spray	Suitable for all types of resistance mechanisms		Easy to apply and require less amount of time, residual activity	Presently available formulation is expensive	n/a
Botanical/natural products	Suitable for all types of resistance mechanisms		Easy to apply and require less amount of time	Unless apply directly onto the bed bugs, it is unlikely going to achieve good control.	Lee et al. (2018)
Fumigants	Suitable for all types of resistance mechanisms		Kill all stages of bed bugs including eggs	Requires license to carry out fumigation, may not work for multi-unit housing, high cost, no residual activity	You et al. (2014); Kells (2018); Todd et al. (2021)
Desiccant dust	All, except penetration resistance		Easy to apply and require less amount of time, residual activity	Slow action (especially for diatomaceous earth), not suitable to be used in high human traffic area and with air movement	Akhtar and Isman (2016); Lilly, Latham, et al. (2016); Lilly, Webb, et al. (2016); Singh et al. (2016); Aak et al. (2017)
Heat treatment	Suitable for all types of resistance mechanisms		Kill all stages of bed bugs including eggs	High cost, requires longer time for proper treatment, no residual activity.	Wang et al. (2018); Ramos et al. (2023); Kong et al. (2024)
Cold treatment (eg. cryonite)	Suitable for all types of resistance mechanisms		Kill all stages of bed bugs including eggs	Requires longer time for proper treatment, no residual activity.	Brown and Loughlin (2008); Olson et al. (2013)
Entomopathogenic fungi spray	Suitable for all types of resistance mechanisms		Easy to apply and require less amount of time, residual activity	Slow action, need at least 3–7 days to kill, and may take up to 2 months for complete eradication	Barbarin et al. (2017); Shikano (2020), Shikano et al. (2021); Aak et al. (2023); Principato and DeVries (2024)

federal efficacy or toxicity regulations, although state registration may still be required under local laws. While some of these products prove effective, primarily when used as direct sprays, others are less effective against bed bugs.

4.3 | Fumigants

Fumigants such as sulfuryl fluoride, methyl bromide (now largely phased out), and inert gases like CO_2 and N_2 have been used for bed bug control (Kells 2018). Fumigants are highly effective because they can penetrate deep into hidden areas and harborages, killing all life stages of bed bugs, including eggs, within 18–24 h, depending on the concentration. They are ideal for challenging infestations, including those in airplanes where insecticide application is heavily regulated. However, fumigation is a complex process requiring thorough planning and adherence to strict safety measures. Despite their effectiveness, fumigants lack residual activity, meaning re-infestation can occur once the treated area is ventilated. Inert gases like CO_2 and N_2, on the other hand, have limited penetration ability and require longer exposure times to be effective. No resistance to fumigants has been reported in bed bugs, making them a reliable option in integrated pest management strategies.

You et al. (2014) used sulfuryl fluoride to fumigate an old vessel infested with bed bugs and killed all stages (adults, nymphs, and eggs). Todd et al. (2021) investigated the use of sulfuryl fluoride (Vikane) fumigation at a 1.9× dosage factor for eliminating resistant bed bugs (*C. lectularius*), including eggs, nymphs, and adults, from vehicles and cargo trailers densely packed with household items. The results showed 100% mortality across all bed bug life stages, with no significant damage to electronics, such as LCD monitors, present during fumigation. This method effectively addressed challenging infestations in inaccessible locations and household belongings. The study concluded that sulfuryl fluoride fumigation is a practical alternative for managing bed bugs in vehicles, trailers, and other spaces where conventional insecticides or heat treatments are impossible due to poor penetration and potential damage.

4.4 | Repellent

Tests using DEET, a common repellent, revealed conflicting results. A pyrethroid-resistant strain of *C. lectularius* collected from the field in Argentina exhibited lower sensitivity to DEET than the insecticide-susceptible Harlan strain (Vassena et al. 2019). Conversely, Hayes and Schal (2024) reported that the multi-resistant FM strain was repelled by DEET at a dose 100 times lower than required for the Harlan strain, indicating greater sensitivity to DEET.

4.5 | Desiccant Dust

Desiccant dust, such as diatomaceous earth (DE) (Akhtar and Isman 2016; Singh et al. 2016) and silica gel (Choe and Campbell 2014; Singh et al. 2016), dehydrate bed bugs by damaging their waxy cuticle. These inorganic and mineral compounds also remove moisture from the harborages, making them unsuitable for aggregation. Most of these products are in dust formulation, although aerosolized formulation is also available now. Their actions are relatively slow, often taking between 24 h to several weeks to provide complete mortality of all stages. Silicon dioxide (silica gel) has faster action than diatomaceous earth (Singh et al. 2016). When combined with carbon dioxide (CO_2), it has been shown that it performs better than when using desiccant dust alone, likely because CO_2 stimulates the movement of bed bugs, increasing the chances of them contacting with the dust (Aak et al. 2017).

4.6 | Entomopathogenic Fungi

One biopesticide product (Aprehend®) containing an entomopathogenic fungus, *Beauveria bassiana* (Bals.-Criv.), is presently available for bed bug management. It is a ready-to-use spore-oil mixture formulation. Unlike most insecticides that could kill very quickly (provided the insects are not resistant), bed bugs will only be killed in 3–7 days upon contact and may take 4–8 weeks for complete eradication. Barbarin et al. (2017) evaluated the performance of Aprehend® and a pyrethroid formulation containing deltamethrin against three pyrethroid-resistant *C. lectularius* in the laboratory. All resistant strains were susceptible to *B. bassiana* with a mean survival time of < 6 d and >94% mortality. The deltamethrin formulation only caused 16–14% mortality of these resistant strains over 14 days. Aprehend is also effective when combined with other insecticides (Shikano 2020; Shikano et al. 2021).

Principato and DeVries (2024) assessed Aprehend across different surfaces and distances, finding that non-porous materials like vinyl and cotton enhanced spore transfer and mortality, while porous surfaces reduced efficacy. Aak et al. (2018) explored the horizontal transfer of fungal spores, demonstrating that *B. bassiana* can spread among bed bug populations, significantly increasing mortality, with behavior like aggregation and CO2-stimulated activity influencing transmission. Another study by Aak et al. (2023) investigated dosage, substrate, and application strategies, showing that higher spore concentrations (2%) and multiple applications improved control. Bed bug age, reproductive status, and feeding influenced mortality timing, and fungal treatments reduced egg production and hatching rates. They also found that the oil-based formulation demonstrated faster mortality and greater efficacy than the water-based formulation. Complete population mortality was achieved only with the oil-based product at high doses (2%).

4.7 | Physical Methods

Physical control methods include the use of cold, heat, and vacuuming (Kells 2018). These techniques target all life stages, including eggs, and are particularly effective in severe infestations. Cold treatment, such as the Cryonite system, which uses CO_2 snow, freezes bed bugs instantly (Brown and Loughlin 2008). Other systems use liquid nitrogen. A temperature of −18°C for 72 h is required to kill 100% of test bed bugs (Olson et al. 2013).

Dry heat or steam treatment can be carried out using handheld devices, heating chambers, or whole-room heating. A heat exposure of >50°C will kill all stages of bed bugs for both *C. lectularius* and *C. hemipterus*. Bed bugs do not have the ability to develop heat resistance (Ashbrook et al. 2019). Laboratory studies demonstrated that steam treatment achieved near-instant mortality when bed bugs were directly exposed, with 100% efficacy for surface-dwelling or crack-hidden individuals. However, efficacy decreased to ~89% when bugs were protected under fabric due to reduced heat penetration (Kong et al. 2024). The survivors exhibited reduced feeding activity, potentially slowing population growth (Wang et al. 2018). In simulated field conditions, steam outperformed insecticide sprays, achieving comparable elimination rates while avoiding chemical residues (Ramos et al. 2023). However, steam lacks residual action, necessitating repeated applications (Kong et al. 2024). Combining steam with diatomaceous earth (DE) dust, which causes lethal desiccation, enhances long-term control; extended field trials (37 weeks) showed 97–100% elimination rates for integrated treatments (Kong et al. 2024). Despite requiring longer application times than insecticides, steam's safety and penetration into harborages make it an ideal option against insecticide-resistant bed bugs, especially in sensitive environments (Ramos et al. 2023).

4.8 | Other Methods Under Development

RNA interference (RNAi) has emerged as a promising tool for pest control by silencing critical genes involved in key biological processes such as molting, sperm release, larval development, reproduction, and locomotor activity in insects. Research has demonstrated that RNAi can significantly affect bed bugs' reproduction, survivorship, and insecticide tolerance (Basnet and Kamble 2017, 2018a, 2018b). Another interest is the development of bed bug baits, made possible by the discovery that certain blood constituents, particularly ATP, act as strong phagostimulants (Romero and Schal 2014). This has led to several studies exploring various toxicants that could be incorporated into bait formulations (Sierras and Schal 2017; Sierras et al. 2018). However, both RNAi-based approaches and bait development face a major challenge: ensuring the oral ingestion of the toxicant by bed bugs. The challenge lies in creating a practical, low-cost formulation for oral delivery system to effectively attract and target bed bugs in pest management operations. Overcoming this barrier is essential for advancing these novel control strategies.

5 | Bed Bug Reservoir

Managing bed bug infestations is a major challenge, especially in low-income housing and disadvantaged communities, where financial constraints prevent tenants from seeking proper treatment. Without effective control measures, these infestations often escalate, creating large populations of insecticide-resistant bed bugs that serve as reservoirs that could further spread throughout the community. The issue is not simply an individual hygiene problem, but a broader socioeconomic issue linked to income levels, eviction rates, and overcrowding (Sutherland et al. 2020). Studies have shown that bed bug infestations disproportionately affect underprivileged communities living in crowded and dilapidated housing, as seen in Hong Kong (Fung et al. 2021). Tenants in these areas often have little choice but to accept whatever minimal assistance they receive from building management, which is usually insufficient to address the problem. In most situations, minimal fund allocations are provided for pest management in these buildings, often using ineffective products and resulting in poor pest management services. Both government and society must step in with proactive policies and resources to ensure comprehensive and sustainable bed bug management. Only by treating bed bug infestations as a community issue can we hope to control their spread and protect vulnerable populations from their ongoing impact.

6 | Summary and Conclusion

The widespread issue of insecticide resistance, particularly pyrethroid resistance, presents a significant challenge in managing both common and tropical bed bugs. While resistance management strategies such as insecticide rotation and mixture applications can be effective, success has been limited in managing populations with metabolic resistance mechanisms, such as cytochrome P450. Alternative approaches, including biopesticides, desiccant dust, fumigants, and physical methods, provide viable solutions for controlling resistant bed bug populations. However, financial constraints pose a major obstacle to implementing physical control strategies, particularly in low-income housing, which serves as a reservoir for bed bug infestations. The persistent challenge of bed bug management lies in the search for low-toxicity, cost-effective, and time-efficient solutions. Future research and government-industry collaboration are crucial in addressing these challenges and ensuring the successful management of bed bugs in the future.

Acknowledgments

This review was based on a keynote paper presented at the 2024 International Symposium on Urban Entomology and the Entomological Society of Korea Annual Meeting in Incheon, South Korea, from November 28–30, 2024. This review is made possible by the UC Riverside Urban Entomology Endowed Chair Research Fund.

Data Availability Statement

Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.

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