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A Review on the Mechanism of Different Insecticide Resistance in German Cockroach (*Blattella Germanica*) in Worldwide

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ABSTRACT

German cockroach is one of the most important pests in public dwellings and health facilities. This insect can transmit many pathogens such as bacteria, viruses, fungi, protozoa and parasite eggs to humans through mechanical methods or their digestive tract. Using chemical insecticides is the most popular way to control these pests. Naturally one of the serious problems for controlling German cockroach is increase of resistance to insecticides due to long-term insecticide spraying and extreme utilization. Increasing resistance of German cockroach to different classes of insecticides including organochlorine, organophosphate, carbamate, and pyrethroid has been reported. The aim of this article was to assemble and review studies conducted on resistance of German cockroaches to insecticides to evaluate the current knowledge and gaps and provides an insight into the pest management.

Keywords: Cockroach; Insecticide Resistance; *Blattella Germanica*

Background

Cockroaches have existed for 300 million years [1]. Among more than 4,600 known species of cockroaches globally, only thirty are considered household pests [2]. Among them, the Germanallergiesch, *Blattella germanica* (Figure 1) is a common domestic pest species of medical and economic importance [3] because they have high adaptability to human life and a wide range of habitats for survival [4] and transmits various pathogens Mechanically via feeding mechanisms, cast skins originating from the molting, feces and secretions and causes allergic [5]. So, the control of this important human home pest is necessary. Control German cockroaches as the important indoor sanitary pests in urban worldwide are increasingly hard due to their high adaptability, strong fecundity and extensive insecticide resistance [6]. The utility of chemical pesticides is still the most important tool for control of these cockroaches [7]. World Health Organization (WHO) lists insecticides used to control cockroaches [8]. A wide range of chemical insecticides are approved.

Figure 1: Different stages of German Cockroach (*Blattella germanica*).

These are organophosphates (chlorpyrifos, chlorpyrifos-methyl, diazinon, fenitrothion, malathion, pirimiphosmethyl), neonicotinoids (dinotefuran, imidacloprid), carbamates (bendiocarb), hydrazine (hydramethylnon), arylpyrazole (fipronil) inorganic (boric acid), insect growth regulators (fenoxycarb, flufenoxuron, pyriproxyfen, hydroprene), pyrethroids (alpha-cypermethrin, beta-cyfluthrin, bifenthrin, cyfluthrin, cyphenothrin, d,d-trans-cyphenothrin, cypermethrin, deltamethrin, esfenvalerate, etofenprox, lambda-cyhalothrin, permethrin), and sulfonamide (sulfluramid). Unfortunately, use of approved insecticides are limited due to resistance to these products [9]. Insecticide Resistance Action Committee (IRAC) defines resistance to toxins as follows [10] 'a heritable change in the sensitivity of a pest population that is reflected in the repeated failure of a product to achieve the expected level of control when used according to the label recommendation for that pest species. Frequency in response to insecticide selection pressure increases because alleles confer appropriate resistance factors. As a result, a population can survive the lethal concentration of an insecticide that normally kills a wild population [11].

Resistance Mechanisms

Behavioral resistance, target site insensitivity, reduced cuticular penetration and metabolic detoxification are mechanisms of insecticide resistance in German cockroaches [12].

Monitoring Techniques

The most widely used bioassay methods on the susceptibility of cockroaches to insecticides are surface contact bioassays (jar test), topical application and toxic baits [13]. In topical applications, a specific amount of insecticide is placed on either the ventral thorax or abdomen of insects. The jar test that accepted worldwide standard method for monitoring resistance in the German cockroach depends on tarsal contact with deposits of insecticide in a glass jar. these methods were tested with numerous insecticides: diazinon, bendiocarb; chlorpyrifos; propoxur, cypermethrin and propoxur, chlorpyrifos, fenitrothion, pyrethrins, and cypermethrin and detected that regardless of the insecticide, jar tests are more practical because they rely on tarsal contact with insecticide deposits, but compared with the more precise topical applications, not sufficiently sensitive because they always produce smaller resistance ratios.

Insecticide Resistance in German Cockroaches

The present research desirable to develop database and monitoring strategies to estimate the susceptibility of German cockroach populations in worldwide with the aim to advance judicious use of insecticides in cockroach control program. Most cockroach susceptibility tests worldwide are performed on *Blattella germanica*, the results of which are classified into groups of insecticides and are presented. After the housefly, the German cockroach is the second most insecticide resistant urban pest, reported to be resistant to 45 insecticides [9]. Heretofore, more than 282 cases resistance are observed worldwide that first resistance was reported with Organochlorines (chlordane) in Texas in 1952 [14], in 1964 to organophosphates, in 1968 to carbamates, in mid-1980s for pyrethroids, in 1992 to sulfluramid, and in 1994 to abamectin. Among forty-five field-collected strains of German cockroaches examined for resistance to insecticides by the time-mortality response method, only low to moderate resistance to chlorpyrifos, and acephate was detected. strains showed high Resistance to malathion, carbamates, propoxur and bendiocarb and detected resistance to pyrethrins in half of the strains. High resistance was uncommon with propoxur. in some of the strains was detected resistance to the pyrethroids allethrin, permethrin, phenothrin, fenvalerate, and cyfluthrin [15].

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Among seven fields collected population of German cockroaches from Tehran City, five showed high resistance to organochlorine DDT indicating the possible cross resistance between three pyrethroid insecticides permethrin, cypermethrin and cyfluthrin and the organochlorine DDT [16]. Pyrethroids are synthetic derivates of pyrethrins, which extract of Chrysanthemum cinerariaefolium flower. These pyrethroids are now used in many synthetic insecticides and are highly effective and efficient neurotoxic insecticides against insects with mode of action on the voltage-sensitive sodium channels [17]. Due to the low efficacy and mammalian toxicity of pyrethroid insecticides, these compounds have become very popular for the control of German cockroaches, but in some populations has been documented control failures due to the development of resistance in many parts of the world [18,19]. *Blattella germanica* has shown Resistance level till now about up to 468.00× against pyrethroids (beta-cyfluthrin, deltamethrin), 62.50× against the carbamates (propoxur), up to 28.80× against OPs (chlorpyrifos), and 10.0× against phenyl pyrazole (fipronil). As well as moderate level of resistance is found in cockroaches against neonicotinoids including imidacloprid (0.8–3.8×) and the oxadiazines like indoxacarb (1.4–5.3×) [20].

At the study used of 2 German cockroaches' strain and the H strain was more resistant to all of the three carbamate insecticides than the D strain, that the order of resistance for H strain was carbaryl > propoxur > bendiocarb [21]. Resistance to the carbamate insecticides in several strains of B. germanica have previously been reported in the Britain, United States, Malaysia, Cuba, India, China, Singapore, Taiwan, South Korea, and Iran [21]. In a project investigated the resistance development of the German cockroach to Chlorpyrifos for 23 generations from the 5th instar nymphs of susceptible cockroaches, using Chlorpyrifos 50% lethal dose (LD50) as the insecticide selection pressure by topical application method. Obtained a highly resistant German cockroach cohort to Chlorpyrifos, which the resistance ratio was 21.63, after 23 generations of selection from susceptible strain cockroaches [22]. Two strains of German cockroach (Baygon-R and Pyr-R) showed 4-fold cross-resistance to imidacloprid that even do not be suppressed by PBO [23]. The Munsyana strain of German cockroach collected in Indana and was found to have high-level resistance to fenvalerate, displaying 825-fold levels of resistance by topical application [24].

A German cockroach, *Blattella germanica* (L.), strain Cincy was collected in Cincinnati, OH that gel bait-resistant and showed a high level of behavioral resistance to Avert (0.05% abamectin) and Maxforce FC (0.01% fipronil) gel baits. Topical application assays demonstrated moderate levels of physiological resistance to abamectin and fipronil with resistance ratios (based on LD50 values from topical applications) 2.5 and 8.7, respectively [25]. A German cockroach showed level of resistance to permethrin and deltamethrin 97 and 480-fold respectively compared with a susceptible strain [26]. German cockroaches collected from a number of field locations, ranging from Florida to South Korea, exhibitioned an avoidance behavior to a bait formulation. Cockroaches collected from locations that exposed with this formulation and had a history of treatment illustrated bait avoidance, whiles field and laboratory strains with no prior exposure ingested and were susceptible to the toxic bait. so, behavioral resistance had developed in these insects. Selection experiments showed that several susceptible strains were potentially capable of developing behavioral resistance [27]. populations of the *Blattella germanica* collected from various localities in peninsular Malaysia were tested for their susceptibility to commonly used insecticides.

The result showed Low to high levels of resistance to carbamates (1.8 – 65.2X) while resistance to organophosphates was low (1.1 – 4.3X). One strain exhibited high resistance to malathion (>275X). Eleven strains tested showed low to high resistance to DDT (1.3 – 40.7X). Resistance to pyrethroids ranged from 1.1 – 17.6X [28]. A strain of *Blattella germanica* with highly resistant to DDT has been reported from Europe [29]. Some populations of German cockroach were collected for testing susceptibility to several different insecticides by a topical application method in compared to an insecticide-susceptible strain. Extremely high to high levels of resistance in bifenthrin, deltamethrin, fenvalerate and low to moderate levels of resistance were observed in cypermethrin, permethrin, chlorpyrifos, chlorpyrifos-methyl and fenthion [30]. The three strains of the German cockroach observed different levels of resistance to permethrin and cypermethrin and low to moderate levels of bendiocarb resistance and low level of chlorpyrifos resistance based on resistance ratios compared with susceptible strain [31]. Collected populations of B. germanica from different localities in Taiwan island were evaluated for their resistance to deltamethrin, propoxur, and fipronil using the surface-contact method. Results had indicated that resistance exist and high deltamethrin resistance in some strains could affect in reducing effectiveness of indoxacarb, fipronil and imidacloprid baits [32].

The German cockroaches were provided from Sanandaj in Iran and evaluated with Surface contact method for bioassay using standard glass jar procedure. The results indicated that the German cockroach was resistant to malathion and propoxur while susceptible to lambda-cyhalothrin [7]. DDT has a long residual action of more than 6 months and is relatively economical, similar to pyrethroids. However, existence of high frequency of mutations in the knockdown resistance gene (kdr), cause conferring cross-resistance to DDT and pyrethroid insecticides; as well as several countries reluctant to register or utilize DDT due to perceived environmental or export concerns [33]. The German beetle (Blatella germanica (L)) strain, Apyr-R, was collected from Opelika, Alabama after control failure with pyrethroid insecticides and the levels of resistance to permethrin and deltamethrin were 97 and 480 times higher than the susceptible strain, respectively. Incomplete suppression of pyrethroid resistance with DEF and PBO shows that one or more mechanisms have rol in resistance. cuticular penetration is one of the barriers for the efficacy of pyrethroids against German cockroaches [26].

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Survey the effect of exposure to baits containing fipronil, indoxacarb, or hydramethylnon on the development of physiological resistance to the same and other insecticides in a number of German cockroach strains indicate that long exposure to baits fipronil or indoxacarb developed physiological resistance to these compounds but no increase was detected in response to hydramethylnon bait. Furthermore, exposure to fipronil bait caused increased cross-resistance to indoxacarb and exposure to indoxacarb bait did not increase cross-resistance to fipronil. Neither fipronil nor indoxacarb bait exposure enhancement resistance to hydramethylnon. exposure to toxic baits, particularly fipronil, have an important role in the expansion of insecticide resistance, including cross-resistance, in German cockroaches [34,35] (Table 1). This review shows studies conducted have great different test in the using insecticides, concentrations methods and formulations. The notable point is that a considerable population of German cockroaches have become resistant to large numbers of insecticides from different groups in over of world. Multiple physiological-based mechanisms including reduced penetration by thickening or remodeling cuticle, metabolic resistance and target site insensitivity (kdr mutations) are associated with *Blattella germanica* insecticide resistance.

Table 1: Reports of resistance to insecticides in German cockroach populations [35].

Group	Mode of action	Insecticide	Years	Location
Organochlorine	Sodium chann	DDT	1959	Trinidad
			1960	UK
			1961	Germany, France
			1962	Poland
			1967	USA-Nebraska-Kansas
			1968	USA-Kansas
			1969	Australia-Queensland
			1971	Puerto Rico, Cuba,Bahamas
			1972	Czechoslovakia
			1988	Japan
lodiene organochlorines	GABA-gated chloride channel antagonists	Dieldrin	1960	UK
			1964	Denmark
			1965	Australia
			1968	Australia
			1969	Finland
			1972	Czechoslovakia
			2005	Denmark
Cyclodiene organochlorines	GABA-gated chloride channel antagonists	aldrin	1960	UK
			1964	Denmark
			1965	Australia
			1968	Australia-Queensland
			1969	Finland
			1972	Czechoslovakia
				Gemany, Canada
				Poland, Japan
				USA-Hawaii
				USA-Kansas
				Trinidad
			1961	USA-Texas

Cyclodiene organo-chlorines	GABA-gated chloride channel antagonists	BHC/Cyclodienes	1962	Puerto Rico
			1965	Panama
			1968	Cuba
			1971	USA-California
			1953	USA-Texas
		Chlordane	1960	USA-California
			1961	UK
			1965	Australia-New Guinea
			1967	USA-Nebraska
			1968	USA-Louisiana
			1971	USA
			1974	USA-Utah
			1977	Canada
Organophosphorus	Acetylcholine esterase inhib-itors	Chlorpyrifos	1983	USA-Veberaska
			1986	Panama
			1987	USA-Florida
			1990	USA
			1991	USA-California
			1993	USA, Panama, Denmark
			1996	USA-Malaysia
			1997	USA-Indiana
			2000	Cuba-Playa
			2010	South Korea
			2016	China-Beijing
			2017	South Korea-Busan
		Chlorpyrifos-methyl	1990	USA
			2017	South Korea-Busan
		Diazinon	1961	USA
			1968	USA
			1974	USA
			1978	USA
			1983	UK
			1986	Panama
			1993	USA

Organophosphorus	Organophosphorus	fenthion	1965	USA
			1968	USA
			2010	South Korea
			2017	South Korea
		malathion	1965	USA-Texas
			1968	USA-Louisinia
			1971	USA
			1973	USA-Virginia
			1983	UK
			1984	Czechoslovakia
			1986	Poland
			1988	USA-California
			1990	USA
			2000	Cuba
		Parathion	1990	USA
		Pirimiphos-methyl	2000	Cuba
Carbamate	Acetylcholine esterase inhibitors	Bendiocarb	1987	USA(Virginia, Carolina, Florida, California)
			1988	USA-Kentucky
			1990	USA
			1993	USA
			1996	USA-Georgia-Ashburn
		Carbamates	1986	Denmark
			1986	Panama
		Dioxacarb	1983	UK
			1984	Czechoslovakia
		propoxur	1968	USA
			1988	USA
			1990	USA
			1993	USA, Dubai, Denmark, Panama
			1996	USA, Malaysia
Pyrethroid	Sodium channel modulators	alletrin	1988	USA
			1988	Japan
		bifenthrin	2010	South Korea
			2017	South Korea-Busan
		Cyfluthrin	1988	USA-Kentucky
		Cyhalothrin	1991	USA
		Lambda- Cyhalothrin	1991	USA
			1997	USA
			2000	Cuba

Pyrethroid	Sodium channel modulators	Cypermethrin	1988	Japan
			1990	USA
			1991	USA-Florida
			1992	USA-Virginia
			1993	USA
			1996	Malaysia-USA
			1997	USA-Indiana
			2000	Cuba
			2010	South Korea
			2011	Iran-Kermanshah
			2017	South Korea-Busan
		Deltamethrin	2000	Cuba
			2005	Denmark
			2010	South Korea
			2017	South Korea-Busan
			2018	Argentina
		Esfenvalerate	1991	USA-Florida
			1994	USA
			2010	South Korea
			2017	South Korea-Busan
		Etofenprox	1988	Japan
		Fenvalerate	1988	USA, Japan
			1991	USA
		Permethrin	1988	USA, Japan
			1991	USA
			1996	USA
			2010	South Korea
			2011	Iran-Kermanshah
			2017	USA, South Korea
Pyrethroid	Sodium channel modulators	Phenothrin	1988	USA
			1991	USA
		Pyrethrin	1956	USA
			1973	USA
			1985	Finland
			1987	USA
			1988	USA
			1990	USA
		Resmethrin	1991	USA
		Tetramethrin	1979	USSR
			1984	Czechoslovakia
			1988	Japan

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Neonicotinoids	Nicotinic Acetylcholine receptor agonists	Imidacloprid	1997	USA
		Clothianidin	2022	USA
Phenylpyrazole	GABA-gated chloride channel antagonists	Fipronil	2003	USA
			2004	USA
			2022	USA
Voltage-dependent sodium channel blocker, Indoxacarb		Indoxicarb	2022	USA

Despite the spread of resistance in this pest, various application methods such as sprays and baits using different modes of action classes rather than insecticides from within the same IRAC mode of action group should be applied in a rotational strategy to provide control and delay the rapid extension of resistance in all species. The use of insecticides is an important element of health and urban pests' management. Resistance to insecticides and the significant shortage of pesticides suitable for control is a serious threat that requires special and immediate attention from health authorities, researchers and the pesticide industry. Insecticide resistance management should be an integral part of pests control programs, and the structure, human resources, and other resources required should be given high priority.

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