



Insecticide Resistance in Urban Pests with Emphasis on Urban Pests Resistance in Iran: A Review

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ABSTRACT

Introduction and Objectives: Pests may transmit deadly parasites or pathogens to humans or cause illness, pain and suffering through bites and stings, infected wounds or allergic reactions. Chemical pesticides are considered as the main pest control tool. Insect resistance to the synthetic insecticide occurred following extensive use of this chemical to control pests. Insecticide resistance is a basic threat to urban pest management in the world, to design more applicable Insecticide Resistance Management (IRM) strategies in urban ecosystems. It is necessary to determine the pesticides used for urban pest control and identify various mechanisms underlying insecticide resistance by the pests. **Materials and Methods:** The review search was performed on the medical and health-related literature. Our search strategy provided us with a total of 374 studies, of which 108 of them were excluded and a total of 266 papers were analyzed and presented in this review article. **Results:** The common insecticides used to control four urban insect pests: house fly, German cockroach, mosquitoes and scorpions will be described. We will also discuss different mechanisms of resistance developed by these pests. **Conclusions:** The extensive application of insecticides and increasing the pesticide resistance species cause high economic costs and threaten human health. Environment improvement programs to make an undesirable condition for growing arthropods had a reduction effect on the pest population. As well as alternative technologies such as genetic and biological approaches have the potential to control the pest abundance in urban ecosystems. The application of any technology to control the pest to improve human health should not have side-effects on the environment.

Keywords: Urban Pests, Insecticide, Resistance, Mechanism

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INTRODUCTION:

The use of various pesticides to protect crops and control vectors has a long history. The first identified pesticide was sulphur compounds which used about 4500 years ago by the Sumerians to control insects and mites. While about 3200 years ago, arsenical and mercury compounds were utilized by the Chinese to

exterminate body lice. The powder of pyrethrum which is gotten from the dried flowers of *Chrysanthemum cinerariaefolium*, as a natural insecticide has been used by Persians for over 2000 years to protect stored grain [1, 2].

The term pesticides include insecticide, herbicide, fungicide, acaricide, molluscicide, nematicide, rodenticide, bactericide, and ovicide. These chemical compounds not only are

toxic to pests but are also potentially toxic to other vertebrate and invertebrate organisms, including humans, because of sustainability in nature [3, 4].

Annually, on an average, insects, plant pathogen and weed pests cause damage to more than 40% of all potential food production in agriculture. The application of pesticides to save agricultural production has increased to three million tons by the year in the world. In Iran, about 14,000 tons of agriculture pesticides were annually used [1, 5].

While ecologically, all organisms have their specific functions in the ecosystem, the use of pesticides to control arthropods and other animals as human competitors in the use of agricultural products, or vectors of human diseases can cause bio-ecological degradation [6]. Every year, a large number of pesticides can enter the environment in different ways. According to pesticide solubility, they enter the natural ecosystems. Lipophilic pesticides including chlorines get absorbed in the fatty tissues of animals, resulting in their persistence in food chains for a long time, While Water-soluble pesticides get dissolved in water and enter groundwater, streams, rivers, and lakes, causing environmental contamination and harm effects to untargeted species [1, 7, 8].

Since the production of artificial insecticides and their application in medical programs especially during the world war, the emergence of resistance in insects was a great problem. Most of the researchers did not know that the successive failures in pest control were as a result of pest resistance until 1956 [1].

Insecticidal properties of Dichloro Diphenyl Trichloroethane (DDT) were discovered in 1939 and the malaria eradication program was commenced by the World Health Organization (WHO) in 1955. Initially, the program was greatly successful, but resistance to DDT soon emerged in the insect population including *Anopheles* mosquitoes. Then the goal of eradication was abandoned [9].

Many arthropods including mosquitoes, cockroaches, flies, bedbugs, sucking lice, scorpions, mites and some vertebrates including rodents are major pests that are threats to agriculture and livestock production and human health [10- 26]. A lot of insecticides are used in houses, restaurants, hospitals, hotels and the

other infected places in urban environments to control these pest species. Both pest control professionals and homeowners use pesticides in urban environments for medical and agricultural purposes [27]. Repeatedly using the same types of pesticide to control a pest can lead to the pest developing resistance [28]. Resistance to various classes of insecticides is now widespread among medically important insects. This is a basic threat to urban pest management in the world. More than 550 arthropod species have developed some level of resistance to pesticide. [29]. More than 100 species of mosquito (56 *Anopheles* spp., 39 Culicine species) are resistant to at least one insecticide. Findings have shown that, in 60 countries, since 2010, pests have developed resistance to at least one type of insecticide. Forty-nine countries have reported that the pests have developed a resistance to two or more classes of insecticides [30, 31].

Insecticide resistance phenomena can be varied over time in response to a range of factors, and can also differ greatly over short distances. It is necessary to preserve current insecticides through implementation and development of resistance management strategies. Then identification of insecticides used for urban pest control and mechanisms underlying resistance developed by these arthropods is essential. The present study provides a review on the frequently used insecticides and also the resistance of four common insect pests: German cockroach, house fly, mosquitoes and scorpions to insecticides and the mechanisms of resistance as well, to design more sustainable Insecticide Resistance Management (IRM) strategies pests and decrease the prospect of insecticide resistance in urban regions.

MATERIALS AND METHODS:

This review search was performed on the medical and health-related literature. The databases included MEDLINE, Web of Science, Cochrane Library Database, Google Scholar as well as SID and Iran Medex. Search terms were such as, insecticide, resistance, pesticide, insect, pest, mosquito, housefly, German cockroach, scorpion and Iran to achieve Persian and English pieces of literature from 1978 to 2019. Our search strategy yielded a total of 374 studies, in

which 108 of them were excluded after initial screening, because of the lack of relevance to the aims of this study. Totally, 266 searched papers were analyzed and presented in this review article. Ethical subjects (Including plagiarism, double submission and/or publication, redundancy, misbehavior, information fabrication and/or falsification, etc.) have been entirely considered by the researchers. All data were analyzed according to the relevant laws and guidelines of the ethical standards of the Declaration of Helsinki.

RESULTS AND DISCUSSION:

Insecticide Resistance in studied urban pests Houseflies

The housefly, *Musca domestica* Linnaeus, is a well-known cosmopolitan pest of urban ecosystems. This species has an association with humans and livestock for a long time. The house fly found on hog and poultry farms, animal shelters, garbage dumps, and food storage. The housefly is not only an annoyance pest, but also a vector that can transmit more than 100 of animal and human diseases mechanically which are caused by many deadly antibiotic-resistant zoonotic pathogens [32].

Application of chemical insecticides to control *M. Domestica* has a long history which unfortunately leads to a well-documented resistance to many insecticides, including, Organochlorines (OCs), Organophosphates (OPs), Carbamates (CBs) and Pyrethroids (PYs). The housefly is resistant to 62 unique insecticides [28, 33-35].

Resistance to propoxur and malathion in *M. domestica* is associated with cross-resistance to OPs compound used in agriculture. Likewise increased metabolic resistance to DDT is attributed to extreme usage of cypermethrin [36].

Musca domestica has multiple Glutathione S Transferase (GST) genes and the relationship between OPs resistance and GST activity has been reported. Two and probably more of these genes are responsible for elevated GST activity excess transcript in organophosphate insecticide-resistant housefly strain Cornell-R [37]. Resistance to tetrachlorvinphos in this fly is a metabolic resistance in which this OP compound is demethylated by GST [38].

Organophosphate or carbamate resistance in housefly is associated with a reduction in the carboxylesterase activity. Five mutations in the acetylcholinesterase gene (V260L, G342A, G342V, F407Y, and G445A) that either singly or in combination, confer various spectra of insecticide resistance to these chemicals in housefly [33, 39-41]. The *kdr* insecticide resistance trait in the housefly confers resistance to the rapid paralysis (knockdown) and lethal effects of DDT and PYs. The *kdr* is the main mechanism for pyrethroid resistance in the *M. Domestica* [42-44].

The important mechanism of resistance to pyrethroid insecticides in the *M. Domestica* that causes target site insensitivity is the mutations in the Voltage-Sensitive Sodium Channel Gene (VSSC). Five known VSSC mutations confer resistance to PYs in the house fly: knockdown resistance (*kdr*; L1014F), super-*kdr* (M918T + L1014F) and *kdr*-his (L1014H), super-*kdr* (D600N) and *kdr* (T929I) were found in the resistant housefly. It was discovered that super-*kdr* + D600N conferred higher levels of resistance to PYs than super-*kdr*, and *kdr* + T929I showed super-*kdr*-like levels of resistance in house flies population [33, 34, 44-49]. Studies showed that the monooxygenase and hydrolase mediated detoxication are involved in resistance to permethrin, beta cypermethrin, cypermethrin, deltamethrin and propoxur in housefly [35].

Application of insecticides to control houseflies in urban environments has resulted in the pests developing resistance to not only four main classes of insecticides but also to biopesticides, Insect Growth Regulators (IGRs), the triazine cyromazine, [50-52] and imidacloprid (neonicotinoid) [53, 54]. The metabolic resistance mechanism was responsible for resistance to this insecticide in the CYR-SEL strain from Punjab, Pakistan [52]. Resistance development to spinosad in the studied field strain of housefly has been reported. The resistance was a recessive trait linked to autosome one, related to an altered target site mechanism, without any cross-resistance with other insecticides (abamectin, deltamethrin, and indoxacarb). These results indicated that spinosad resistance in the housefly is due to a unique mechanism of resistance [55-57]. It was discovered that the neonicotinoid resistance in

housefly is associated with the CYP6G4 as an important insecticide resistance gene [58]. It was selected as a strain of housefly that was resistant to indoxacarb following three generations. Resistance was related to major and minor factors on autosomes 4 and 3, respectively [59]. The Imidacloprid resistance is emerging in housefly in Florida, and this species showed tolerance to both imidacloprid and nithiazine [60]. In the results of several studies, it was shown that multiple controlled factors imidacloprid. Resistance to imidacloprid in housefly is autosomally inherited, incompletely recessive and phylogenetic [53, 61]. The result of a study revealed that *M. domestica* can develop resistance with continued selection pressure with fipronil. But the level of resistance to lambda-cyhalothrin, profenofos, and indoxacarb did not increase due to this selection. Then there was no cross-resistance to these insecticides [62]. Monooxygenases and esterases mediated fipronil resistance in *M. domestica* have been reported [63]. Likewise the housefly showed the reduced sensitivity to emamectin benzoate, a broad-spectrum agrochemical belonging to the avermectin group of pesticides. The metabolic resistance mechanism does not account for the development of emamectin resistance in the EB-SEL strain [64].

Resistance to pyriproxyfen in the Pyri-SEL strain of the housefly was detected. This resistance in *M. Domestica* was autosomally inherited, completely dominant and polygenic [65, 66].

Mosquitoes

Mosquitoes are the most important vectors of diseases including malaria, lymphatic filariasis, arboviral encephalitis, dengue, and yellow fever. Malaria and dengue fever are the most important mosquito-borne disease. Malaria is transmitted by the female of *Anopheles* mosquito species. In 2015, 212 million cases of malaria occurred worldwide and 429000 deaths from malaria are estimated to have occurred globally, which 303000 cases of them are estimated to have occurred in children aged less than 5 years [67].

The number of reported cases of dengue fever transmitted by *Aedes* species increased from 2.2 million in 2010 to 3.2 million in 2015. The global annual incidence has been estimated at 50 million – 100 million [68]. *Aedes* species are also

vectors of yellow fever and chikungunya. Various species of *Culex* are vectors of West Nile, filariasis and mosquito-borne encephalitis [69-72].

Vector control is the most important part of the global approach for the management of mosquito-borne diseases. In this case, one of the very important elements is applying insecticides. Mosquito-borne diseases have become resurgent due to the development of insecticide resistance in mosquito vectors. Six classes of insecticides including OCs, OPs, CBs, PYs, pyrroles, and phenyl pyrazoles are recommended in adult mosquito control programs [73]. Insecticide-Treated Nets (ITNs), Indoor Residual Spraying (IRS) and Long-Lasting Insecticide-Treated Bednets (LLITs) are the insecticide-based approaches for control of adult mosquitoes recommended by WHO. Four main classes of insecticides including, OCs, OPs, CBs, PYs suggested for IRS and the last ones are the only insecticides that are applying for treated bednets according to WHO recommendation [74-81].

The global eradication of malaria was failed soon after the emergence of resistance in the vector mosquitoes to DDT. Then WHO officially switched the program from malaria eradication to malaria control in 1976 [9]. DDT was first applied to control mosquito in 1946. The first mosquito resistance to DDT was reported in *Aedes tritaeniorhynchus* and *Ae. sollicitans* in 1947 [82] and *Anopheles sacharovi* in Greece by 1954 [83]. Resistance to DDT or dieldrin had developed in ten confirmed malaria vectors in nineteen countries by the end of 1958 [84]. Since hundreds of mosquito species including 50 Anopheline species were resistant to DDT and at least one or two more insecticides [30]. Findings show that since 2010, the species that have developed resistance to at least one class of insecticide have been reported in 60 countries, fifty of these countries reported resistance to 2 or more classes [85].

The development of insecticide resistance is widespread in mosquitoes and this phenomenon is a global problem for control programs in the world. Resistance to the DDT and dieldrin was reported in mosquito vectors in the world, particularly in malarious areas. Studies detected the resistance of *An. gambiae*, *An. sudaicus*, *An. stephensi*, *An. quadrimaculatus*, *An. subpictus*, *An.*

sacharovi, *Aedes aegypti*, *Culex fatigans* and *Cu. tarsalis* to these two OCs from 1956 to 1957 [86]. Resistance to DDT, dieldrin in adults of *An. stephensi* has been widespread in the Persian Gulf, the Middle East and Indian-subcontinent areas [87]. Subsequently, the resistance of the other malaria vectors to OCs (DDT, dieldrin, and HCH) was detected from malarious areas including *An. fluviatilis* in Afghanistan, Pakistan, India, and Nepal to DDT, in Saudi Arabia and Pakistan to dieldrin and in India to HCH [87, 88], *An. pulcherrimus* in Afghanistan, Iraq, Saudi Arabia and Syria to DDT, in Afghanistan, and Pakistan to dieldrin [89-91] and *An. sacharovi* population in Turkey [92]. Following the application of the other classes of insecticides in the malaria vector programs, resistance in *Anopheles* species to OPs, CBs, and PYs was detected in numerous countries [93-99]. Widespread resistance to PYs has been reported for malaria vectors from different countries in sub-Saharan Africa as well as central and south-east Asia [95, 100].

The resistance to DDT in *Ae. aegypti* was developed in regions that this vector mosquito distributed. Subsequently, OPs, CBs and Pyrethroid resistance were detected in some regions of the world [87, 101-107]. It was showed that resistance to the OCs in *Ae. aegypti* populations were consistently high while resistance to the CBs was more variable. However resistance to these insecticides has been reported in Asia, Africa, and Latin America and the resistance to PYs in this dengue vector is widespread [108, 109]. Southeast Asia reported the resistance of this vector mosquito population to all four important classes of insecticides although fewer studies assessed the susceptibility of *Ae. albopictus* to insecticides compared to the susceptibility of *Ae. Aegypti*. Resistance to the OPs has also been reported from America [108]. Moderate resistance to new chemical insecticides like imidacloprid and spinosad in *Ae. aegypti* is also reported [110].

In Iran resistance to DDT and dieldrin in *An. stephensi*, the main vector of malaria in southern of this country, was first reported from Khuzestan, Fars and Hormozgan Provinces in 1957 and 1960, respectively [111]. Studies have been shown the resistance of this species in Iran to both of these chlorinated insecticides and also fipronil, a phenyl pyrazole insecticide [112-118].

This mosquito vector showed resistance to DDT but a low level of tolerance to dieldrin in southern Iran [119]. The resistance of *An. stephensi* larvae to fenitrothion and tolerance of adults to malathion have been reported from Hormozgan and Fars Provinces of Iran [119-121]. The susceptibility of this major malaria vector to malathion was shown in recent studies in Iran. However the resistance of *An. stephensi* to this insecticide had been reported in 1976, [122] but substituted propoxur in 1978 in malarious areas caused the susceptibility back [117, 123]. The first indication of pyrethroid resistance in *An. stephensi* was reported in a malarious area, from southern Iran [122]. A study carried out in Jask County in the Hormozgan Province southeastern Iran revealed that the field strain of *An. stephensi* was resistant to DDT and lambda-cyhalothrin [124]. Similarly, the resistance of *An. culicifacies* to DDT and dieldrin has been reported from Baluchistan Province, south of Iran [125-127]. The resistance of this malaria vector to dieldrin, tolerance to propoxur, and susceptibility to DDT, malathion, and bendiocarb from these areas were reported [126]. The results of a study carried in Hormozgan Province, southern Iran, showed some indication of tolerance to DDT, propoxur, and deltamethrin in this mosquito [117]. The resistance of this species to pyrethroid insecticides was also reported in Baluchistan, Iran [128]. Likewise, *An. maculipennis* vector of malaria in north and central of Iran, showed resistance to DDT [129]. This mosquito species displayed resistance to propoxur, bendiocarb and malathion in West Azarbaijan Province, northwestern Iran, [130] and DDT and dieldrin in Astra County, borderline of Iran and Republic of Azarbaijan [131]. The extensive application of DDT against cotton pests in the north part of the country and the other agricultural pesticides in West Azarbaijan Province, known to be able to cause the development of resistance in Anopheline mosquitoes in these areas. The major vector of malaria which is the resistance of *An. sacharovi* to DDT first occurred in 1959 from Kazeroon, subsequently from Izeh and Meshkinshahr, Iran [132]. This species showed resistance to DDT and tolerant to dieldrin in East Azarbaijan Province; Iran; and Borderline of Iran, Armenia, Naxcivan, and Turkey [133, 134]. Resistance to

DDT and deildrin was also detected in *An. Sacharovi* from Ardebil Province, Iran [135]. Similarly, resistance to DDT in an adult of malaria vector *An. d'thali* has been reported from Iran [30].

Culex quinquefasciatus is considered as the main nuisance mosquito in Iran. Transmission of the sindbis virus by *Cx. quinquefasciatus* has been reported in Iran [136]. This species could be a vector of microfilaria, *Dirofilaria immitis* [137]. Studies evaluated the susceptibility of field strains of *Culex* species revealed the resistance of these mosquitoes to DDT, OPs (chlorpyrifos, malathion), CBs (propoxur) and PYs (deltamethrin, lambda-cyhalothrin and cyfluthrin) [118, 138-144]. Tolerant to malathion, permethrin, deltamethrin, lambda-cyhalothrin, and etofenprox in this urban species was also reported [118, 143, 145-147]. The two important mechanisms that are involved in insecticide resistance in insects including mosquitoes are target-site insensitivity and increased metabolic detoxification of insecticides. Sodium channels are target-site for insecticides such as DDT and PYs [73, 148, 149] and the reduction of sensitivity of this target site is described by the knockdown resistance (kdr) [108, 150-152]. By now, kdr mutations have already been reported from African, Asian and, more recently, American continents in at least 13 species: *An. gambiae*, *An. arabiensis*, *An. sinensis*, *An. stephensi*, *An. subpictus*, *An. sacharovi*, *An. culicifacies*, *An. sudaicus*, *An. aconitus*, *An. vagus*, *An. paraliae*, *An. peditaeniatus* and *An. albimanus* [153]. Four mutations (L1014 F/C/S/W), (I1011M/V), (V1016G), and (F1534C) have been correlated with the resistance to these two classes of insecticides in mosquito species [97, 149, 154]. Multiple mutation combinations have been also identified in insecticide resistance mosquitoes including; (L1014F) and (N1575Y) in *An. gambiae*, [155] (V1010L) and (L1014S) in *An. culicifacies* [156], (S989P) and (V1016G), [157] (V1016G) and (D1794Y) [158] and (V1016) and (F1534) in *Ae. aegypti* [159]. The cross-resistance between DDT and PYs which occurred by target-site mutations in the para voltage-gated sodium channel gene kdr, has been detected in several mosquito species [108, 150, 160-163]. A Leu to His amino acid substitution in *An. culicifacies* detected upstream

the formerly known knockdown resistance (kdr) mutation site in this vector of malaria in Baluchistan of Iran; confer resistance to DDT and PYs [128]. The kdr-type nerve insensitivity mechanism may be involved in resistance to both DDT and deltamethrin insecticides in two strains of *Ae. Aegypti* [164]. Similarly, *Cu. quinquefasciatus* showed high levels of resistance to DDT, permethrin, and deltamethrin [165].

The target site for both OP and carbamate insecticides is Acetylcholinesterase (AChE) which is a key enzyme in the nervous system, hydrolyzing acetylcholine neurotransmitters and terminating nerve impulses [74, 166]. At least five-point mutations in the acetylcholinesterase insecticide-binding site have been identified that singly or in combination are related to resistance to OPs and carbamate insecticides [167]. The γ -Aminobutyric Acid (GABA) receptors are the target for Cyclodiene and fipronil insecticides [168-170].

In addition to mutations at the target site, resistance can also be related to over-expression of certain enzyme families that metabolize or sequester the insecticide molecules, like GST, P450s and esterases [144, 149, 150, 163]. High GST activity has been associated with resistance to all the major classes of insecticides. Detoxification of DDT is catalyzed by GSTs which detected in many insects including *Ae. aegypti*, *An. gambiae* and *An. dirus* [74, 161-165]. GSTs are also responsible for OPs resistance in many insects [171-179].

The other detoxification enzymes, P450s have highly been associated with pyrethroid resistance. The overexpressions of CYP6BB2, CYP9J32, and CYP9J28 have been detected in pyrethroid-resistant strains of *Ae. aegypti* [180, 181]. It was shown that CYP6M2 is an efficient metabolizer of DDT and PYs in the *An. Gambiae* [182, 183]. While CYP6P3 metabolizes PYs [184] and has also potential to metabolize the carbamate, bendiocarb in this vector mosquito [185]. It was detected that the resistance of larvae of *Cx. quinquefasciatus*, *Ae. aegypti* and *An. stephensi* to deltamethrin was mainly due to the detoxification of this pyrethroid insecticide by microsomal mono-oxygenases [186]. The correlation of esterases, monooxygenases and possibly GSTs in pyrethroid resistance of *An.*

stephensi from the south of Iran was confirmed by biochemical assays [187]. The carboxylesterases (CCEs) have been related to resistance to Ops, [188] particularly in *Culex sp* mosquitoes. These enzymes produce resistance through sequestration [189]. The resistance to temephos in *Ae. aegypti* is associated with raised esterase activity [109]. Two CCE genes, CCEae3a and CCEae6a, were detected in temephos resistance strains of *Ae. Albopictus* [149]. Elevated activity of esterases, monooxygenases and glutathione S-transferases in the permethrin resistant than in the susceptible strain of *An. stephensi* was detected, which confer to pyrethroid-resistance in this major vector of malaria in several countries of the Middle East and Indian subcontinent [150]. The existence of behavioral and cuticular resistance in mosquitoes has also been reported [74].

Cockroaches

Cockroaches are considered the most common pests in residential areas and public housing, hospitals, and restaurants. These insects act as mechanical vectors of many, bacteria, fungi, viruses, Protozoa and parasites egg [190]. The German cockroach, *Blattella germanica* (L.) is the most important species of cockroaches which have adapted to human life in cities. The feces, secretions and cast skins originating from the molting process of these urban pests, have allergic substances causing dermatitis, itches and many respiratory disorders. Cockroaches are considered as the second important factor of asthma after dust sensitivities [191].

In 1952, the first insecticide resistance in German cockroaches was reported from the USA against chlordane. Subsequently, Resistance to linden in Poland, linden and dieldrin in Turkey and malathion, diazinon and phenthiene in the USA, in 1959, 1962 and 1970s respectively were reported [192]. The German cockroach is resistant to forty-two insecticides of OCs, OPs, and CBs. This species is the No. 2 insecticide-resistant urban pest in the world [193].

Extensive application of four major classes of insecticides including OCs, OPs, CBs, and PYs to control this urban pest, have been led to high-level resistance of *B.germanica* to these insecticides in many field populations. Resistance to DDT, [192, 194], OPs [192, 195-198] CBs [197, 198-201] and PYs, [197,198, 202-

205] was reported from different countries in the world. Moderate level of resistance is also found in cockroaches against neonicotinoids (imidacloprid), oxadiazines (indoxacarb) and the phenylpyrazole (fipronil) [198].

In Iran, many studies have been carried out to monitoring insecticides resistance in the German cockroach population from various parts of this country. Resistance to at least four main classes of insecticides has been detected in a field population of this urban pest. Resistance to DDT, [206, 207] OPs, [208-214] CBs [212, 213, 215, 216] and PYs [206-208, 211-213, 214, 217-219] have been reported from various places in different cities of Iran. In German cockroach moderate levels of resistance to fipronil were also discovered [220]. Susceptibility of the *B. germanica* to the spinosad has been reported from Iran [221]. Studies showed the cross-resistance between DDT and pyrethroids in this insect species [197, 207, 208, 217]. Likewise, the limited cross-resistance in DDT and chlordane resistant strains of the German cockroach was observed [195].

The same as the other insects, both target-site insensitivity, and increased metabolic detoxification of insecticides are the two major mechanisms involved in insecticide resistance in cockroaches. It was detected that four-point mutation; glutamic acid to lysine (E434→K434), cysteine to arginine (C764→R764), aspartic acid to glycine (D58→G58), proline to leucine (P1880→L1888) are associated with pyrethroid resistance in cockroaches [222]. Molecular evaluation detected the *kdr* mutation, the substitution of G for C (L1014F), in collected *B. germanica* from three different locations of Urmia city, northwestern Iran. However, the super-*kdr* mutation (M918T), was not found in the sequences of the current study [218]. Additional resistance mechanisms such as *kdr* type and *rdl* mutation confer to pyrethroids and fipronil resistance in German cockroach [198]. Numerous studies revealed that the metabolic mechanisms were involved in pyrethroid-resistant in German cockroaches which are related to elevated oxidases and esterases in this urban pest [204, 223, 224]. Several studies in Iran also showed the involvement of oxidases, esterases, and GSTs in pyrethroid resistance in *B.germanica* [206, 207, 212]. Multiple

mechanisms of resistance to pyrethroids, including *kdr*, decreasing of cuticular penetration and elevated metabolism was detected in a strain of German cockroach [222]. Overexpression of GST confers broad-spectrum resistance to a range of OPs and carbamates [225]. Increased level of CYP4G19 is also involved in pyrethroid resistance in *B. germanica* [226]. Studies detected that the detoxification by cytochrome P450s and target site insensitivity, mutation of the alanine to serine (A302S) involved resistance to new chemical insecticides, such as fipronil [227, 228]. Fenvalerate resistance in a strain of *B. germanica* was not omitted by either PBO, MGK-246, or DEF completely. Then additional mechanisms, probably including sodium channel insensitivity, are related to this resistance [229]. Studies revealed that aside from the Leu993Phe mutation in *kdr*, decreased cuticular penetration may also be involved in cypermethrin resistance in German cockroach [205].

Scorpions

Scorpions are medically important arthropods that are considered as urban pests distributed in a 52N and 5S [230, 231]. In addition to pain caused by a scorpion sting, sometimes it may result in death. Scorpions are predators and feed on other insects or tiny animals. Regarding the variant climate in Iran, a variety of arthropods exist in Iran. Reports showed that there are 59 scorpion species in Iran [232, 233-236]. About 40000-50000 scorpion stings are reported annually from different parts of this country [237, 238].

Scorpions are considered as major pests in the human environment, in the south and southwest of Iran, as well as in some central and eastern parts of this country [239-241]. Different insecticides applied for scorpion control that showed this species are susceptible to insecticide but the continuous use of insecticides may result in resistance [242]. The application of pesticides against scorpions may affect non-target animals including their predators, therefore attention to non-chemical methods to control this arthropod is important [243, 244].

Urban Integrated Pest Management

Arthropods including insects are the most serious threats to the health of humans in the

urban ecosystem. The various classes of insecticides have produced in the past fifty years to reduce the pest population. However, Extensive use of insecticides and emphasis on killing pests soon resulted in pesticide-resistant populations of some major insect pests along with some undesirable environmental effects [245]. When only a unique insecticide class is suggested for a particular application, Resistance management is challenging, as is the case of bed [246]. Studies have revealed that Integrated Pest Management (IPM) can be more efficient and successful than conventional pest control [247, 248]. The overall goal of urban IPM is to decrease the pest population while avoiding excessive and ineffective pesticide use [249]. IPM is a combination system of different protection approaches with careful evaluating of pests and their natural enemies to manage them below levels that cause economic damage [250] and endangers human health.

Insecticide resistance monitoring is an essential part of IPM programs. Determination of the susceptibility of pest to insecticides and mechanisms of resistance are the two fundamental points of a pest control program. The molecular methods are preferable since insecticide resistance can be detected before it reaches the maximum level and the insecticide is completely ineffective [251]. Several strategies can be effective to reduce the selection pressure of an insecticide, such as the application of several insecticides in rotation, mixtures, and mosaic formats [252]. Nonchemical techniques like Genetic control should be the powerful new methods that, integrated with current methods to control insect pests [253].

Sterile Insect Technique (SIT) which was introduced in 1955, [254] is one of these methods. By this method, several sterile male mosquitoes (using the irradiation) [255] are released to mate with the wild females which causes a reduction in the reproductive potential. This method is environmentally friendly and is specified for species [28, 256]. SIT has been successfully used to control the New World screwworm (*Cochliomyia hominivorax*) and the Mediterranean fruit fly (*Ceratitis capitata*), tsetse fly (*Glossina fuscipes*) in Zanzibar [257]. Release of engineered male insects that are carriers of a dominant lethal gene (RIDL) to

mate with wild females led to die the progeny [258]. Likewise, Homing Endonuclease Genes (HEGs) is the other molecular and genetic approach to reduce the population of mosquitoes and control mosquito-borne diseases [259, 260].

Biopesticide is the agents produced from living microorganisms or natural products for pest control. These Green chemicals usually have specificity against their target insects with limited impacts on non-target organisms. They are biodegradable with various structures and modes of action, which prohibit the development of resistance. Biopesticides classified as three different types according to the active substance: microorganisms; e.g. *Bacillus thuringiensis*, biochemicals; e.g. pyrethrins, produced by *Chrysanthemum cinerariaefolium*, neem oil, an extract from seeds of *Azadirachta indica*, semiochemicals; e.g. insect sex pheromones [261- 263].

Spinosad is a mixture of two chemicals from *Saccharopolyspora spinosa* which introduced in 1997. The resistance of some pests to this biopesticide has been reported [264]. Similarly, abamectin is a macrocyclic lactone compound produced by *Streptomyces avermitilis*, which resistance has also developed to it in some pests [265].

In recent years, the use of Essential Oils (EOs) derived from aromatic plants has increased to control urban pests. These phytochemicals have repellent, insecticidal, and growth-reducing effects on various species of insects. According to literature, EOs is extracted from different parts of four plant families including Myrtaceae, Lauraceae, Lamiaceae, and Asteraceae [266].

Resistance can be delayed by strategies such as responsive alternation, mosaic, periodic application, and combinations. Other strategies such as cultural and biological control and also environment improvement techniques should also be considered in resistance management programs Education of the residents should be an important component of an IPM program. It was reported that educational programs had a positive impact on residents' attitudes [252].

CONCLUSIONS:

The extensive application of insecticides and increasing the pesticide resistance species cause

high economic costs and threaten human health. Then the evaluation of resistance to different classes of insecticides in urban pests as well as understanding the mechanism of resistance in these arthropods are necessary to apply the best strategy in IPM programs to control them in urban ecosystems. In this regard, recognizing the biology and ecology of pests is an important issue.

Environment improvement programs to make an undesirable condition for growing arthropods had a reduction effect on the pest population. As well as alternative technologies such as genetic and biological approaches have the potential to control the pest abundance in urban ecosystems. The application of any technology to control the pest to improve human health should not have adverse effects on the environment.

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