



Insect Resistance to Insecticides and Approaches to Its Identification

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ABSTRACT

Pesticide resistance has become one of the pressing problems of ecology and agriculture because it makes it difficult to deal with pests and ectoparasites while increasing the chemical load on the environment. This paper focuses on the importance of studying insecticidal resistance in agricultural, veterinary, and medical insects. Brief information is given concerning the resistance of ectoparasites and crop insect pests in different world regions to commonly used insecticides. The main approaches for identifying insecticide resistance in field insect populations are listed. The progress achieved in understanding the molecular basis of insecticidal resistance in insects is briefly described, and the primary areas of recent research are outlined. The importance of assessing the resistance profile and the potential for insecticide resistance developing in field insect populations are emphasized. The study of molecular mechanisms of insecticidal resistance to specific compounds is important for searching for new active agents and developing strategies for their application.

Keywords: Pests, Insecticide, Resistance profile, Resistance diagnostic, Molecular mechanism.

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INTRODUCTION

Historically, the use of chemicals has been practiced as the primary method of insect pests and ectoparasites control [1, 2], and by far, the use of pesticides remains the most common way to control their population [3-5]. The use of pesticides in agriculture has increased over the past few decades with the continuous growth of global food production [6, 7]. Food and Agricultural Organization data show that in 2019 the consumption of pesticides reached 4.2 million tons, with insecticides being the third most used (17%) after herbicides (53%), fungicides, and bactericides (23%) [7]. According to BusinesStat estimates, pesticide production in Russia has increased by 1.7 times between 2017 and 2021: from 86.8 thousand tons to 148.9 thousand tons, while the share of insecticides by 2021 amounted to 12.5% [8].

The use of insecticides in agriculture is essential to enhance crop yields [2, 7]. However, the intensive use of insecticides, the long-term use of the same agents, the increase in the applied doses and frequency of treatments, and the rapid life cycle of pests result in a high potential for pesticide resistance selection in insects and mites [9]. Pesticide resistance has become one of the pressing problems of ecology and agriculture [10] because it makes it difficult to deal with pests and ectoparasites while increasing the chemical load on the environment [11]. A great number of researches are devoted to studying insecticide resistance and the degree of its prevalence in insect populations, revealing the mechanisms and patterns of its formation. The relevance of this topic is evidenced by the increase in the number of publications indexed in the Scopus database, which for the last ten years (between 2011 and 2021) has almost doubled

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(from 616 to 1302) and remains consistently high over the past five years. Currently, there are more than 330 known insecticides, resistance to which has been recorded in one or more arthropod species [12]. Bass *et al.* (2015) collected and analyzed data on resistance to neonicotinoids and its formation mechanisms in pest populations (Cotton whitefly *Bemisia tabaci*, green peach aphid *Myzus persicae*, cotton aphid *Aphis gossypii*, brown planthopper *Nilaparvata lugens*, Colorado beetle *Leptinotarsa decemlineata*, etc.) that bear serious economic importance [13]. The variation of insecticide resistance in populations of diamondback moth *Plutella xylostella* (Linnaeus), a cruciferous pest inhabiting different geographical regions of the world, to OPCs, pyrethroids, and biopesticides have been described [14, 15]. High resistance levels to OPCs and growth regulators and the formation of tolerance to neonicotinoids have been detected between 2019 and 2020 in China in populations of the white-backed planthopper, the rice pest, *Sogatella furcifera* [16]. Van den Berg *et al.* (2022) illustrated the potential for insecticide resistance development in African countries' cotton, corn, vigna, and tomato pests [17]. The research conducted by Russian scientists also indicates the presence of resistant populations of insects inside the country. For instance, the constant growth of the multiple resistance of the Colorado beetle, a major potato pest, to chemical insecticides (OPCs, pyrethroids, neonicotinoids) was previously reported in the North Caucasian, Central, and North-Western regions [18], in the Republic of Bashkortostan and Novosibirsk Region [19, 20]. The researchers observed the development of resistance to insecticides of the same classes in the populations of green peach aphids *Myzus persicae* (Sulz.) in the Astrakhan Region, as well as the development of resistance to Thiamethoxam agents in foxglove aphids *Aulacorthum solani* (Kalt.) in Leningrad Region and wireworms *Agriotes* spp. in Pskov Region [18].

The problem of insecticide resistance is relevant not only in plant protection but also in medicine and animal health [21-26]. Studies demonstrate that resistance, including cross-resistance, is widespread in various countries in medically important mosquito populations. For example, in Iran, between 2000 and 2020, the populations of

mosquitoes of the *Anopheles*, *Culex*, *Aedes*, and *Culiseta* genera with multiple resistance to four groups of insecticides (COCs, OPCs, pyrethroids, and carbamates) were reported [27]. In South Asian countries during the same interval, an increase in the spread of resistance to these compounds in the populations of *Aedes* mosquitoes was identified, which are the vectors of such viral diseases as Dengue fever, Zika fever, yellow fever, etc. [28, 29]. Resistance to pyrethroids, neonicotinoids, and fipronil has been described in populations of the bed bug *Cimex lectularius* L. [24]. Juache-Villagrana *et al.* (2022) examined the effect of insecticidal resistance in insect vectors of arthropod-borne infections on their vector competence [30]. Tolerance to the pyrethroid deltamethrin was found in red louse *Bovicola bovis*, collected on livestock farms in Ireland [31]. Medical and veterinary organizations worldwide face the problem of insecticide resistance in the population of the housefly *Musca domestica* L. [32]. Thus far, the resistance of *M. domestica* to insecticides of widely used classes of chemical compounds has been described. For example, in North and South America, Africa, and Asia, insect populations resistant to organophosphorus (OPCs) and carbamate insecticides were recorded [33, 34]. Researchers from various countries have reported populations of pyrethroid- and neonicotinoid-resistant flies inhabiting livestock and poultry farms [35-37]. In Russian housefly populations, the resistance to COCs, OPCs, carbamates, pyrethroids, and neonicotinoids was also reported [32].

Many researchers in their works emphasize the need for timely diagnosis of insecticide resistance, more thorough monitoring of its spread in insect populations and resistance management through the use of strategies [11, 17, 20, 24, 38]. According to the World Health Organization, only 38% of the surveyed countries in the European region consider insecticide susceptibility levels when choosing insecticides for insect vector population control, while in the Asia-Pacific, African, and South American regions, the percentage of countries using this indicator amounts to 80-92% [39]. Meanwhile, the information about the resistance profile of insect populations can not only allow for easier and less costly pest and parasite control but also help to reduce the chemical and environmental

load.

To successfully prevent and combat insecticide resistance in parasitic and pest insects, it is necessary to possess data on the resistance profile of natural populations. Toxicological and molecular-genetic methods are used to establish this profile. Toxicological methods involve biotesting to assess the insecticide's toxicity for the studied population's insects, the results of which establish the resistance ratio (RR) and the proportion of specimens susceptible to the insecticide at a diagnostic concentration (dose). The resistance ratio is calculated by dividing the median lethal concentration (LC₅₀) value of the insecticide for the studied insect population by the LC₅₀ value for the susceptible strain of that species. World Health Organization recommends the use of diagnostic (discriminatory) concentrations or doses of the insecticide to quickly establish resistance. The dose or concentration is considered diagnostic when it is equal to two doses or concentrations, which cause 95% (99%) mortality in a susceptible insect population of a given species [26]. Experts calculate diagnostic concentrations (doses) of a particular insecticide for each insect species. An insect population is considered sensitive (or susceptible) to an insecticide if 98-100% mortality is achieved using a diagnostic concentration and is considered resistant (tolerant) to an insecticide if less than 90% mortality is achieved [26]. The methods for assessing the toxicity of an insecticide correspond to the way they are used and the biological characteristics of certain species or groups of insects. WHO experts have developed methods for detecting insecticide resistance in populations of insect vectors of vector-borne diseases and other synanthropic insects [<https://apps.who.int/iris/>]. A thorough description of methods for testing populations of plant pests and some other arthropods can be found on the website of the Insecticide Resistance Action Committee [<https://irac-online.org/>].

According to the diagnostic procedure described in the WHO guidelines, it is necessary not only to establish the presence of a resistant phenotype in an insect population but also to characterize the intensity of resistance and the underlying mechanism [26]. Biochemical and molecular methods are used to establish the mechanism

that provides resistance to insecticides in a particular population. In this case, the detoxification enzyme systems [40, 41], molecular targets of insecticides [3, 42], as well as the presence and prevalence of alleles associated with insecticide resistance [43, 44] are studied. Nowadays, progress has been made in understanding the mechanisms of resistance to commonly used insecticides: pyrethroids, OPCs, neonicotinoids, spinosyns, pyrazoles, etc. Five alleles responsible for target insensitivity and hence pyrethroid resistance in insects have been described in the scientific literature: *kdr*-his (L1014H), *kdr* (L1014F), *super-kdr* (M929I+L1014F), Type N (D600N+M918T+L1014F) и 1B (T929I+L1014F) [44]. For still commonly used OPCs, Gly137Asp and Trp251Leu/Ser mutations in carboxylesterase genes are reported, which lead to changes in the structure of the enzyme active center, resulting in increased hydrolytic activity towards OPCs [45]. Carboxylesterases of the cotton bollworm *Helicoverpa armigera* Hbn. are involved in the resistance to organophosphorus and pyrethroid insecticides through enhanced sequestration due to gene overexpression [46]. The review by Feyereisen *et al.* (2015) is devoted to the analysis of mutations affecting acetylcholinesterase genes found in different insect species, which cause resistance to OPCs [47]. As for the relatively new insecticides, such as chlorfenapyr and chlorantraniliprole, the exact mechanism of resistance development is not fully established. A possible mechanism of resistance development to chlorfenapyr has been described for the spider mite [48] and boll weevil [49]. It is associated with an increase in esterase and glutathione-S-transferase activity, as well as with a decrease in cuticle permeability.

Meanwhile, the study on resistant cabbage moth populations concluded that the enzymes mentioned above are not involved in forming a resistance to chlorfenapyr [50]. When studying insect resistance to insecticides, a lot of attention is paid to epigenetic effects, the interaction of resistance-related genes, and the regulatory factors triggering their expression [38]. Identifying specific genetic mutations associated with resistance to certain insecticides may be useful for developing molecular diagnostic methods for insecticide resistance [38]. In addition, the study of molecular mechanisms of

insecticidal resistance to specific compounds and the potential for its formation in field insect populations is important for the search for new active agents and the development of new pesticide formulations and strategies for their application.

CONCLUSION

The examples presented in this review show that insecticidal resistance in insects is one of the urgent issues of ecology and agriculture. The toxicological and molecular studies of the resistance profile of insect populations can help develop a more appropriate strategy for resistance management and thereby reduce the chemical load on the environment.

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