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Novel Insecticides and Resistance Challenges

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ABSTRACT

Insecticides remain indispensable tools in global agriculture and vector control; however, resistance evolution among pest species poses a major threat to their long-term efficacy. This paper examines the dynamics of insecticide resistance and emerging strategies to mitigate it, focusing on rotation of insecticides, resistant crop varieties, regulatory oversight, and innovative formulations. Insecticide rotation alternating compounds with different modes of action has proven effective in delaying resistance onset in pests such as Diaphorina citri and Plutella xylostella. Similarly, the use of genetically resistant crop varieties provides sustainable pest suppression through mechanisms like antibiosis and tolerance. Regulatory and safety frameworks govern the approval and deployment of novel insecticides, ensuring risk assessment, toxicological review, and environmental safety. Recent advancements include the development of biologically derived insecticides, micro- and nano-formulations, and targeted delivery systems that minimize non-target exposure while maintaining field efficacy. Nevertheless, economic, environmental, and public health risks necessitate rigorous evaluation before widespread adoption. Public perception, education, and stakeholder engagement play decisive roles in the acceptance and success of new insecticidal technologies. Awareness campaigns and participatory frameworks enhance understanding and encourage responsible usage. Globally, regulatory differences across regions including restrictions on neonicotinoids in the European Union and tolerance-based policies in the United States reflect varying priorities in balancing productivity with ecological safety. Future directions emphasize integrated pest management (IPM), improved formulation design, advanced risk modeling, and multi-sectoral cooperation. A global shift toward innovation, sustainability, and informed regulation is essential to mitigate resistance, preserve ecosystem integrity, and ensure the continued viability of insecticidal technologies for agriculture and public health.

Keywords: Insecticide Resistance Management (IRM), Novel Insecticides, Integrated Pest Management (IPM), Risk Assessment and Regulation and Stakeholder Engagement and Public Perception.

INTRODUCTION

Insecticides are chemical substances used to kill insects. Their application is an important branch of pest management and crop protection [2]. Attention is increasingly shifting to the development of novel insecticides, as well as the challenges posed by insecticide resistance [1]. Historically, pesticide development remains a global issue, demanding immediate solutions. Food production relies heavily on effective agrochemicals, a capacity threatened by widespread insecticide resistance [2, 3]. Insecticides exert their effects on target organisms via two principal physiological routes: those targeting the insect nervous system and those affecting other metabolic pathways 1. Resistance to pesticides is a natural phenomenon intrinsically linked to the genome of microorganisms and therefore considered unavoidable [6, 7]. Where development of novel compounds is hindered by resistance, other methods aimed at preserving or revitalizing the efficacy of existing compounds will become increasingly important [3].

Historical Overview of Insecticide Development

Insecticides comprise substances designed to kill or mitigate the severity of insect pests and parasites. Although the term was initially derived for pesticides targeting insects exclusively, it is now often extended to substances acting on other non-arthropod pests such as nematodes [1]. The development of insecticides has encompassed various strategies, culminating in an emphasis on novel compounds devised to manage resistance and environmental concerns [7]. Early pest management employed plant or animal extracts, followed by a succession of inorganic and industrial compounds [8]. The advent of synthetic organic pesticides marked a significant advance, with chlorinated hydrocarbons, organophosphates, carbamates, and pyrethroids gaining widespread use after World War II[8]. As resistance emerged, the focus shifted toward compounds with enhanced safety profiles and new mechanisms of action, including biopesticides, neonicotinoids, insect growth regulators, and RNA interference-based insecticides [7]. Numerous insecticides induce neurotoxic effects, altering the normal function of the insect nervous system and resulting in paralysis; others perturb crucial metabolic processes, impairing amino acid synthesis, molting, cuticle formation, and vitellogenesis[3]. The widespread deployment of insecticides has led to diverse genetic, physiological, and behavioural adaptations, bolstering the fitness of invasive and vector species under continued selection pressure and culminating in resistance [4]. Although the majority of compounds target agricultural pests, resistance has also proliferated in urban insect populations exposed to domestic-use insecticides and metals, raising salience for species that serve as vector reservoirs in close association with human habitation [5].

Types of Novel Insecticides

In the 21st century, insecticide development has evolved from organophosphates, carbamates, and pyrethroids to nicotinic and diamide insecticides, introducing new compounds with various modes of action for resistance management [1]. Novel insecticides include biopesticides, neonicotinoids, insect growth regulators, and RNA interference–based insecticides. Biopesticides comprise substances derived from naturally occurring materials such as plants, bacteria, and certain minerals [8]. Neonicotinoids, similar to nicotine, are nicotinic insecticides widely applied worldwide, predominantly in agriculture [3]. Insect growth regulators disrupt growth and reproduction processes, making them effective against both pyrethroid-resistant and susceptible strains. RNA interference, a biological process used by most eukaryotes to regulate gene expression, can be harnessed in RNA interference based insecticides [9].

Biopesticides

Biopesticides consist of several different types of natural pest control agents derived from living organisms, including bacteria, fungi, viruses, plants, and certain minerals[7]. Fungal biopesticides are formulated as wettable powders, dry powders, granules, or ultra-low-volume liquids [6]. The use of botanical insecticides, which are derived from plants, represents a significant form of pest management compared with synthetic insecticides[3]. Prior to the invention of synthetic insecticides, botanicals were the principal method of pest control. Several classes of water-soluble botanical chemicals have been identified worldwide, with at least 2500 exotic plant species known for possible insecticidal activity [7]. Early records of ethnobotanical insecticide use appeared in Pliny's Natural History, which stated that "If your neighbour's vines are being eaten by a caterpillar, it is the practice to take a handful of torn earth and seedlings and spread it above them to ward off the pest." Of the numerous natural macro-compounds mentioned in the literature (such as alkaloids and pyrethrum), approximately 200 have been investigated for insecticidal properties [6, 7].

Neonicotinoids

Neonicotinoids are a class of neuro-active insecticides chemically similar to nicotine [15]. They exhibit selective action on insects through interaction with the nicotinic acetylcholine receptor (nAChR). Since the early 1990s, when the first products imidacloprid and acetamiprid were launched on the market, neonicotinoids have been extensively used in agriculture and urban pest control [11]. By the end of 2010, seven molecules belonging to the neonicotinoids family had gained a worldwide market share of approximately 24 % in terms of production volume [5]. The peach-potato aphid, Myzus persicae, causes severe damage and transmits more than 100 different plant viruses. Over recent decades, the species has evolved resistance to insecticides including organophosphates, carbamates, and pyrethroids by developing gene amplification of a major detoxifying enzyme, a G119S biochemical resistance mutation in acetylcholinesterase (AChE), and a L925V target site mutation in the voltage-gated sodium channel [8]. Neonicotinoids, such as imidacloprid and clothianidin, are currently the main insecticides used for the control of M. persicae in many regions. Resistance to this molecule is emerging, with first cases reported in field populations from Europe, the USA, and Japan [2, 8]. The Colorado potato beetle, Leptinotarsa decemlineata, the brown planthopper, Nilaparvata lugens, and the tobacco whitefly, Bemisia tabaci, all display some resistance to neonicotinoids. The use of neonicotinoids for bed bug control has rapidly expanded since 2005 when other compounds such as pyrethroids, carbamates, and organophosphates lost their effectiveness [7]. High resistance ratios (>1000-fold) to neonicotinoids indicate that target site resistance or other mechanisms are involved. Investigation of nAChR sequences and evaluation of detoxification enzymes using synergists are recommended to assess the prevalence and importance of these mechanisms [2, 8].

Insect Growth Regulators

Insect growth regulators (IGRs) postpone insect development and suppress adult emergence by disrupting the synthesis or action of hormones that usually propel insects from larval stages to pupae or from pupae to adults. IGRs are also regarded as an alternative to pyrethroids, especially in locations of elevated long-lasting insecticide-treated bed net coverage [8, 10]. IGRs induce morphogenetic anomalies or mortality, usually dosage dependent, in immature stages and typically require 4 to 10 days to manifest effects, unlike rapid-acting larvicides. Due to their specific modes of action perturbing endocrine functions or chitin synthesis they exhibit heightened safety profiles toward non-target organisms and the environment [1, 9]. For instance, fenoxycarb mimics juvenile hormone activity and directly influences insect moulting and reproductive processes; low concentrations impede embryonic development, whereas elevated concentrations cause adults to retain larval characteristics and render them incapable of reproduction [1, 10].

RNA Interference-based Insecticides

RNAi (RNA interference)-based insecticides constitute a novel and environmentally friendly class of insect control agents designed for use in crop protection scenarios and reducing urban pest populations. No transgenic plants are required for their deployment [3, 25]. Upon ingestion, RNAi insecticides are metabolized into small interfering RNAs (siRNAs) that bind to complementary messenger RNAs, suppressing the translation or expression of essential genes and consequently causing developmental disruptions, growth inhibition, and mortality [24]. The high degree of sequence specificity ensures reduced toxicity to non-target organisms and enables incorporation into integrated pest-management programs without compromising biological control agents, pollinator populations, or other beneficial arthropods [13]. RNAi insecticides can be applied via sprays, trunk injections, or root drenches, and they are actively degraded by environmental nucleases [12]. The first transgenic crop containing an RNAi active ingredient was approved for control of corn rootworms, and various commercial RNAi products are becoming available for crop and urban insect-pest management worldwide [3, 11]. Insects can develop resistance to RNAi insecticides through multiple mechanisms. Gene mutations or polymorphisms may prevent double-stranded RNA (dsRNA) from matching target mRNA sequences, and impediments to cellular uptake of dsRNA further reduce sensitivity. Resistance observed in some populations is linked to decreased internalization of dsRNA and down-regulation of RNAi machinery genes. Variations in physiological and genetic background among the major pest species influence the effectiveness of RNAi products [11]. To mitigate resistance caused by target-gene mutations, different gene regions can be targeted; a strategy unique to RNA-based insecticides [12]. Designing specific dsRNAs is therefore crucial; bioinformatic analyses ensure minimal effects on beneficial and non-target organisms. Excessively high concentrations of dsRNA may also trigger non-specific immune responses or saturate the RNAi machinery, posing additional challenges. Association with nanoparticles or other formulations prolongs dsRNA persistence and efficacy, although the potential risks of such additives warrant careful consideration [13].

Mechanisms of Action

Insecticides react with their targets inside pest organisms; these targets are a broad range of molecules involved in essential metabolic processes [1, 13]. The vast majority of insecticides try to affect the behaviour of insects; the most target molecules are proteins of the central nervous system [4]. Insecticides may lead to the contraction or paralysis of muscles in the insect body, insecticide poisoning, and death. During their mechanism of action, insecticides can cause excitation of the brain and peripheral nervous system (metabolite of organophosphates, betacypermethrin, bifenthrin, neonicotinoids) or inhibition of nerve excitation (dieldrin, fipronil). Insecticides can also affect insect nerve channels, such as the metabotropic GABA receptors, in which the antagonists bifenthrin, lindane and dieldrin interact and the nicotinergic acetylcholine receptors (nAChRs) which can be ivermectin agonists [13]. These acute neurotoxic effects can block the nerve interaction leading to the death of the insect. The other important groups of insecticides block developmental stages of insects, such as insect growth regulators (IGRs)[13]. They can disturb molting, pupation or cuticle formation and lead to death. The last group of insecticides disturb protein synthesis, energy production, and other metabolic activities (fluazinam, dimethoate, heptenophos, phosphamidon)[15].

Neurotoxic Effects

Agricultural and urban pests threaten global food security and public health, raising annual control costs in the billions of dollars. In response, a variety of insecticides have been developed, including spinosyns, neonicotinoids, ryanoids, butenolides, METIs, and diamides[14]. Several of these novel classes are reaching wide-scale use, while others rapidly face resistance issues. Pesticides that act on insect nervous systems are valuable tools to protect crops and control insect vectors. Spiroindolines are a chemical class with such activity, representing a novel mode of action that makes them eligible for resistance management programmes[17]. Multiple lines of evidence in insects and nematodes reveal that these chemicals selectively target the vesicular acetylcholine transporter [14]. The vesicular acetylcholine transporter is essential for neuronal function and represents a new target site for insecticide development [31].

Metabolic Disruption

Insecticides can affect non-neuronal targets such as egg production, metabolism, or energy production. The neonicotinoids, for example, have an ovariotoxic effect which causes a reduction in the number and viability of eggs laid by insects [5]. The neonicotinoids appear to exert this metabolic effect by binding to an acetylcholine receptor on the ovary tissue [12]. Conventional insecticides, including the organophosphates, carbamate, and pyrethroids act by inhibiting key metabolic enzymes in insects [11]. The mode of action varies: for example, the organophosphate malathion is metabolised by carboxylesterases in the insect body, which create a compound that inhibits mitochondrial ATP production; propoxur inhibits insect acetylcholinesterase; deltamethrin binds to the voltage-gated sodium channel; and avermectin opens glutamate-gated chloride channels[13].

Resistance Mechanisms in Insects

Resistance challenges both natural and synthetic insecticides. Several physiological adaptations decrease the likelihood of toxic interactions between insecticides and their target sites, ultimately reducing insecticide efficacy and the overall toxicity of insecticides [15]. Insecticide-resistance mechanisms involve reduced penetration of the insecticide, enhanced efflux activities, metabolic detoxification, and modification of the target-site of the insecticide that lowers sensitivity [16]. Resistance mechanisms occur due to naturally existing genetic variations in the population, and those genetic variations endure selection pressure caused by frequent insecticide applications, and the resistant individuals survive and eventually leave more offspring Selecting for those variation results in a constant reduction of the susceptible gene pool and renders the insecticides ineffective[15, 16]. The continuous use and exposure of insecticide over time with repeated applications may result in the rapid development of insecticide resistance, especially if insecticide use is inappropriate or sublethal[15].

Genetic Adaptations

The evolution of insecticide-resistant insects provides a powerful model to study rapid acquisition of novel complex adaptations and evolutionary rescue from extinction [16]. Prior molecular analyses of major resistance mechanisms revealed three common routes: effective sequestration of insecticides via amplification and/or upregulation of carboxylesterases; rapid active degradation associated with structural changes in key enzymes, including modified cytochrome P450s and EPSP synthase; and target site insensitivity caused by mutations affecting insecticide-binding proteins such as acetylcholinesterase (AChE), gamma-aminobutyric acid (GABA) receptors, and voltage-gated sodium channels[13, 16]. Remarkably, multiple, geographically separate incidences of resistance within a species often depend on the same limited set of mutation hotspots, and the mutations can spread swiftly among populations[9, 20]. High-throughput genomic approaches presently extend the investigation to mechanisms of resistance that had previously appeared intractable, including resistance to a broad range of chemical insecticides and to toxins from the biopesticide bacterium Bacillus thuringiensis[3, 17].

Physiological Resistance

Resistance is the result of behavioral, physiological, and genetic adaptation by insects to reduce the harmful effects of a toxic agent [17]. Physiological mechanisms include biochemical changes (metabolic resistance), decreased cuticular penetration, enhanced excretion, and target-site changes [18]. Metabolic resistance occurs when the insect is able to detoxify the insecticide before it reaches the target site. Decreased cuticular penetration is a mechanism that slows the passage of insecticide through the insect's cuticle, allowing more time for metabolic detoxification [15]. Enhanced excretion increases the rate at which the insecticide is eliminated from the insect's body prior to reaching the target site entrance. Target-site resistance results from a structural modification to the insecticide's specific binding site, rendering it less sensitive or insensitive to the toxic compound [2, 6].

Behavioral Resistance

Behavioural resistance has received comparatively little attention yet can substantially reduce the effectiveness of insecticide applications [19]. Concerns increased rapidly after the introduction of novel and non-repellent compounds such as neonicotinoids and fipronil, both of which require pests to be exposed continuously to a lethal dose during the period of residual killing [14, 15]. Behavioural resistance poses a particularly serious threat to vector-borne disease control because it has the potential to render all non-repellent classes of insecticide effectively useless if tightly cross-resistance occurs as documented for Anopheles mosquitoes [20]. However, unlike physiological resistance, the underlying genetic and physiological basis for behavioural resistance remains unknown for any system and it also appears to be far less common than physiological resistance [7, 17].

Case Studies of Resistance Development

Innate resistance to novel insecticides, including imidacloprid and thiamethoxam, has evolved in populations of key urban pest species such as the bed bug and German cockroach [6, 19]. Although comparative resistance studies in agricultural pests highlight a rapid increase of tolerance towards novel compounds, resistance research into pest arthropods of human health and production facility environments remains sparse [24]. The continual introduction of novel compounds within these urban grain and floricultural systems, coupled with growing concerns regarding insecticide safety assessments, necessitates an improved understanding of resistance trends and the development of evidence-based management strategies [21].

Agricultural Pests

Insecticides are substances used to kill insect pests that damage agricultural crops and transmit human and animal diseases [11]. Various insecticides are available to control insect pests, including organochlorines, organophosphates, carbamates, synthetic pyrethroids, neonicotinoids, insect growth regulators (IGRs), botanical, Mycoinsecticides, and Microbial Pesticides [18]. Recently developed insecticides differ from traditional insecticides in biological activity, physico-chemical properties, mode of action, applications, and the target insect spectrum. Recent innovations include biopesticides, neonicotinoids, insect growth regulators, and RNA interference–based insecticides. Most novel insecticides exhibit neurotoxic activity, while some act via metabolic disruption [7]. Agricultural pests are insect species that feed on plants and reduce crop yields [9]. They are also vectors of many plant diseases. Approximately 20%–40% of global crop production is lost annually due to insect pests [10]. The most devastating agricultural pests worldwide belong to the Coleoptera, Hemiptera, Thysanoptera, Lepidoptera, and Diptera orders [4]. Resurgence and resistance to insecticides cause many pest outbreaks, including aphids, diamondback moth, whitefly, armyworms, and stored grain pests. Agricultural pests have evolved resistance against nearly all commercial pesticides, including novel and older insecticides, such as organophosphates, pyrethroids, neonicotinoids, IGRs, and biopesticides [18]. Therefore, it is imperative to understand the mechanisms involved in insecticide resistance [12].

Urban Pest Control

Urban pest control strategies encompass the management of insects, arachnids, annelids, gastropods, and scorpions that pose risks to human and animal health, as well as economic interests in urban environments [7, 29]. Besides safeguarding public health, these strategies protect natural ecosystems and preserve the structural integrity of urban infrastructures [3, 32]. Insecticides have become pivotal in mitigating the risks associated with pest infestations, especially as pests evolve to tolerate and resist traditional compounds [21]. Increasing the toxicity of conventional insecticides often results in detrimental effects on non-target species and escalates contamination concerns [5, 26]. Consequently, the focus has shifted towards developing novel insecticides that exhibit enhanced efficacy, reduced environmental impact, and diminished potential for resistance development. Urban pest management has also embraced biopesticides and ultraviolet light-based applications, with a burgeoning interest in plant extracts and semiochemicals as alternative control agents. These advancements signify a multidisciplinary effort to address the multifaceted challenges inherent in urban pest control [5].

Impact of Resistance on Pest Management

Insecticide resistance contributes to the largest direct annual economic losses to agriculture worldwide 22. Additional indirect costs include expenses for resistance monitoring and management, increased emphases on non-chemical tactics, and efforts to develop new control technologies. Resistance to insecticides can result in loss of key compounds from existing pest-management programs [7]. In addition, intensive reliance on a single insecticide increases risks of insect resistance[9]Resistance to insecticides results in the reduction of the utility of these products and cannot be managed effectively without an understanding of insecticide modes of action and resistance.In addition to economic costs, resistance raises environmental concerns, as resistance can lead to increased applications of insecticides, potential disturbance to ecosystems, and health risks to humans and other non-target organisms[8]. The ability of insects to develop resistance to new chemicals has led to an increasing use of insecticides worldwide, resulting in applications of over 1.5 million tonnes per year. Resistance is a global problem, and there are only limited options available under regulations aimed at reducing the adverse effects of insecticides on human health, non-target species, and the environment [31]. Many compounds are regulated to such an extent that the risk of resistance development cannot be monitored easily, and the tolerance of the pest population cannot be maintained effectively [16].

Economic Consequences

Insecticides are compounds designed to kill insect pests [10]. They have long been and continue to be indispensable in combating pests of agricultural and public health importance [13]. Over the past several decades, resistance development has forced farmers to rely on other insecticides to control pests, although many of the alternatives in use today are novel and, in many cases, have been marketed only within the last 20 years. Insecticides remain the fastest and most accessible method of pest control, with their more recent development, alongside improvements in the formulation and delivery of older chemistries, offering new options to farmers worldwide [12, 17]. These technological advances in insecticide science are examined before their relationship to resistance development is discussed. Insecticides are one of many tools available for pest management, and their utility, like that of other control options, is diminished when pests develop strategies to circumvent efficacy. Pest management failure, particularly the failure of insecticides, exacts an economic toll thereby threatening food security [16]. When an insecticide is unable to effectively control a pest population, more insecticide may be required to reduce pest bite damage and the quality and quantity losses caused by the higher numbers of pests;

alternatively, other, possibly more expensive, insecticides may be deployed[18]. Data from the United States House of Representatives (2007) highlight that the rise in pesticide costs coupled with the cost of managing pesticide resistance were considered to be major contributing factors to the $10 billion loss to the United States economy caused by insect, disease, weed and nematode infestations in soybean[19].

Environmental Implications

The widespread application of novel insecticides in agriculture and urban pest control has elicited concerns about potential environmental hazards [14]. Prompted by a looming global food shortage, emerging insecticides bind reversibly at nicotinic acetylcholine receptors in a manner distinct from typical nitrite insecticides, leading to elevated acetylcholine accumulation at synapses and subsequent insect paralysis in various resistant strains 23. Concerns focus on neonicotinoid insecticides such as carbamates, fenitrothion, phosphides, and pyrethroids. Under laboratory conditions, exposure to these chemicals, even at concentrations well below maximum residue limits, adversely affects beneficial insects and other nontarget species [24]. Similarly, residues of novel insecticides have been detected in cocoons, rendered unsafe for silk production and raising threats to public health [11]. The onset of resistance may diminish the efficacy of these new insecticides [2], rising fears of trophic disruption. Given that novel insecticides are synthesized using less toxic compounds, their adoption could alleviate some environmental disturbances associated with pest control in agricultural regions where food sustainability is critical [10].

Strategies to Combat Resistance

Combating insecticide resistance presents a fundamental hurdle in the application of novel compounds for commercial crop protection and human health [9]. If no insecticide resistance management strategy is implemented or if a strategy is implemented incorrectly, insecticide resistance can rapidly develop, substantially increasing regulatory approval and marketing costs [25]. Insecticide resistance management (IRM) 20 represents a set of practices designed to prevent or delay the development of insecticide resistance in pest populations. The principal goal of IRM is to lengthen the effective life of insecticide chemistries, to reduce product development and registration costs, and to increase the public acceptance and adoption of new products [18]. The basic components of IRM center on the integration of tactics that reduce pest populations to an economic or tolerable level that may be a combination of pest-resistant varieties, biological control, crop rotation, and applications of insecticides. An optimal ERM program includes the implementation of economic thresholds so chemical control is only implemented when necessary. IRM programs revolve around the proper use of insecticides that includes following label directions, the use of the highest label rate, the correct application equipment, and timing [28]. Most importantly, the program consists of the proper rotation of insecticide modes-of-action to delay the development of resistance. The repeated use of the same insecticide mode-of-action has been shown to ultimately result in insecticide resistance, and therefore its use is not recommended by any IRM program [25]. Rotations must alternate insecticide modes-of-action and mixtures are not recommended. When insecticide resistance is suspected, a comprehensive evaluation of the pest population and pest management program is necessary because there are other reasons that may result in reduced efficacy [17]. Factors such as applying the wrong insecticide, the use of an insufficient application rate, the incorrect application equipment, adverse weather conditions, poor spray coverage, using the insecticide at the wrong time, pest life stage that is not susceptible to the insecticide, or recolonization of a treated area that was effectively controlled may all be misdiagnosed as resistance [17]. A well-designed IRM program prolongs the effectiveness of insecticide chemistries, reduces pest-management costs, limits yield and commodity losses, decreases environmental pollution and off-target effects, reduces insecticide exposure to workers, increases the adoption of new insecticide products, increases the value of products to growers, reduces brand switching, and increases investor confidence[25].

Integrated Pest Management (IPM)

The first step in insecticide resistance management is to determine the risks posed by, and the extent of, insecticide resistance in targeted pest populations [5]. Resistance arises because of the strong selection pressure imposed by the intensive use of insecticides and is defined as any inherited change in the sensitivity of a pest population that reduces the efficacy of a pesticide [26]. In-response, modern pest-management programs often rely on resistance-management plans designed to delay the onset of resistance [20]. Before assuming resistance is the cause of control failure, misapplication of insecticides, weather conditions, timing of application, and re-colonization by the pest should be considered as factors [27]. An important element of insecticide resistance management (IRM) is to avoid or reduce use of insecticides to slow the development of resistance. Integrating other management tactics with insecticide applications reduces the amount of insecticide needed [6]. Regular scouting is necessary to make accurate and timely management decisions, with insecticide application preferably guided by economic thresholds, rather than a calendar schedule [26, 7]. If insecticides are applied, label instructions should be carefully followed, and the same population of pests should not be subjected repeatedly to insecticides with the same mode of action [25, 27]. A more holistic program now recognized as a key component of achieving sustainable agriculture worldwide is Integrated Pest Management (IPM) 26. Its adoption during the last 30 years in cropping systems for smallholders and resource-poor farmers from many parts of the world has increased substantially with numerous positive impacts [25, 33]. Yet IPM adoption remains low among the majority of farm households and there is little evidence that it has reduced overall pesticide use or eliminated negative externalities [32]. New invasive pests and diseases continue to emerge on a regular basis due to global trade and climate change. Effective IPM commonly involves deploying multiple, complementary methods of controlling weeds, pests, and diseases within a cropping system [30].

Rotation of Insecticides

Insecticide rotation represents a key tactic for managing insecticide resistance, involving alternate applications of insecticides with different modes of action [27]. Given the widespread emergence of resistance in pest species, insecticides from different classes and modes of action should be rotated to extend product efficacy and delay resistance onset [27]. This practice has proven effective for controlling P. xylostella on cruciferous vegetables in Australia, small aphids such as Myzus persicae under orchard crops in Israel, and Diaphorina citri in Florida citrus groves [27]. Adhering to resistance-management recommendations, some insecticide products suggest rotation strategies to maintain and enhance effectiveness. Resistance shifts in Florida's D. citri populations have been documented for several insecticides [11]. Rotation of modes of action within annual programs is a common resistance-management strategy, particularly for pests like D. citri that occur year-round and require multiple sprays [3, 9]. Three evaluated rotation models effectively prevented resistance development in D. citri. Resistance to dimethoate increased only after repeated applications in the no-rotation control; rotations with multiple modes of action showed no resistance decrease [7, 14]. Other studies indicate that rotations are superior to mixtures for managing resistance. Sequential application of the same mode of action is not recommended and has been linked to resistance development [6, 23]. Resistance to insecticides such as organophosphates can reach levels predictive of field failure. Although yield was not measured, no differences in D. citri numbers were observed among rotation treatments; larger-scale and multi-season studies are necessary [6, 18]. Insecticide rotation prevents or delays resistance onset, even over short periods, despite small plots where adult movement may dilute effects. More extensive evaluations are needed to assess efficacy across diverse populations and determine the duration of susceptibility restoration after resistance development [8, 19].

Use of Resistant Crop Varieties

Crop protection methods often target insects, using resistant plant varieties that exhibit antibiosis, antixenosis, or tolerance to pests and pathogens [32]. Plants with resistance to sap-sucking insects deter or suppress feeding activity [28]. Nonetheless, insect damage and outbreak intensities have surged in recent decades, adversely affecting productivity and causing economic losses. Since 1945, management of pyrethroid-resistance in Helicoverpa armigera and Plutella xylostella mainly relied on chemical options until the emergence of transgenic cotton in 1996[26]. The initial wave of resistance to pyrethroids developed before 2000, whereas resistance to Bacillus thuringiensis (Bt) insecticides also appeared around that time [27].

Regulatory and Safety Considerations

Insecticides form a critical component of integrated pest management programs [6]. Used increasingly in combined formulations, insecticides in the mid- and late twentieth century had longer residual activity and broader pest control spectra than did previous materials[4, 8]. The pace of discovery and development has slowed dramatically in recent years; emphasis therefore shifted to compounds of novel chemistry or biological origin. Novel insecticides include new chemical groups, insect-growth regulators, and naturally derived materials such as botanical oils, azadirachtin, and microbial control agents [9]. Registration of insecticides and other crop protection products involves an extensive review process. An application is first evaluated for completeness and is reviewed in the context of earlier submissions for a similar material. A new compound is subjected to a thorough toxicological review and residue assessment [9, 10]. Economic losses from insecticide resistance are estimated in the hundreds of millions of dollars each year in the United States alone [4]. Several types of resistance have been described that cover a range of genetic, physiological, or behavioural adaptations. Individual examples illustrate the frequent nature of resistance development in agricultural pests such as the Colorado potato beetle and diamondback moth as well as in urban pests such as German cockroach, cat flea, and bed bug. Resistance therefore remains a major concern in both traditional crop production and in growing sectors such as organic farming, where broad-spectrum insecticides commonly are not approved for use [5].

Approval Processes for New Insecticides

New insecticides are chemical or biological materials intended to kill or prevent insect attacks, with emphasis on novel insecticides and resistance problems briefly discussed. Rapid approval is desirable, but safety and environmental risks must be assessed. Appropriate risk analysis is becoming increasingly complex and costly. The method of application represents a critical factor, because it influences the risk of insecticide exposure to nontarget organisms and the economic feasibility of new pest control techniques. Resistance reflects the adjustments of an insect pest population to the effect of an insecticide. Physiological resistance results from a high frequency of genetically based physiological traits in the population that confer some degree of tolerance to the insecticide. Such resistance has been described after widespread or repeated use of many insecticides, with neonicotinoid resistance readily developing in both agricultural and urban pests. Resistance is a major factor controlling the success of pest management programs. The development of resistance in the diamondback moth Plutella xylostella to the original and novel insecticides points out the need for a continuing supply of new insecticides. The accelerating economic cost of the development of insecticide resistance emphasizes the need to develop alternative solutions or reduce resistance development by sustainable pesticide control strategies. If novel insecticides are relevant for controlling the destructive Cochliomyia hominivorax, neonicotinoids could become involved in the control.

Risk Assessment and Management

Novel insecticides require rigorous toxicity assessment to ensure safe and effective pest control, validated through dose–response experiments [15, 16]. Assessing chemical, biological, environmental, human health and ecological risks provides a comprehensive understanding of potential hazards [12, 10]. Deployment according to recommended "maximum doses" and "spray intervals" safeguards public health by minimizing over-application. Historically, insecticide registration programs utilised mammalian toxicity metrics such as the median lethal dose (LD50) and the no observable effect level (NOEL) to establish safety requirements. Combined with residue analyses, these parameters formed the basis of models estimating the environmental, human health, and pesticide exposure risks associated with registered insecticides [15, 17]. More recently, the conceptual framework for governing the development and deployment of novel insecticides incorporates steps such as research and development, safety evaluations, target product profiling, efficacy testing, designation of target pests, and risk management an approach that supports the creation of insecticides with reduced toxicities and environmental impacts. Reflecting these priorities, insecticide exposure risk assessments first consider the targeted pest species [3, 8]. Beyond establishing a target profile, potential environmental toxicity is also examined, followed by evaluation of non-target risks [7]. When in-use risks emerge, risk-management options must be identified; these include reduced application rates, shorter or longer spray intervals, or changes to insecticide formulations. Ensuring that the range of potential risks attributable to any insecticide is documented remains central to the design of risk-assessment and management approaches [5].

Future Directions in Insecticide Research

Future strategies for managing insecticide resistance focus on innovative formulations and targeted delivery systems, which concentrate insecticidal activity on the intended pests while minimizing environmental dispersion and exposure of beneficial organisms [6, 9]. Such approaches also aim to address the loss of activity from common formulation ingredients that can trigger physiological defenses in the insect. Protection-targeted formulations (PTFs) combine an insecticidal agent typically an acetylcholinesterase (AChE) inhibitor with a repellent or irritant ("protection") and a thickening agent ("Formulation") to deliver efficient field control[23, 26]. The protective compounds prevent insect contact irritation by acting as chemical barriers, enabling the insecticide to remain in place. Examples include liquid sprays, gels, liquid formulations for ultra-low volume (ULV) application, sprays-without-wash, and polymer-enhanced binary systems [29]. Pyrethroid sprays with fans, wraps, and rollers serve as prototypes for similar delivery systems [7, 18]. The ongoing challenges posed by insecticide resistance underscore the need to develop new compounds within existing classes boosted by complementary agents and, more importantly, to identify chemically novel insecticides with new modes of action for long-term sustainability[10, 15]. While initiatives such as those described by Hemingway (2014) focus on discovering new insecticides, the broader problem calls for a dual approach that balances innovation with practical management strategies[5, 7].

Innovative Formulations

Besides the active chemical agent in the spray preparation, other constituents of the formulation concern the user as well. For example, solvents and some spray adjuvants that form a major proportion of the mixture, present additional risk of hazard to humans and non-target organisms [25]. Both the public and spray operators dislike the products emitting strong odours and are averse to smelling them. The unpleasant, penetrating odour of many spray formulations, in particular organophosphates and carbamates, is indicative of active ingredient vapour and suggests that spray operators might be inhaling dosages exceeding the levels of exposure that cause adverse health effects[28]. Therefore, the organoleptic characteristics of a spray formulation are not simply cosmetic; they are related to the bioefficacy and safety of the product [25]. The evaluation, registration and sales appeal of insecticide formulations often depend more on the perceived advantages of the product using physical and operational criteria rather than the assessment of toxicological and ecotoxicological data. Market surveys show that cosmetic appearance and attractive packaging strongly influence buyers' choice [19]. It is not surprising that insecticide manufacturers have spent large amounts of time and money on research directed towards producing formulations with cosmetically desirable colours, odours and physical appearance, which have ready sales appeal and are likely to reduce incriminations by spray operators and the general public. Consequently, the area of formulation research is currently directed not only towards enhanced biological efficacy and tolerance but also towards increased user acceptability and marketability [18].

Targeted Delivery Systems

Improving delivery techniques also bears promise for more sustainable insecticide usage [17, 18]. Nebulisation, for example, enhances activity with reduced quantities; micro-encapsulation releases active ingredient in a sustained way, prolonging the effective period of establishments of the treatment; gel formulation increases persistence and provides the basis for long-term residual formulations; and nano-formulations yield similar advantages to gel formulations while allowing finer tailoring [17]. The precise regulation of dosage and consequent exposition of various entomological targets at different development stages potentially leads to the apparition of effective insecticide compounds with a reduced rate of resistance to deployment and a smaller environmental impact compared with conventional treatments [14].

Public Perception and Acceptance

Public perception and acceptance of novel insecticides are critical components of successful pest-management programs [30]. Awareness of the benefits and limitations of new insecticide classes can enhance acceptance and promote adoption by key stakeholders [30]. Effective communication strategies are therefore crucial to foster understanding and trust in novel compounds that can reduce selection pressure on resistance [17]. The importance of public attitudes towards emerging insecticides transcends technical and regulatory platforms, influencing governmental decision-making and policy formulation [27]. Comprehensive information on a new compound and its public perception exists in diverse language patterns. Extracting independent data and insights from such large-scale, qualitatively diverse text samples can be challenging [28]. A structured methodology is needed to process heterogeneous text and identify acceptance trends within expansive document collections [29].

Education and Awareness

Education and awareness are essential elements of integrated strategies to manage resistance and minimise excessive cycles of costly replacement with novel insecticides [23]. Over the last half-century, insecticides have become an absolute necessity in global pest management systems [4, 7]. Yet, while humans are reliant upon these powerful synthetic tools, humanity remains fearful of what their extensive, and often indiscriminate, use may have on the environment and individual health. The development of new insecticide classes is an ever-persistent global call to arms in filling the gap left by resistance to old classes [32]. Following the pyrethroids, carbamates and organophosphates, new classes have emerged in the shape of neonicotinoids and, more recently, spinosins and aryloxyphenoxy-propionates. However, the World Health Organization (WHO) specified that the introduction of genuinely new insecticidal modes of action had not been observed in public health for over 30 years, and there remain only a limited number of classes to use in the framework of resistance management strategies [33]. New modes of action, as witnessed with neonicotinoid insecticides, generally require a substantial burst of funding to develop, indicating the vast industrial challenge of this task; hence, it is conceivable that the drive will continue to develop new insecticidal formulations and delivery strategies to improve the efficacy of the existing chemistries, rather than focusing on the development of genuinely new classes [31]. In any event, insecticides will therefore continue to play a dominant role in pest management and, given current predictions, the development of resistance will accelerate and continue to be one of the defining characteristics of the next century [30]. Novel modes of action must be defined at the outset of the research and development process if the global call for novel classes, and thereby the future of the multi-billion-dollar insecticide sector, is to be sustained. In parallel, management strategies directed at limiting the development and further spread of resistance are a necessity [30]. Effective resistance management programmes in all sectors are an essential component in delaying the development of resistance to existing and novel insecticides, in order to minimise its impact on pest control. In addition, extending the effective life span of any newly developed insecticide will ensure not only that the existing commercial investment is maximised, but that the development of novel insecticidal classes can be maintained over the long-term in the absence of new financial models that are currently deemed to be necessary by the market[17]. Principles of resistance management can be applied on local, national or global scales, but their success will be dictated by the cooperation and organisation of all sectors engaged in the development and application of these integrated strategies; from the chemical companies, through to the producers and distributors, and ultimately to the end-users[19]. The construction of effective information networks that communicate the relevant scientific evidence to those responsible for the adoption of responsible pest control practices (and that disseminate the information to the wider farming community) is, therefore, essential if production continues to be maintained, and novel classes are to be discovered [26].

Engagement

The development and deployment of novel insecticides is a political, economic, and societal challenge to research scientists and governments [30]. Public acceptance of new insect control products is crucial as their success hinges on societal support [31]. Awareness therefore, of both public perceptions and stakeholder motivations, and concerns must be considered at an early stage of product development [32]. Early engagement allows open discussions that, in turn, enable the integration of societal needs and concerns into the development pathway to increase learnings on components of the technology that are viewed positively and those of concern [32]. This information then allows scientists to develop potential mitigation strategies around the obstacles, where possible.

Global Perspectives on Insecticide Use

Vector insects develop several resistance mechanisms, including single gene mutations that alter molecular target sites, enhanced metabolic detoxification through increased production or modification of detoxifying enzymes, reduced penetration rates of insecticides through the integument, and behavioural changes that limit insect contact with insecticides [8, 19]. Resistance development has major economic and environmental impacts, as it compromises control efforts using registered products with negative effects on productive activities and the vector ecology [33]. Developing effective resistance countermeasures is challenging, but integrated management programmes may assist in resistance control and slow its progression [12]. Important tactics include insecticide rotation, integrated pest management approaches that combine chemical and nonchemical alternatives, mosaic treatments, the use of mixtures or combinations of insecticides, and the development of resistant crop varieties with enhanced tolerance to insect pest damage [5]. Insecticide regulation and authorization also play key roles, since safety evaluation and risk assessment ensure oversight of active substances that require registration and approval before use[8]. Novel active ingredients continue to be developed and reinforce the insecticide toolbox [7, 14]. Alternatives include new formulations such as timed-release microcapsules or nanoformulations that allow controlled or targeted delivery, increasing efficacy while reducing environmental impact [11, 13]. However, public perception and user acceptance remain determinants in the successful adoption of novel insecticides. Increased awareness, education, and participatory initiatives involving stakeholders and end users in decision-making and policy design can facilitate the penetration and use of innovative materials [16, 26].

Comparative Analysis of Different Regions

Diverse regions and countries02in particular, South America, North America, Europe, India, Africa, and Canada02form a complex mosaic of insecticide use and regulatory frameworks[24]. The administrative and agronomic efficacy of insecticide residues varies considerably, with time-limited approval undergirding widespread concerns about contamination and water pollution. Current neonicotinoid regulations in the European Union, Switzerland, and some United States states have prohibited or constrained seed treated products on certain crops [30]. The United States Environmental Protection Agency enforces a leeway limit tolerance policy based on detection levels for untreated crops. Surveys of international seed trade reveal that untreated seeds commonly contain residues of immidacloprid, thiamethoxam, and clothianidin, creating second02hand exposure for treated crop production elsewhere [34].

International Regulations and Agreements

Insecticides kill insects or inhibit their development [20]. They are used widely in human health and crop protectionto protect foodstuffs for human consumption and to limit the spread of disease. Insecticides can be grouped by the timing of their usage from historic to contemporary [32]. Traditional insecticides, such as organochlorines and organophosphates, have been phased out in many countries. Novel insecticides, such as biopesticides, neonicotinoids, insect growth regulators, and RNA interference insecticides, have been developed and are progressively replacing traditional insecticides [5].The majority of novel insecticides also have neurotoxic effects [19]. A smaller number affect the metabolic processes of the target insect. This relatively narrow range of mechanisms of action makes the discovery of novel modes of action especially desirable [33].

CONCLUSION

The persistence of insecticide resistance represents a critical global challenge, undermining agricultural productivity, food security, and disease control. As resistance evolves across diverse pest species through genetic and physiological adaptations, it threatens the sustainability of conventional chemical control methods. Rotational use of insecticides with different modes of action, combined with the deployment of resistant crop varieties, provides a practical means to delay resistance and maintain control efficacy. However, such strategies must be underpinned by robust regulatory oversight, systematic risk assessments, and continuous innovation in formulation technology. Emerging advances, such as targeted delivery systems, nano- and micro-formulations, and biologically derived agents, offer promising alternatives that enhance precision, reduce toxicity, and minimize environmental contamination. Nonetheless, public perception, education, and stakeholder cooperation remain decisive for the acceptance and responsible use of these technologies. Effective resistance management depends on global coordination among researchers, policymakers, manufacturers, and end-users, supported by transparent communication and participatory governance. The future of insecticide use will rely on harmonizing innovation with ecological stewardship and regulatory accountability. International collaboration, data-driven risk evaluation, and inclusive engagement will ensure that new insecticidal tools not only preserve their efficacy but also promote long-term environmental and human health. Thus, sustainable pest management in the twenty-first century must transcend chemical dependence, integrating science, society, and policy to achieve resilient and responsible control of pest populations worldwide.

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