

## Review Article

# Biomimetic and Synthetic Advances in Natural Pesticides: Balancing Efficiency and Environmental Safety

**Mohammad Harun-Ur-Rashid**  <sup>1</sup> and **Abu Bin Imran**  <sup>2</sup>

<sup>1</sup>Department of Chemistry, International University of Business Agriculture and Technology, Dhaka, Bangladesh

<sup>2</sup>Department of Chemistry, Bangladesh University of Engineering and Technology, Dhaka, Bangladesh

Correspondence should be addressed to Abu Bin Imran; abimran@chem.buet.ac.bd

Received 4 February 2025; Accepted 10 June 2025

Academic Editor: Mahmood Ahmed

Copyright © 2025 Mohammad Harun-Ur-Rashid and Abu Bin Imran. *Journal of Chemistry* published by John Wiley & Sons Ltd. This is an open access article under the terms of the Creative Commons Attribution License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited.

Biomimetic and synthetic advancements in natural pesticides are driving a transformative shift toward sustainable pest management, promoting agricultural productivity while preserving ecological balance. These innovative approaches are inspired by nature's defense mechanisms, integrating cutting-edge science to develop precise, effective, and environmentally safe alternatives to traditional chemical pesticides. The review explores the evolution of natural pesticides, historical milestones, biomimicry principles, and the synergies achieved through hybrid formulations that combine natural and synthetic elements. Key findings highlight the exceptional specificity of biomimetic pesticides, such as azadirachtin from neem and pyrethrins from chrysanthemum, which disrupt pest physiological pathways while minimizing harm to nontarget organisms. Advances in green chemistry and nanotechnology have further enhanced these compounds' stability, efficacy, and scalability, addressing challenges related to environmental degradation and cost-efficiency. Synthetic analogs, designed to mimic natural bioactives, complement biomimetic solutions by offering extended durability and broad-spectrum activity, thus bridging field performance and scalability gaps. The review also emphasizes the critical role of interdisciplinary research, policy support, and technological innovation in overcoming barriers to adoption, such as regulatory complexities, pest resistance, and economic accessibility. By harmonizing efficacy with sustainability, these advancements pave the way for next-generation agricultural practices that ensure food security while preserving biodiversity and soil health. This synthesis provides a comprehensive roadmap for researchers, policymakers, and industry stakeholders aiming to redefine the future of eco-friendly pest control.

**Keywords:** biomimetic pesticides; green chemistry; integrated pest management (IPM); nanotechnology in agriculture; sustainable pest management; synthetic pesticides

## 1. Introduction

Natural pesticides have long been recognized as a cornerstone of sustainable agriculture, drawing from nature's defenses to manage pests without the unintended consequences often associated with synthetic chemical pesticides [1–3]. Unlike their synthetic counterparts, natural pesticides are generally biodegradable and exhibit lower risks of environmental contamination [4, 5]. For instance, the neem tree (*Azadirachta indica*) produces compounds that deter various pests while being relatively safe for nontarget organisms, showcasing the potential of plant-derived solutions to revolutionize pest management [6].

However, the broader adoption of natural pesticides remains limited by challenges such as inconsistent efficacy, scalability, and economic viability [7]. With increasing societal demand for environmentally friendly farming practices and stricter regulatory frameworks surrounding synthetic pesticide usage, the role of natural pesticides has become more pivotal than ever. As global agricultural systems face growing pressures from climate change, biodiversity loss, and the need for higher productivity, natural pesticides offer an opportunity to harmonize agricultural innovation with ecological sustainability [8, 9].

Despite their promise, natural pesticides are not without challenges. A primary hurdle lies in their variable effectiveness

under diverse environmental conditions. Factors such as temperature, humidity, and ultraviolet exposure can degrade natural compounds, diminishing their efficacy [10–12]. For instance, pyrethrins, derived from chrysanthemum flowers, are highly effective in pest control but degrade rapidly when exposed to sunlight, limiting their application in open-field conditions [13–15]. Additionally, extracting bioactive compounds at scale often demands significant resources, making cost-competitiveness a persistent concern. Another key challenge is the narrow spectrum of activity exhibited by many natural pesticides, necessitating the development of formulations or blends to target a broader range of pests [16]. Furthermore, the lack of rigorous quality standards and regulatory inconsistencies across regions complicate their global adoption. Bridging these gaps requires a multidisciplinary approach that integrates advances in biomimicry, synthetic biology, and green chemistry to enhance the performance and accessibility of natural pesticides while reducing their ecological footprint [17].

This review aims to comprehensively analyze recent advancements in biomimetic and synthetic approaches to natural pesticide development, focusing on bridging the gap between efficacy and sustainability. By examining the underlying principles, innovative technologies, and practical applications, this article seeks to:

- Highlight the scientific principles driving biomimetic pesticide innovation.
- Explore state-of-the-art synthetic methods inspired by natural compounds.
- Compare the environmental, economic, and societal impacts of biomimetic and synthetic approaches.
- Identify key knowledge gaps and propose future research directions to accelerate the adoption of natural pesticides in sustainable agriculture.

The overarching goal is to offer actionable insights for researchers, policymakers, and industry stakeholders striving to develop next-generation pesticides that meet the dual objectives of high efficacy and ecological stewardship. It begins with historical perspectives on traditional uses and the evolution of these technologies, followed by analyses of biomimetic advances and synthetic techniques to enhance efficacy. A comparative evaluation of biomimetic and synthetic approaches focuses on performance, sustainability, and economic viability. Strategies to overcome limitations and align innovations with global sustainability goals are discussed alongside real-world examples and field studies. Emerging trends and interdisciplinary collaborations are highlighted, ensuring a balanced discussion with theoretical insights and practical recommendations to advance the field.

## 2. Historical Perspectives on Natural Pesticides

**2.1. Early Uses of Natural Pesticides in Agriculture.** The use of natural pesticides in agriculture can be traced back to ancient civilizations, where farmers relied on nature's resources to protect their crops. Ancient Egyptians utilized garlic and onion extracts as insect repellents, demonstrating an intuitive

understanding of plant-derived bioactive compounds. In China, chrysanthemum flowers rich in pyrethrins were employed to combat crop-damaging pests, an approach that remains relevant in modern pest control practices [3]. These early techniques were innovative for their time and showcased humanity's ability to harness nature for sustainable agricultural practices, even without scientific knowledge.

**2.2. Transition From Natural to Synthetic Pesticides.** As agricultural demands intensified during the Industrial Revolution, the limitations of natural pesticides became apparent. Extracting bioactive compounds was labor-intensive, and variability in efficacy posed challenges for large-scale applications. This led to the advent of synthetic pesticides, such as dichlorodiphenyltrichloroethane (DDT), which improved pest management. During World War II, DDT offered unprecedented efficiency, uniformity, and scalability compared to natural alternatives [18]. However, this transition marked a key moment in agriculture, where pursuing higher yields began to outweigh ecological considerations.

The widespread use of synthetic pesticides came with consequences. Issues such as bioaccumulation in the food chain, environmental contamination, and pest resistance emerged as significant challenges. Public awareness of these risks gained momentum following the publication of Rachel Carson's *Silent Spring*, highlighting the environmental damage caused by synthetic pesticides and spurred regulatory changes [19]. Despite their transformative impact on agriculture, synthetic pesticides underscored the need for a balance between productivity and sustainability.

**2.3. Limitations of Traditional Approaches.** While natural pesticides are environmentally friendly, they face several inherent limitations. Their reliance on environmental stability means external factors like temperature, humidity, and UV exposure can degrade their efficacy. For instance, neem-based pesticides have shown great potential in controlled conditions but often fail to perform consistently in the field [20]. Additionally, natural pesticides exhibit narrow-spectrum activity, necessitating combinations to target multiple pests. These limitations made them less practical for large-scale use, particularly in industrial agriculture.

Despite addressing scalability and efficacy issues, synthetic pesticides introduced their own set of problems. Overuse and improper application led to developing pesticide-resistant pests and ecological imbalances. Furthermore, synthetic pesticides frequently harmed nontarget species, contributing to biodiversity loss. These challenges emphasized the need for innovative approaches that could combine natural pesticides' ecological benefits with synthetic solutions' stability and effectiveness.

**2.4. Historical Milestones in Natural Pesticides Development.** The timeline traces the evolution of natural pesticides, beginning in the 1900s when farmers relied on traditional plant-based remedies for pest control, reflecting centuries of knowledge passed down through generations [21]. By the

1920s, scientific advancements led to the isolation of pyrethrins from chrysanthemum flowers, marking the first step in understanding the potential of natural bioactives for targeted pest control. In the 1940s, the development of synthetic pesticides like DDT marked a transformative shift, offering scalable and effective solutions while diverting attention from natural pest control methods [22]. In the 1960s, Rachel Carson's *Silent Spring* highlighted the ecological risks of synthetic pesticides, prompting renewed interest in safer alternatives [19]. The 1970s marked a significant moment with the global recognition of neem as an eco-friendly and sustainable pesticide. In the 1980s, integrated pest management (IPM) emerged, emphasizing a balanced use of synthetic and natural methods to reduce environmental impact [23]. The 1990s brought advances in biotechnology, with genetically engineered crops like those producing *Bacillus thuringiensis* (Bt) toxins demonstrating the integration of bioengineering in pest management [24]. The 2000s saw global policies restricting harmful synthetic pesticides, driving innovation in biopesticides and natural alternatives aligned with sustainability goals [25]. During the 2010s, biomimetic approaches gained prominence, with scientists designing nature-inspired solutions to enhance the stability and efficacy of natural pesticides. By the 2020s, technologies such as nanotechnology and advanced formulations optimized natural pesticides, establishing their role in sustainable agriculture and IPM systems. Figure 1 illustrates the evolution of natural pesticides, a historical journey from traditional practices to cutting-edge sustainable solutions in agricultural pest management.

### 3. Biomimetic Advances in Natural Pesticides

**3.1. Principles of Biomimicry in Pesticide Design.** Biomimicry in pesticide design harnesses mechanisms evolved in nature to develop precise, sustainable, and ecologically aligned pest control strategies. A prominent example is azadirachtin, a bioactive compound derived from the neem tree (*Azadirachta indica*), which disrupts insect growth and reproduction by interfering with hormonal regulation. Similarly, pyrethrins, extracted from chrysanthemum flowers (*Chrysanthemum cinerariifolium*), target the insect nervous system, causing paralysis and death with minimal impact on mammals and beneficial species [26]. These examples reflect how biomimetic pesticides achieve high specificity, reducing collateral damage to nontarget organisms. In addition to biochemical mimicry, recent advances also explore structural inspirations from nature. For instance, the micro- and nanoscale architecture of insect cuticles has inspired the design of interface materials that enhance pesticide adhesion and controlled delivery, improving efficacy while minimizing runoff and environmental exposure [27].

Biomimetic pesticide designs also prioritize biodegradability, ensuring active agents break down naturally in the environment, thereby reducing ecological disruption and chemical persistence [28]. Integrating computational biology and artificial intelligence (AI) further accelerates this process. These tools enable modeling natural compound

interactions with pest targets, facilitating the design of synthetic analogs that replicate natural efficacy with improved stability or delivery properties [29]. Biomimicry offers a holistic framework for pesticide development that draws from biochemical, structural, and ecological cues in nature. It fosters innovation that is precise, adaptive, and sustainable. Figure 2 illustrates the cycle of biomimetic pesticide development in a holistic process inspired by nature that emphasizes the development of natural compounds, ensures specificity, achieves sustainability, leverages AI tools, and addresses agricultural challenges.

#### 3.2. Case Studies of Biomimetic Natural Pesticides

**3.2.1. Neem-Based Pesticides.** The neem tree (*Azadirachta indica*), often called "nature's pharmacy," is a cornerstone of biomimetic pesticide development. Neem produces azadirachtin, a bioactive compound with multiple insecticidal properties, including acting as an antifeedant, growth inhibitor, and reproductive suppressant. Neem-based products are widely regarded for their biodegradability and minimal toxicity to beneficial species, making them a vital component of IPM systems [30]. However, due to environmental factors, their efficacy can be hindered by rapid degradation under UV light and variability in active compound concentrations. Advances in nanoformulation technologies are addressing these challenges, improving the stability and performance of neem-based pesticides.

Kamaraj et al. emphasized the potential of neem-based nanoformulations, particularly neem gum nano formulation (NGNF), as an innovative solution for environmentally friendly pest control [31]. The NGNF demonstrated significant antifeedant, larvicidal, and pupicidal activities against key agricultural pests such as *Helicoverpa armigera* and *Spodoptera litura*. Its effectiveness was attributed to its ability to disrupt larval development and enzyme activities critical for pest survival. This formulation also showed minimal toxicity to earthworms, highlighting its eco-friendly attributes, unlike traditional chemical pesticides that often harm nontarget organisms and the environment.

**3.2.2. Pyrethroids Derived From Chrysanthemum.** Inspired by natural pyrethrins extracted from chrysanthemum flowers, pyrethroids represent another landmark achievement in biomimetic pesticide design [32]. Pyrethrins act on insect nervous systems, leading to paralysis and eventual death, while exhibiting low toxicity to mammals. Synthetic pyrethroids, modeled after natural pyrethrins, have enhanced stability and extended shelf life, overcoming the natural degradation challenges of pyrethrins. However, the overuse of synthetic pyrethroids has contributed to pest resistance, highlighting the need for responsible usage and further refinement of biomimetic strategies [33].

Nagar et al. demonstrated the effectiveness of various extraction and enrichment techniques for isolating pyrethrins, the active insecticidal compounds derived from *Chrysanthemum cinerariaefolium* [34]. They found that pyrethrins act by targeting the insect nervous system,

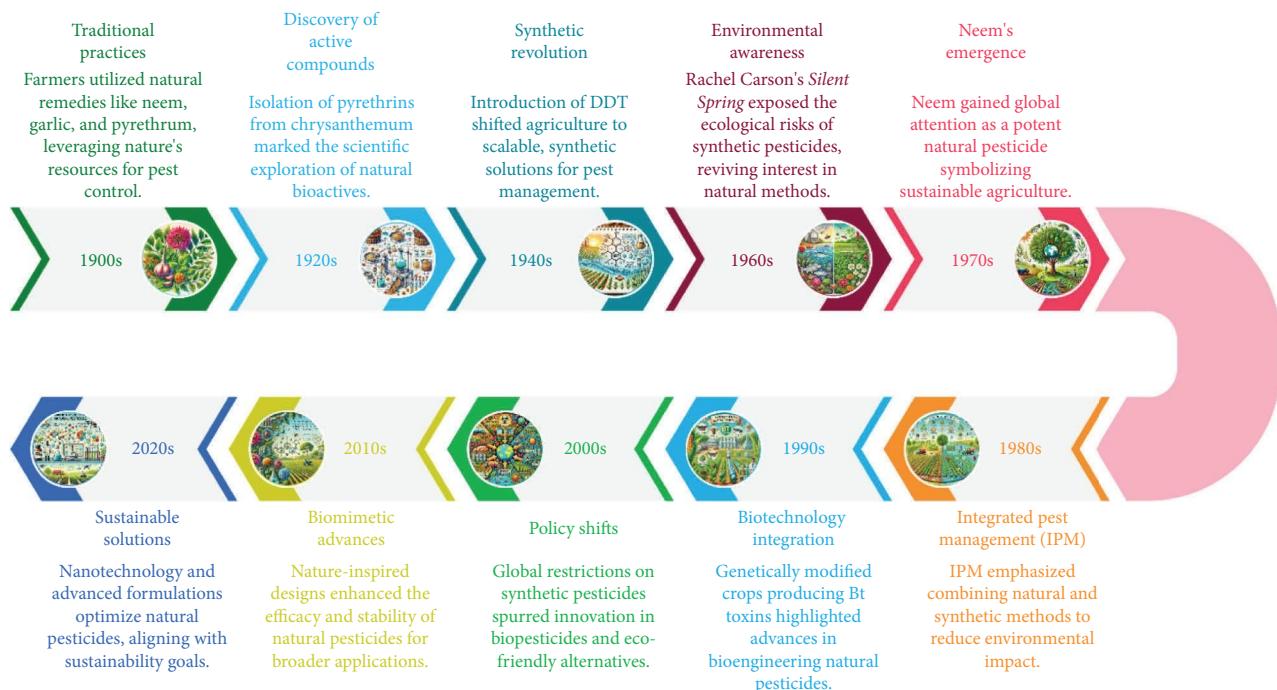


FIGURE 1: Timeline of historical milestones in natural pesticides development.

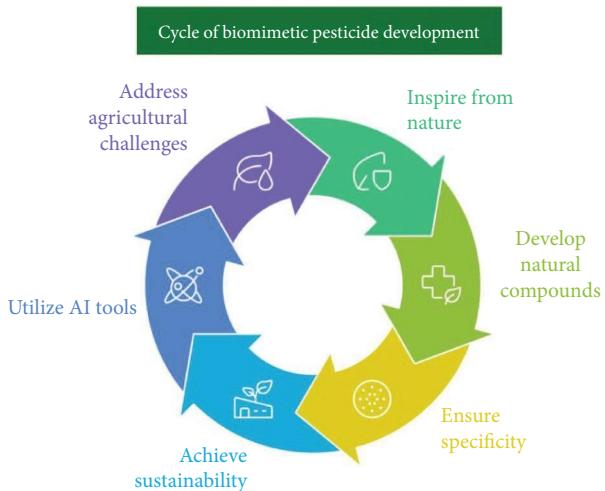


FIGURE 2: The cycle of biomimetic pesticide development.

causing rapid paralysis and eventual death, a mechanism that reflects their high specificity and low mammalian toxicity. Among the extraction methods tested, the Soxhlet technique using methanol provided the highest yield. At the same time, acetonitrile was the most effective solvent for enrichment, achieving pyrethrin concentrations of up to 60.37% through solid-matrix partitioning. Their study emphasized the environmental benefits of these natural compounds in organic farming and IPM systems. The insecticidal properties of pyrethrum extract arise from six compounds, all of which share a characteristic stereochemical configuration, as illustrated in Figure 3.

**3.3. Mechanisms of Action: Mimicking Nature's Strategies.** Biomimetic pesticides mimic nature's precision and efficacy in pest control. Azadirachtin, a tetraterpenoid compound extracted from the seeds and leaves of the neem tree (*Azadirachta indica*), is renowned for its multifaceted insecticidal properties [35]. It primarily disrupts the endocrine system of insects, mainly through interference with the production and activity of ecdysone, a hormone critical for molting and metamorphosis [36]. This disruption halts the growth and development of larvae, preventing them from reaching maturity. Azadirachtin also inhibits the synthesis of juvenile hormones, which are essential for maintaining normal insect development and reproductive processes. This dual interference in hormonal regulation prevents insects from progressing through their life cycle stages, effectively controlling their populations. In addition to its effects on hormonal pathways, azadirachtin acts as a potent anti-feedant, deterring insects from consuming treated plants. It achieves this by disrupting the neurosensory functions associated with feeding, leading to reduced nutrient intake and eventual starvation. Furthermore, azadirachtin has been shown to impair oviposition in female insects by disrupting egg-laying behavior and reducing the viability of laid eggs.

One of the most significant advantages of azadirachtin is its specificity; it selectively targets the physiological pathways of insect pests while leaving nontarget organisms such as pollinators, earthworms, and other beneficial species unharmed. This makes it an invaluable component in IPM systems [37]. Its natural origin and rapid biodegradability also minimize environmental persistence and reduce the risk of bioaccumulation, aligning with sustainability goals in

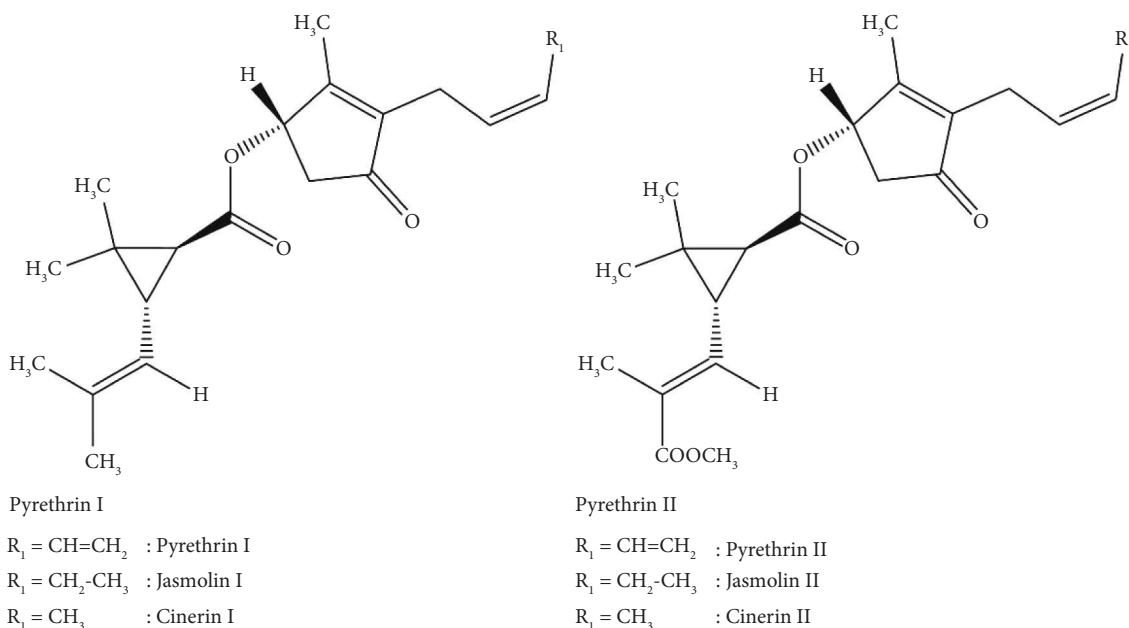


FIGURE 3: Structural representation of six stereochemically configured compounds responsible for the insecticidal activity of pyrethrum extract. The figure has been reproduced with the permission from [34]. Copyright 2015 by Elsevier.

agriculture. These properties investigate azadirachtin's potential as a cornerstone for eco-friendly pest management practices in modern farming systems. Figure 4 represents the mechanism of action of azadirachtin as a natural pesticide.

Pyrethrins, derived from chrysanthemum flowers (*Chrysanthemum cinerariaefolium*), are natural insecticidal compounds that target voltage-gated sodium ion channels in insect neurons [38]. By prolonging the open state of these channels, pyrethrins disrupt the normal flow of sodium ions across the neuronal membrane, causing hyperexcitation of the nervous system [39]. This leads to paralysis and eventual death of the insect. Known for their rapid knockdown effect, pyrethrins are highly effective against various pests. Their low affinity for mammalian sodium channels ensures safety for humans and nontarget species. Unlike synthetic pesticides, pyrethrins degrade quickly in sunlight and air, reducing environmental persistence and contamination risks. This biodegradability makes them a valuable component of organic farming and IPM systems. However, their susceptibility to UV degradation can limit field efficacy, necessitating improved formulations. Pyrethrins exemplify the potential of natural compounds for eco-friendly pest control, balancing efficacy with environmental safety. Figure 5 illustrates the mechanism of action of pyrethrins, derived from chrysanthemum flowers.

**3.4. Sustainability Impacts of Biomimetic Approaches.** Biomimetic pesticides significantly contribute to environmental sustainability by aligning with natural ecological processes. Their reduced persistence in the environment minimizes risks of bioaccumulation and contamination in water bodies. Additionally, biomimetic pesticide production often employs greener chemistry, avoiding toxic solvents and reducing waste. For instance, recent advancements in

the extraction and formulation of neem and pyrethrin-based pesticides have lowered their environmental impact and carbon footprint [40]. By emulating nature, biomimetic approaches inherently support ecological balance while meeting the demands of modern agriculture. Biomimetic advances in pesticide development showcase the potential to harmonize efficacy with sustainability. These innovations provide transformative solutions to contemporary agricultural challenges, fostering a future where productivity and ecological preservation coexist. Continued investment in biomimetic research is essential to realizing the full potential of these groundbreaking strategies. Table 1 provides a detailed comparison of biomimetic and synthetic pesticides across key sustainability and functional aspects.

#### 4. Synthetic Advances in Natural Pesticides

**4.1. Evolution of Synthetic Techniques Inspired by Nature.** The evolution of synthetic techniques in pesticide development has been profoundly influenced by natural bioactive compounds, which serve as structural and functional templates for chemical innovation. These efforts aim to replicate and enhance nature's efficacy, selectivity, and ecological safety in pest control agents. A well-established example is the development of pyrethroids, synthetic analogs of pyrethrins—pesticidal esters derived from *Chrysanthemum* flowers. While natural pyrethrins are effective but photolabile, pyrethroids incorporate structural modifications to improve thermal and photostability, resulting in prolonged field efficacy and reduced application frequency [41]. Advancements in molecular modeling and structure-activity relationship (SAR) analysis further drive the rational design of synthetic pesticides. These computational tools facilitate the development of derivatives with enhanced pest

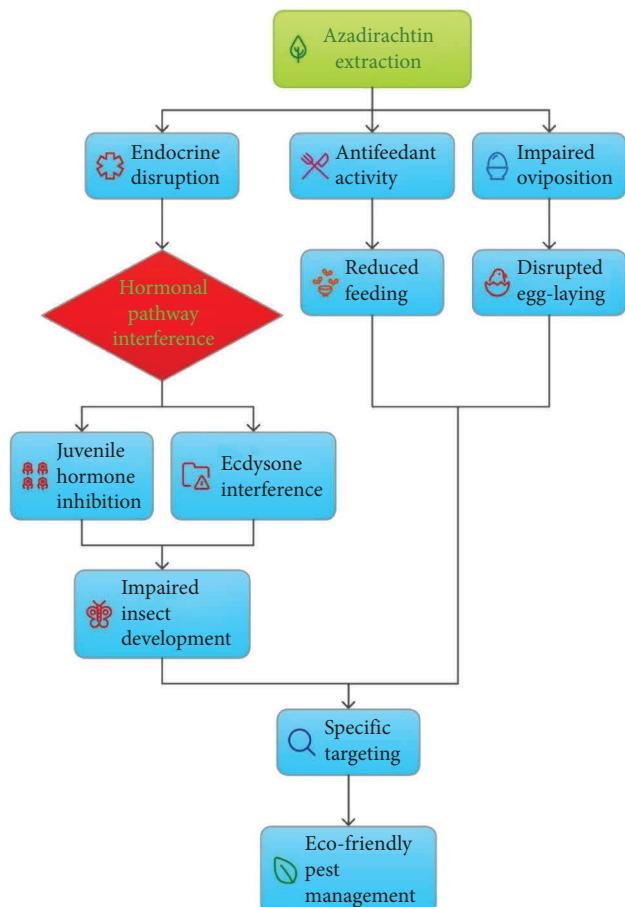


FIGURE 4: Mechanism of action of azadirachtin, extracted from neem, showing its multifunctional impacts on pest control, including endocrine disruption, antifeedant activity, and impaired oviposition, ultimately leading to impaired insect development and eco-friendly pest management.

specificity and environmental resilience, allowing researchers to simulate molecular interactions and optimize binding affinities before synthesis [42]. For example, cyclopropane-based structures, known for their rigid triangular geometry and conformational stability, have been increasingly incorporated into pesticide molecules to enhance target specificity, chemical durability, and resistance to metabolic degradation. The cyclopropane moiety acts as a conformational lock, mimicking the compact, active-site-binding features found in certain natural compounds. Recent studies demonstrate that cyclopropane-containing synthetic pesticides exhibit improved biological activity and reduced volatility, making them promising candidates for durable pest control solutions [43]. These biomimetic strategies highlight the role of nature-inspired chemical design in advancing modern, sustainable pesticide technologies.

**4.2. Hybrid Pesticides: Combining Natural and Synthetic Features.** Hybrid pesticides, which integrate natural and synthetic components, is a promising solution to address the limitations of traditional natural pesticides and conventional

synthetics. These formulations leverage the bioactivity of natural compounds while incorporating synthetic enhancements to improve stability, scalability, and efficacy. A notable example is the development of hybrid formulations combining neem oil with synthetic stabilizers to counteract its rapid degradation under UV light, significantly extending its field effectiveness [44, 45]. Another breakthrough involves hybrid formulations of pyrethroids, which combine the fast action of natural pyrethrins with synthetic modifications to prevent pest resistance. These hybrid approaches underscore the potential to harmonize the strengths of natural and synthetic methodologies, offering versatile tools for sustainable pest management. However, careful regulation and monitoring are essential to maintain these formulations' environmental compatibility.

**4.3. Advances in Green Chemistry for Pesticide Synthesis.** Green chemistry has played a pivotal role in transforming synthetic pesticide production, emphasizing sustainability, efficiency, and safety. Innovations in solvent-free synthesis, catalysis, and energy-efficient processes have minimized the environmental impact of pesticide manufacturing. For example, using ionic liquids and water-based reactions in pyrethroid synthesis has significantly reduced the reliance on hazardous organic solvents, aligning production processes with green chemistry principles [46–48]. Similarly, the integration of renewable feedstocks, such as plant-based raw materials, has further reduced the carbon footprint of synthetic pesticide production. Advanced catalytic systems, including enzyme-based and nanoparticle catalysts, have enabled selective synthesis of pesticide molecules, minimizing waste, and improving reaction yields. Figure 6 highlights key advancements in green chemistry for pesticide synthesis, including solvent-free methods using ionic liquids and water-based reactions to reduce hazardous solvents, renewable feedstocks to lower carbon footprints, and advanced catalytic systems like enzyme-based and nanoparticle catalysts for selective synthesis, all of which minimize waste, improve reaction yields, and promote sustainable, eco-friendly agricultural practices.

**4.4. Challenges in Scaling Synthetic Natural Pesticides.** Despite significant progress, scaling synthetic natural pesticides for widespread agricultural use remains a complex challenge. One of the primary obstacles lies in balancing production costs with affordability for farmers. While green chemistry processes are environmentally advantageous, they often involve higher initial investment and operational complexity, limiting their adoption in resource-constrained regions [49]. Additionally, achieving consistency in synthesizing complex biomimetic compounds requires advanced technologies and rigorous quality control measures, further reducing production costs. Regulatory hurdles, particularly in the approval and testing phases, impede innovative pesticides' rapid deployment. Furthermore, ensuring that synthetic derivatives maintain the ecological benefits of their natural counterparts while avoiding unintended impacts on nontarget species poses a critical scientific and ethical challenge.

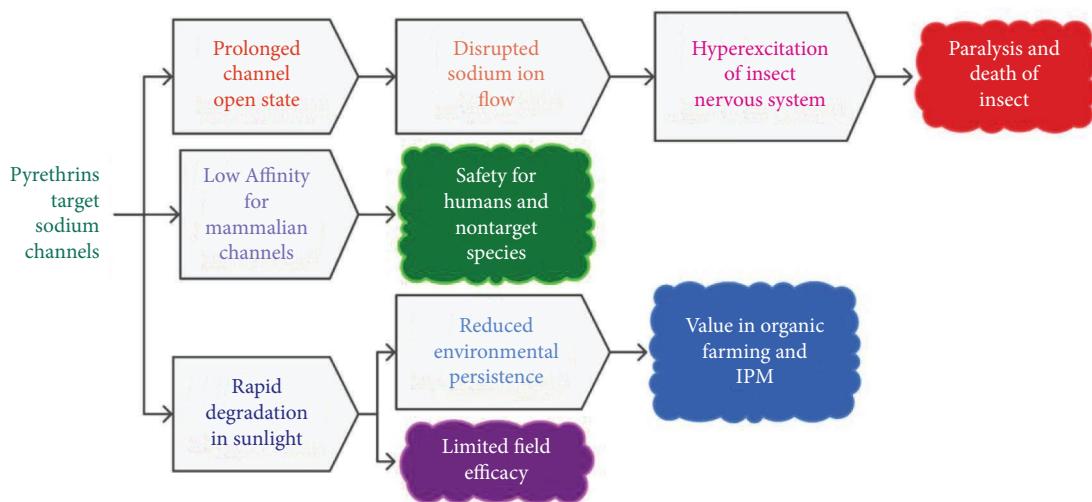


FIGURE 5: Mechanism of action of pyrethrins, derived from chrysanthemum flowers, illustrating their interaction with sodium ion channels in insect neurons, resulting in nervous system hyperexcitation, paralysis, and death, while highlighting their safety for humans, reduced environmental persistence, and value in organic farming and IPM.

To overcome these challenges, interdisciplinary collaboration between chemists, biologists, and agricultural engineers is essential. Investments in research and development, coupled with supportive policy frameworks, can accelerate the scalability of synthetic natural pesticides, bridging the gap between laboratory innovation and field application. These efforts hold the potential to redefine pest management practices, aligning agricultural productivity with ecological sustainability. Table 2 outlines the key challenges in scaling synthetic natural pesticides, including high production costs, operational complexity, consistency in synthesis, regulatory hurdles, ecological compatibility, and limited adoption in resource-constrained regions.

## 5. Comparative Analysis: Biomimetic vs. Synthetic Approaches

**5.1. Efficacy in Pest Control.** Biomimetic pesticides, derived from natural compounds, exhibit highly targeted action by mimicking biological molecules that disrupt pest-specific pathways. Azadirachtin disrupts hormonal systems, while pyrethrins target sodium ion channels, leading to paralysis and death in pests [50, 51]. These mechanisms often ensure high specificity, reducing harm to nontarget organisms. However, their rapid degradation under environmental conditions, such as sunlight and microbial activity, can limit their field longevity, necessitating frequent applications or improved formulations. In contrast, synthetic pesticides, designed for durability and broad-spectrum efficacy, can provide prolonged pest control with fewer applications. For example, synthetic pyrethroids offer enhanced stability and a longer residual effect than their natural counterparts. While this ensures consistent pest suppression, it also increases the likelihood of pest resistance over time, a growing concern in agricultural practices. Balancing these attributes, biomimetic approaches are increasingly integrated into pest management systems to complement synthetic methods, creating a synergistic strategy for sustained efficacy.

**5.2. Environmental and Ecotoxicological Impacts.** Biomimetic pesticides have a clear advantage when it comes to environmental compatibility. Being biodegradable and naturally occurring, they minimize risks of environmental persistence and bioaccumulation. For example, neem-based formulations rapidly degrade into nontoxic residues, ensuring minimal contamination of soil and water bodies [52, 53]. Additionally, their specificity spares beneficial organisms, such as pollinators and natural predators, promoting ecological balance. However, the challenge lies in maintaining efficacy under varying field conditions, where degradation may occur too quickly to provide effective pest control. Conversely, synthetic pesticides often persist in the environment for extended periods, leading to concerns about long-term contamination. Persistent organic pollutants (POPs) from synthetic pesticides can accumulate in ecosystems, affecting nontarget species and disrupting ecological networks. For instance, studies have linked synthetic pesticide runoff to declines in aquatic biodiversity and the contamination of groundwater supplies [54–57]. The trade-off between durability and environmental safety highlights the need for regulatory frameworks to limit the use of highly persistent synthetic pesticides while incentivizing biomimetic alternatives.

**5.3. Cost-Effectiveness and Accessibility.** The economic considerations of pesticide adoption are critical for widespread use, particularly in resource-constrained regions. Synthetic pesticides are generally more cost-effective initially, benefiting from economies of scale in production and distribution. Their durability reduces the need for frequent reapplications, lowering operational costs for farmers. However, the long-term costs associated with environmental remediation, pest resistance management, and health risks often outweigh these initial savings [58–60]. Biomimetic pesticides, while environmentally advantageous, often face higher production costs due to the complexity of extracting

TABLE 1: Comparative analysis of biomimetic and synthetic pesticides highlighting sustainability impacts and practical considerations.

Aspect	Biomimetic pesticides	Synthetic pesticides
Environmental persistence	Reduced persistence; degrades quickly under environmental conditions such as sunlight and microorganisms	Persistent in soil and water; prone to long-term contamination
Bioaccumulation risk	Minimal risk due to rapid biodegradability and natural origins	High risk of bioaccumulation in ecosystems and food chains
Production process	Employs greener chemistry, reducing reliance on toxic solvents and minimizing waste	Often involves the use of hazardous chemicals and generates significant waste
Target specificity	Highly specific, targeting pest species while sparing beneficial organisms	Broad-spectrum activity often affects nontarget organisms
Impact on nontarget organisms	Low impact on nontarget species, including pollinators and soil microbes	High impact on nontarget species, leading to ecological imbalances
Compatibility with IPM	Highly compatible, often integrated as part of sustainable farming practices	Partially compatible but often conflicts with ecological farming principles
Efficacy and stability	Effective but may require advanced formulations for increased stability under field conditions	Stable and long-lasting, but leads to issues like pest resistance
Carbon footprint	Lower carbon footprint due to environmentally friendly production methods	Higher carbon footprint due to energy-intensive manufacturing processes
Economic viability	Generally higher initial cost but potential for long-term savings with reduced environmental harm	Lower initial cost but higher ecological and health remediation costs
Scalability	Scalable with continued advancements in formulation and production technologies	Widely scalable but at the expense of environmental sustainability

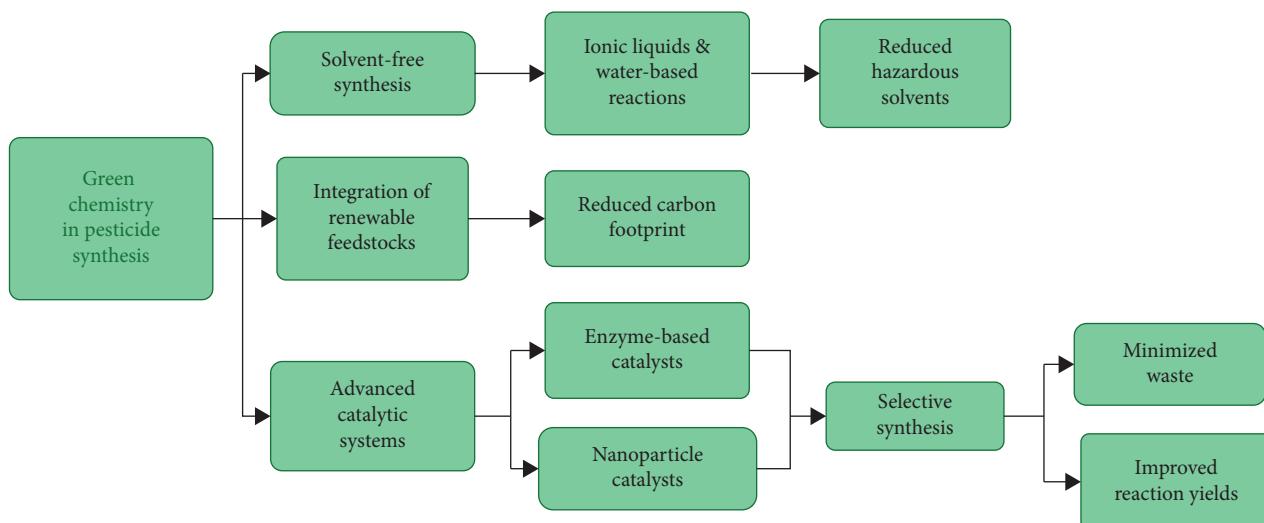


FIGURE 6: Infographic illustration of key advancements in green chemistry applied to pesticide synthesis.

and synthesizing natural compounds. For example, azadirachtin extraction from neem or the synthesis of pyrethrin analogs requires advanced technologies and precision processes, increasing their market price. Despite this, their alignment with sustainable farming practices and reduced environmental liabilities makes them a cost-effective solution in the long term. Subsidies, governmental incentives, and advancements in green chemistry are essential to bridge the affordability gap and make biomimetic pesticides accessible to smallholder farmers [61–63].

**5.4. Long-Term Impacts on Soil and Ecosystems.** The long-term impacts of pesticide usage on soil health and ecosystem functionality further distinguish biomimetic and synthetic approaches. Due to their biodegradability, biomimetic pesticides have minimal residual effects on soil microorganisms and fertility. For instance, neem-based formulations have been shown to enhance soil health by promoting beneficial microbial activity and reducing harmful pathogens [64]. Similarly, using pyrethrin-based products has limited negative effects on earthworm populations and other essential soil fauna, preserving ecosystem services vital for sustainable agriculture. On the other hand, synthetic pesticides can disrupt soil ecosystems by accumulating toxic residues. Prolonged use of such chemicals often leads to the suppression of beneficial microbes, soil acidification, and reduced fertility. Furthermore, the unintended impacts on nontarget organisms, such as earthworms and nitrogen-fixing bacteria, can diminish soil productivity over time [65–67]. These ecological consequences highlight the importance of transitioning to biomimetic solutions to preserve soil and ecosystem health while maintaining agricultural productivity. Table 3 provides a detailed and inclusive comparison between biomimetic and synthetic approaches in natural pesticides across critical aspects such as efficacy, environmental impacts, cost, scalability, and regulatory processes.

## 6. Bridging the Gap Between Efficacy and Sustainability

**6.1. Key Challenges in Achieving Sustainability.** Achieving sustainability in pesticide development and use requires addressing multifaceted environmental, economic, and operational challenges. One significant issue is the environmental persistence of synthetic pesticides, which contributes to soil degradation, water contamination, and bioaccumulation in nontarget organisms. Despite the potential of biomimetic pesticides to mitigate these impacts, their adoption faces hurdles such as higher production costs, limited scalability, and variability in field performance. For example, while eco-friendly, neem-based pesticides often degrade rapidly under ultraviolet light, reducing their efficacy in open agricultural environments [68]. Additionally, resistance management remains a critical concern, as pests can evolve mechanisms to counteract natural and synthetic pesticides, necessitating ongoing innovation in design and delivery mechanisms [69–71]. Economic barriers also persist, especially for small-scale farmers in resource-limited settings who may lack access to affordable, sustainable pesticides. Bridging these gaps requires a systemic approach integrating technological advancements, financial incentives, and targeted education programs to promote sustainable practices while maintaining agricultural productivity. Figure 7 illustrates the critical challenges in achieving sustainable pesticide development, represented as the roots of a tree to signify foundational barriers.

**6.2. Innovations in Delivery Mechanisms.** Advancements in delivery mechanisms are critical to improving the efficacy, environmental stability, and targeted action of natural pesticides. Traditional formulations often suffer from rapid degradation, uncontrolled dispersion, and reduced field performance. Recent innovations—particularly in nano- and microencapsulation technologies—have improved pesticide

TABLE 2: Challenges and solutions in scaling synthetic natural pesticides for sustainable agricultural practices.

Challenges	Description	Potential solutions
High production costs	Green chemistry processes and advanced technologies increase production costs, making affordability for farmers challenging.	Investments in cost-reduction strategies and economies of scale to make production more affordable.
Operational complexity	Scaling synthesis processes involve complex operational requirements that demand significant expertise and infrastructure.	Streamlining processes and automating workflows to reduce complexity and improve efficiency.
Consistency in synthesis	Synthesis of complex biomimetic compounds like azadirachtin analogs requires advanced technologies and strict quality control, adding to the cost.	Developing robust quality control frameworks and scalable technologies for consistent synthesis.
Regulatory hurdles	Lengthy approval processes and stringent regulations delay deployment and add costs to innovative pesticide production.	Advocating for supportive policy frameworks simplifying regulatory processes while ensuring safety and efficacy.
Ecological compatibility	Ensuring synthetic pesticides mimic natural ecological benefits without unintended harm to nontarget species remains a scientific and ethical challenge.	Conducting interdisciplinary research to optimize ecological benefits and mitigate risks to nontarget species.
Adoption in resource-constrained regions	Limited financial and technical resources in certain regions make adopting innovative pesticides difficult.	Providing subsidies, training, and infrastructure support facilitates adoption in under-resourced areas.

TABLE 3: Comparative analysis of biomimetic and synthetic approaches in natural pesticides.

Aspect	Biomimetic approaches	Synthetic approaches
Efficacy in pest control	Highly specific, targeting pests with minimal harm to nontarget organisms, but may require frequent applications due to rapid degradation.	Broad-spectrum and long-lasting efficacy, but can lead to pest resistance over time due to overuse.
Environmental and ecotoxicological impacts	Biodegradable with a low risk of bioaccumulation, preserving ecological balance and sparing beneficial organisms like pollinators and soil microbes.	Persistent in the environment, posing risks of bioaccumulation and contamination, with significant impacts on nontarget species.
Cost-effectiveness and accessibility	Higher production costs but lower long-term environmental remediation expenses; subsidies and advancements are improving accessibility.	Lower initial costs due to mass production and durability, but higher long-term costs from environmental and health consequences.
Long-term impacts on soil and ecosystems	Minimal residual impact, promoting soil health and supporting beneficial microbial activity, with limited disruption to ecosystem services.	Accumulation of toxic residues can harm soil microbes, reduce fertility, and disrupt essential ecosystem functions over time.
Impact on nontarget organisms	Minimal impact on nontarget species due to high specificity, ensuring ecological balance and safety for beneficial organisms.	High impact on nontarget species, often harming pollinators, beneficial insects, and aquatic organisms, disrupting ecological balance.
Compatibility with sustainable practices	Highly compatible with integrated pest management (IPM) and organic farming practices, supporting sustainable agricultural goals.	Partially compatible with sustainable practices but often conflicts with ecological goals due to environmental persistence.
Ease of scalability	Scaling requires advanced technologies and initial investments, but improvements in formulation and processes are making it more feasible.	Easily scalable due to established production processes and global distribution networks, though environmental risks remain high.
Regulatory and approval processes	Fewer regulatory hurdles due to natural origins but requires comprehensive safety and efficacy data to meet global standards.	Stringent regulatory processes due to potential toxicity and environmental persistence, leading to prolonged approval timelines.
Research and development requirements	Significant R&D efforts needed for advanced formulations and extraction methods to improve stability and field efficacy.	Moderate R&D requirements for formulation optimization, with most efforts focused on resistance management and toxicity reduction.

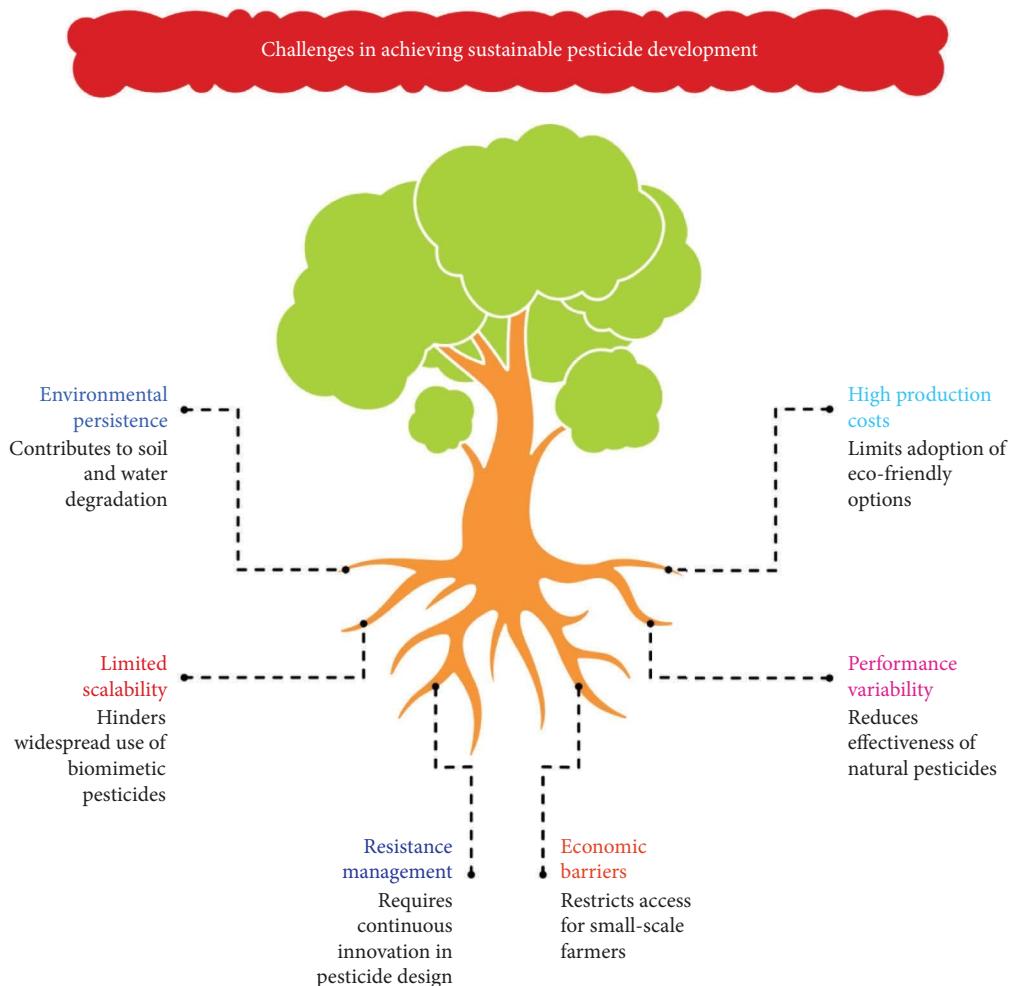


FIGURE 7: Key challenges in achieving sustainable pesticide development highlighting environmental, economic, and operational barriers.

delivery systems by offering protection and precision. One strategy is using polymeric nanoparticles (e.g., PLGA, chitosan, alginate), encapsulating active ingredients like azadirachtin and enabling slow, controlled release. For example, azadirachtin-loaded chitosan nanoparticles (size  $\sim 150$  nm) have shown enhanced UV stability and a 2.5-fold increase in residual activity compared to nonencapsulated formulations.

Another technique involves liposomal encapsulation, where lipids form bilayer vesicles that encapsulate hydrophobic and hydrophilic pesticides. Liposomal pyrethrin formulations have demonstrated improved dispersion in aqueous media and delayed release, extending field efficacy to over 10 days under standard agricultural conditions. Solid lipid nanoparticles (SLNs) and nanostructured lipid carriers (NLCs) are also gaining attention (Figure 8) [72]. SLN-based delivery of neem oil has improved adherence to plant surfaces and increased larvicidal activity by over 40% in *Spodoptera litura* infestations [73–75]. In addition, smart delivery systems have emerged, leveraging stimuli-responsive materials that release active agents in response to environmental triggers such as pH, temperature, or humidity. For instance, pH-sensitive silica-based nanocarriers functionalized with polydopamine have been used to release

pesticide only in the alkaline pH of insect midguts, thereby reducing nontarget exposure [76–78].

Zhao et al. developed a pH-responsive nanopesticide using hollow mesoporous silica nanoparticles loaded with prochloraz and capped with ZnO quantum dots, achieving controlled release, enhanced photostability, and systemic delivery in rice plants (Figure 9) [79]. The nanoformulation showed 2.67-fold higher release under acidic conditions and demonstrated effective fungicidal activity against rice blast disease, highlighting its potential in precision agriculture. These delivery systems not only reduce the frequency of application but also minimize pesticide leaching and environmental persistence, aligning with the goals of sustainable and precision agriculture. Integrating these novel systems represents a shift from conventional pesticide delivery to next-generation biomimetic formulations that are smarter, safer, and more effective.

**6.3. Role of Biotechnology and Nanotechnology.** Biotechnology and nanotechnology are transforming the landscape of pesticide development by providing tools for designing highly specific, environmentally safe, and effective solutions. Biotechnology enables genetically engineering

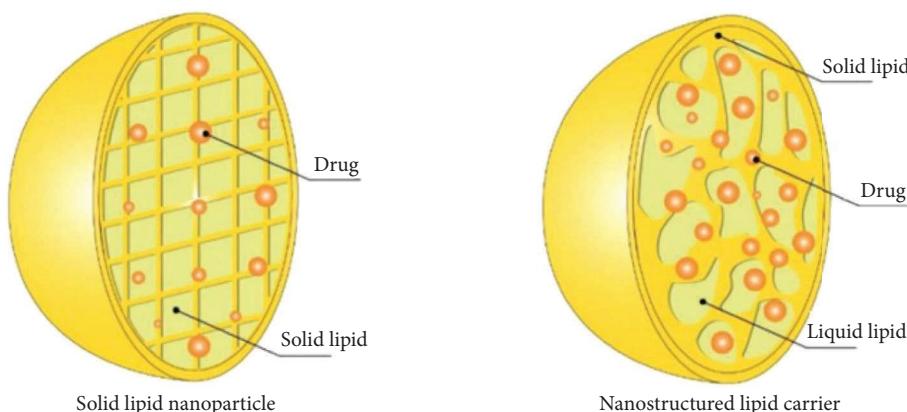


FIGURE 8: Structural matrix of SLN and NLC. Adapted with permission from reference [72].

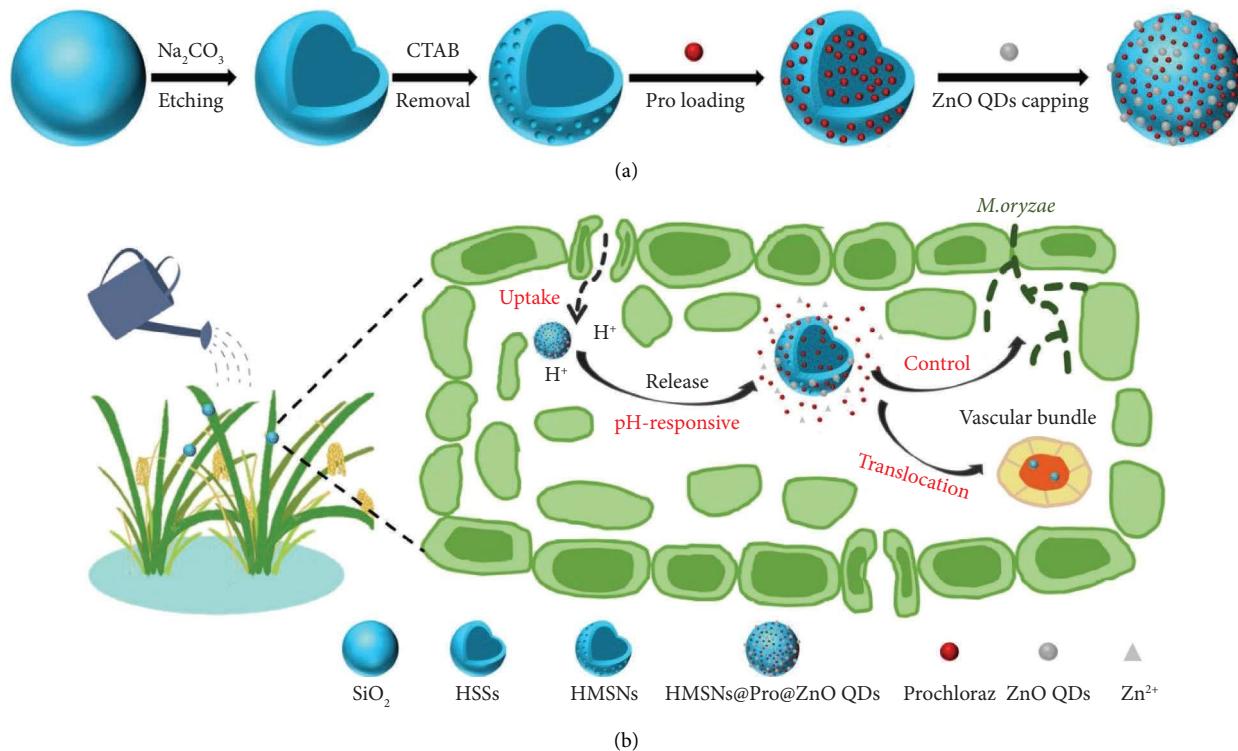


FIGURE 9: Schematic illustration of (a) the synthesis of hollow mesoporous silica nanoparticles loaded with the photosensitive pesticide prochloraz and then combined with ZnO quantum dots (HMSNs@Pro@ZnO QDs) and (b) their application in the smart control of rice blast disease. Reproduced with permission from reference [79].

crops that produce natural pesticides, such as Bt toxins, directly within their tissues. These genetically modified organisms (GMOs) reduce the need for external pesticide applications while precisely targeting specific pests. However, concerns about ecological impacts and public acceptance necessitate robust regulatory frameworks and transparent communication strategies [80, 81]. Nanotechnology complements these efforts by enhancing the formulation and delivery of pesticides. Nanoemulsions, nanosuspensions, and nanocarriers improve active ingredient solubility, stability, and bioavailability, resulting in more efficient pest control. For example, silver nanoparticles

have been investigated for their dual roles as antimicrobial agents and carriers for natural pesticide compounds, providing a synergistic approach to pest and pathogen management [82–84]. These cutting-edge technologies underscore the transformative potential of interdisciplinary research in addressing the dual challenges of efficacy and sustainability.

**6.4. Policy and Regulatory Considerations.** Policy and regulatory frameworks are indispensable in bridging the gap between efficacy and sustainability in pesticide use. A major challenge lies in establishing globally harmonized standards

that balance innovation with safety and environmental protection. Current regulatory processes often involve lengthy approval timelines, particularly for novel biomimetic and nanotechnology-based pesticides, which can hinder their timely adoption [85]. Simplifying these processes while ensuring rigorous safety evaluations is essential for promoting sustainable alternatives. Policies incentivizing the development and adoption of eco-friendly pesticides can accelerate the transition toward sustainability. Subsidies, tax breaks, and research grants for companies and researchers working on biomimetic and green chemistry-based solutions can significantly reduce the financial barriers to innovation. Public awareness campaigns and farmer education programs are equally important to encourage the widespread use of sustainable practices, bridging the gap between laboratory advancements and field application [86].

## 7. Applications and Success Stories

**7.1. Agricultural Applications: Field Studies and Case Examples.** The practical implementation of biomimetic and synthetic pesticides has shown significant promise in diverse agricultural settings. Field studies have demonstrated the efficacy of neem-based pesticides in controlling aphids, whiteflies, and other sap-sucking pests in crops such as potatoes, wheat, peach, chili, okra, cotton, tomatoes, and mangoes (Table 4). Similarly, pyrethrin-based formulations have proven effective in managing fruit fly populations in orchards, with minimal environmental residues, ensuring compliance with export standards [99]. Synthetic pesticides, such as pyrethroids, have also been extensively utilized in large-scale agriculture due to their broad-spectrum activity and residual efficacy [100]. Nizam et al. reported that pyrethroids effectively controlled pests like planthoppers in Southeast Asian rice fields, improving yields. However, improper handling and disposal led to environmental contamination and ecological risks, particularly to aquatic organisms, emphasizing the need for sustainable pesticide practice [101]. These examples underscore the need for a balanced integration of biomimetic and synthetic approaches to optimize productivity and sustainability. Table 4 summarizes the major findings from multiple studies on neem-based and other biopesticides, highlighting their effectiveness against various pests and crops, specific mechanisms of action, and contributions to sustainability.

**7.2. Applications in IPM.** Biomimetic and synthetic pesticides are increasingly being integrated into IPM programs to achieve sustainable pest control [102, 103]. IPM emphasizes using multiple control strategies, including biological, cultural, and chemical methods, to minimize pest populations while reducing reliance on synthetic chemicals. Biomimetic pesticides, such as neem and Bt-based formulations, target specific pests without disrupting natural predators or beneficial organisms. For instance, in maize cultivation, incorporating Bt sprays into IPM strategies effectively controlled corn borers while maintaining ecological balance [104]. Synthetic

pesticides, while not entirely excluded from IPM programs, are used judiciously to manage outbreaks that exceed the control capacity of natural methods. For example, the selective use of synthetic pyrethroids in conjunction with pheromone traps and biological controls has successfully reduced pest damage in vineyards [105]. This integrated approach minimized chemical usage and enhanced the effectiveness of natural pest control agents [106, 107]. The synergy between biomimetic and synthetic pesticides within IPM frameworks demonstrates their potential to harmonize efficacy with environmental stewardship.

**7.3. Commercial Success Stories of Biomimetic and Synthetic Pesticides.** The commercialization of biomimetic and synthetic pesticides has led to several notable success stories, reflecting their market viability and agricultural impact. Neem-based products, such as azadirachtin EC formulations, have gained widespread acceptance in organic farming due to their eco-friendly profile and effectiveness against various pests [108, 109]. The commercial success of a leading neem pesticide brand in Europe has been attributed to its compatibility with organic certification standards and its ability to meet consumer demand for residue-free produce [110–112]. Synthetic pesticides have also achieved significant commercial milestones, particularly in large-scale industrial farming. Pyrethroid-based products, such as deltamethrin and lambda-cyhalothrin, are among the most widely used synthetic pesticides globally, with applications ranging from cotton to vegetable crops [113, 114]. Their broad-spectrum activity, cost-effectiveness, and long-lasting field performance drive their success. However, the increasing regulatory restrictions on synthetic pesticides in regions like the European Union have prompted companies to invest in greener, biomimetic alternatives, signaling a shift toward sustainability [115].

## 8. Future Directions in Natural Pesticide Development

**8.1. Emerging Technologies in Pesticide Design.** The future of natural pesticide development lies in leveraging advanced technologies to enhance efficacy, specificity, and environmental sustainability. One promising avenue is using nanotechnology to create novel formulations that improve the delivery and stability of active compounds. For instance, nanoencapsulation techniques can protect bioactive ingredients like azadirachtin from rapid degradation under UV light, ensuring prolonged effectiveness in field applications [116, 117]. Additionally, smart pesticides incorporating responsive systems that release active ingredients based on environmental triggers such as pH, humidity, or temperature are gaining traction as cutting-edge solutions to reduce waste and environmental impact [118–120]. AI and machine learning are also set to revolutionize pesticide design by enabling predictive modeling of compound efficacy, optimizing formulations, and identifying potential resistance pathways [121, 122]. These

TABLE 4: Key field studies highlighting the efficacy and sustainability of natural pesticides.

Study	Key findings	Pests/crops studied	Mechanism of action	Impact on sustainability	Ref
Santos et al.	Neem seed extracts showed significant mortality (up to 100%) in cotton aphids ( <i>Aphis gossypii</i> ) at higher concentrations (1410 mg/100 mL). Reduced fecundity and developmental disruption were also observed.	Cotton aphids	Azadirachtin disrupts hormonal pathways, affecting molting, growth, and reproduction.	Supports integrated pest management (IPM) by being selective, eco-friendly, and safe for beneficial organisms.	[87]
Pathania et al.	Neem formulations reduced wheat aphids by up to 74.23% after 7 days of application. Coccinellid presence was higher in neem-treated fields compared to synthetic pesticides.	Wheat aphids	Neem-based treatments act as antifeedants and growth inhibitors, with minimal impact on nontarget organisms.	Promotes biodiversity by reducing harm to natural predators and pollinators.	[88]
Shannag et al.	Neem-based biopesticides significantly reduced green peach aphid populations by 50%-75% in greenhouse conditions. Pure neem oil and azatrol eliminated nearly all aphids with two applications.	Green peach aphids	Neem extracts deter feeding and reduce reproductive rates without acting as strong repellents.	Effective alternative for organic farming, reducing reliance on conventional pesticides with fewer residues.	[89]
Tobing et al.	Neem leaf extract at higher concentrations (30%-50%) effectively suppressed aphid severity on chili plants. Increased application frequency enhanced aphid control and improved plant growth metrics like height and leaf area.	Chili aphids	Secondary metabolites (azadirachtin, saponins, meliantriol) function as insect growth regulators, repellents, and stomach poisons.	Reduces dependency on synthetic chemicals while promoting healthy crop development and minimizing environmental harm.	[90]
Ahmad et al.	Neem-white oil emulsions were effective against aphids and leafhoppers on potato crops, with yields close to synthetic bifenthrin.	Potato aphids and leafhoppers	Neem enhanced by white oil acted as an insect growth regulator, disrupting feeding and reproduction.	Promoted eco-friendly pest management with comparable efficacy to synthetic options, reducing toxicity risks.	[91]
Ghosh et al.	Neem oil achieved over 60% reduction in whitefly populations on okra crops while maintaining environmental safety.	Whiteflies on okra	Biological action disrupted whitefly activity, reducing pest loads while maintaining environmental compatibility.	Demonstrated potential for inclusion in organic farming and IPM strategies, reducing chemical pesticide reliance.	[92]
Mann et al.	Neem azal and rakshak gold (2 L/ha) effectively suppressed <i>Bemisia tabaci</i> with only 4 sprays over 48 days, with residual effects persisting for 6-12 days.	<i>Bemisia tabaci</i> , <i>Aphis gossypii</i> , <i>Amrasca biguttula</i> , and bollworms on cotton crops	Neem-based formulations disrupted pest feeding and reproductive cycles, maintaining populations below ETI.	Reduced synthetic pesticide use and minimized secondary pest outbreaks, supporting eco-friendly cotton cultivation.	[93]

TABLE 4: Continued.

Study	Key findings	Pests/crops studied	Mechanism of action	Impact on sustainability	Ref
Aggarwal and Brar Hafeez-ur et al.	<p>Neem formulations (e.g., neem azal T/S) showed lower toxicity to beneficial insects (e.g., parasitoids and predators) than synthetic insecticides like triazophos.</p> <p>Neem oil (4% and 5%) and lambda-cyhalothrin were equally effective in reducing whitefly and jassid populations on okra, enhancing yield and promoting eco-friendly pest management with reduced reliance on synthetic chemicals.</p> <p>Neem oils, combined with a detergent and sticker (Triton X-100), effectively reduced <i>Bemisia tabaci</i> populations in laboratory and field tests, with castor oil showing the highest efficacy. Neem formulations were less effective than chemical treatments. No phytotoxic effects were observed on cotton leaves.</p> <p>Neem oil, in combination with native predators (<i>Chrysoperla carnea</i> larvae and <i>Brumus suturalis</i> adults), effectively reduced mealybug populations (<i>Phenacoccus solenopsis</i>) under semifield and field conditions. Exotic predator <i>Cryptolaemus montrouzieri</i> was effective in semifield conditions but failed in field trials. Synthetic insecticides provided the maximum reduction in mealybug populations.</p>	<p>Cotton whitefly (<i>Bemisia tabaci</i>); cotton</p> <p>Whitefly (<i>Bemisia tabaci</i>), jassid (<i>Amrasca devastans</i>), okra (<i>Abelmoschus esculentus</i>)</p> <p>Whitefly (<i>Bemisia tabaci</i>), cotton</p> <p>Mealybugs (<i>Phenacoccus solenopsis</i>), cotton</p> <p>Thrips (<i>Thysanoptera</i>), mango (<i>Mangifera indica</i>)</p>	<p>Neem acts as a biorational insecticide, disrupting the life stages of pests while preserving natural enemies in the ecosystem.</p> <p>Neem oil acts as an antifeedant and oviposition deterrent, while lambda-cyhalothrin provides rapid knockdown effects.</p> <p>Oils act as suffocants and disrupt whitefly activity, while Triton X-100 ensures effective application and adhesion.</p> <p>Neem oil acts as a natural insecticide, enhancing predator effectiveness, while native predators suppress mealybug populations through biological control.</p> <p>Neem oil acts as an antifeedant, oviposition deterrent, and repellent due to azadirachtin, which disrupts thrips' life cycle and feeding patterns.</p>	<p>Supports (IPM) by reducing reliance on broad-spectrum insecticides and preserving biodiversity.</p> <p>Encourages sustainable agriculture by reducing chemical residues, supporting biodiversity, and fostering environmentally sound pest management practices.</p> <p>Encourages sustainable pest management by reducing reliance on synthetic chemicals, preserving crop health, and ensuring environmental safety.</p> <p>Supports eco-friendly pest management by reducing dependence on synthetic insecticides and promoting biological control methods.</p>	<p>[94]</p> <p>[95]</p> <p>[96]</p> <p>[97]</p> <p>[98]</p>
Mamoon-ur-Rashid et al.	Aliakbarpour et al.			Enhances sustainable pest management by reducing reliance on synthetic insecticides, preserving beneficial pollinator populations, and promoting biodiversity.	

TABLE 5: Comprehensive challenges and solutions for advancing natural pesticide development.

Challenge	Description of challenge	Proposed solutions	Impact on sustainability
Scalability in resource-constrained regions	Limited access to technology and capital in certain regions makes scaling natural pesticide production difficult.	Invest in cost-efficient production using renewable feedstocks and green chemistry techniques to lower manufacturing expenses. Rotate active ingredients with diverse mechanisms of action, deploy combination treatments, and use pest monitoring technologies.	Cost-effective production methods support widespread adoption while minimizing environmental impact.
Evolution of pest resistance	Pests developing resistance to both biomimetic and synthetic pesticides threaten long-term efficacy.	Harmonize international standards, streamline approval processes, and ensure rigorous safety evaluations to promote global adoption.	Diverse strategies reduce reliance on a single pesticide, mitigating resistance risks and ensuring ecological balance.
Complex regulatory landscapes	Regulatory frameworks for biomimetic products are complex, often straddling biological and chemical classifications, delaying approvals.	Provide subsidies, government support, and tailored pricing models to improve affordability for smallholder farmers.	Streamlined approvals enable timely adoption of eco-friendly solutions, fostering global sustainability efforts.
Economic viability for smallholders	High initial production costs of natural pesticides make them less accessible to smallholder farmers in low-income regions.	Launch educational campaigns and community outreach programs to promote understanding and trust in biomimetic products.	Improved affordability expands adoption, promoting sustainable practices in underserved regions.
Public perception and education	Lack of public awareness and skepticism about biomimetic products hinders widespread adoption.	Increased public trust accelerates adoption, integrating biomimetic products into global pest management practices.	

technologies, combined with advances in bioinformatics, allow for the discovery of new bioactive molecules from natural sources, accelerating innovation in biomimetic pesticide development [123].

**8.2. Synergies Between Biomimetic and Synthetic Approaches.** Biomimetic and synthetic approaches, often seen as competing methodologies, have the potential to complement each other when strategically integrated. Biomimetic pesticides excel in their ecological compatibility and specificity, while synthetic pesticides offer durability and broad-spectrum efficacy. Combining these strengths can lead to hybrid formulations that maximize pest control while minimizing environmental risks. The synthetic analogs of natural compounds, such as pyrethroids derived from pyrethrins, provide enhanced stability without compromising biodegradability [114]. Moreover, integrating biomimetic pesticides into synthetic-dominated IPM systems can enhance the overall sustainability of pest control practices. Their treatments can be paired with reduced doses of synthetic chemicals to maintain pest populations below economic threshold levels while reducing the likelihood of resistance development and environmental contamination [80, 124].

**8.3. Interdisciplinary Research and Collaboration Opportunities.** The development of next-generation natural pesticides demands interdisciplinary collaboration, bringing together expertise from chemistry, biology, nanotechnology, data science, and agricultural engineering. Chemists and biologists can work on isolating and synthesizing bioactive molecules, while engineers develop advanced delivery mechanisms to enhance field performance. For example, collaborations between agricultural researchers and materials scientists have already resulted in biodegradable polymers for encapsulating active ingredients, ensuring targeted release and reduced environmental residue [125]. Public-private partnerships also have the potential to accelerate innovation by pooling resources and expertise. Companies investing in sustainable agricultural solutions can collaborate with academic institutions to test new formulations in real-world conditions, bridging the gap between laboratory research and commercial application. Funding agencies and policymakers must prioritize these collaborations by offering incentives for projects focused on ecological pest control [126].

**8.4. Anticipating Future Challenges and Solutions.** As the demand for sustainable pest management grows, the natural pesticide industry must address several challenges to maintain its trajectory of innovation. A critical issue is the scalability of natural pesticide production, particularly in resource-constrained regions where access to technology and capital is limited. Addressing this requires investment in cost-efficient production methods, such as using renewable feedstocks and green chemistry techniques to lower manufacturing expenses [11]. Another pressing challenge is

the evolution of pest resistance, which threatens the long-term efficacy of both biomimetic and synthetic pesticides. Solutions include rotating active ingredients with diverse mechanisms of action, deploying combination treatments, and integrating pest monitoring technologies to ensure timely interventions [127]. Finally, navigating regulatory landscapes remains complex, particularly for novel biomimetic products that straddle the boundaries of biological and chemical classifications. Harmonizing international standards and expediting approval processes while maintaining rigorous safety evaluations will be critical for promoting global adoption [128]. Table 5 comprehensively addresses the critical challenges and proposed solutions while emphasizing their sustainability impact.

## 9. Conclusion

The review discusses the transformative potential of biomimetic and synthetic advances in natural pesticides, presenting a roadmap for achieving sustainable pest management. Key findings highlight that biomimetic pesticides, inspired by nature's precision, provide targeted pest control with minimal ecological disruption. Examples include azadirachtin from neem and pyrethrins from chrysanthemum, which offer specificity, biodegradability, and environmental safety. Synthetic advancements, on the other hand, complement biomimetic approaches by enhancing the stability and scalability of natural analogs, bridging gaps in efficacy and longevity. The implications of this synthesis are significant for both research and policy. From a research perspective, interdisciplinary collaborations integrating chemistry, biotechnology, and nanotechnology are essential to overcoming production, resistance, and regulatory hurdles. Policies must prioritize developing and adopting eco-friendly solutions through streamlined approval processes, subsidies, and education programs for farmers. Regulatory frameworks should also harmonize global standards to facilitate the broader adoption of innovative biomimetic products. Looking forward, the path to sustainable agriculture lies in combining biomimetic and synthetic strengths while addressing challenges such as scalability, pest resistance, and economic accessibility. Continued investment in green chemistry, smart delivery systems, and bioinformatics-driven discovery will be pivotal in aligning agricultural productivity with environmental stewardship. This synergy between innovation and sustainability offers a compelling vision for the future, fostering a balanced ecosystem and ensuring global food security.

## Data Availability Statement

All data are available in the manuscript. Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.

## Conflicts of Interest

The authors declare no conflicts of interest.

## Funding

No funding was received for this manuscript.

## References

- [1] M. Riyaz, P. Mathew, S. M. Zuber, and G. A. Rather, "Botanical Pesticides for an Eco-Friendly and Sustainable Agriculture: New Challenges and Prospects," in *Sustainable Agriculture: Technical Progressions and Transitions*, ed. S. A. Bandh (Cham: Springer International Publishing, 2022), 69–96.
- [2] M. F. B. Mfarrej and F. M. Rara, "Competitive, Sustainable Natural Pesticides," *Acta Ecologica Sinica* 39, no. 2 (2019): 145–151, <https://doi.org/10.1016/j.chnaes.2018.08.005>.
- [3] A. L. Souto, M. Sylvestre, E. D. Tölke, J. F. Tavares, J. M. Barbosa-Filho, and G. Cebrián-Torrejón, "Plant-Derived Pesticides as an Alternative to Pest Management and Sustainable Agricultural Production: Prospects, Applications and Challenges," *Molecules* 26, no. 16 (2021): 4835, <https://doi.org/10.3390/molecules26164835>.
- [4] K. S. Rajmohan, R. Chandrasekaran, and S. Varjani, "A Review on Occurrence of Pesticides in Environment and Current Technologies for Their Remediation and Management," *Indian Journal of Microbiology* 60, no. 2 (2020): 125–138, <https://doi.org/10.1007/s12088-019-00841-x>.
- [5] V. M. Pathak, V. K. Verma, B. S. Rawat, et al., "Current Status of Pesticide Effects on Environment, Human Health and It's Eco-Friendly Management as Bioremediation: A Comprehensive Review," *Frontiers in Microbiology* 13 (2022): <https://doi.org/10.3389/fmicb.2022.962619>.
- [6] E. V. R. Campos, J. L. de Oliveira, M. Pascoli, R. de Lima, and L. F. Fraceto, "Neem Oil and Crop Protection: From Now to the Future," *Frontiers in Plant Science* 7 (2016): <https://doi.org/10.3389/fpls.2016.01494>.
- [7] C. A. Damalas and S. D. Koutroubas, "Botanical Pesticides for Eco-Friendly Pest Management," *Pesticides in Crop Production* (2020): 181–193, <https://doi.org/10.1002/9781119432241.ch10>.
- [8] Z. Jouzi, H. Azadi, F. Taheri, et al., "Organic Farming and Small-Scale Farmers: Main Opportunities and Challenges," *Ecological Economics* 132 (2017): 144–154, <https://doi.org/10.1016/j.ecolecon.2016.10.016>.
- [9] F. Jacquet, M.-H. Jeuffroy, J. Jouan, et al., "Pesticide-free Agriculture as a New Paradigm for Research," *Agronomy for Sustainable Development* 42, no. 1 (2022): 8, <https://doi.org/10.1007/s13593-021-00742-8>.
- [10] P. Gupta, M. Shahnawaz, V. Zambare, N. Kumar, and A. Thakur, "Chapter 21-Natural Compounds as Pesticides, Emerging Trends, Prospects, and Challenges," *New Horizons in Natural Compound Research*, ed. S. N. Meena, V. Nandre, K. Kodam, and R. S. Meena (Academic Press 2023), 391–414.
- [11] M. Lykogianni, E. Bempelou, F. Karamaouna, and K. A. Aliferis, "Do Pesticides Promote or Hinder Sustainability in Agriculture? the Challenge of Sustainable Use of Pesticides in Modern Agriculture," *Science of The Total Environment* 795 (2021): <https://doi.org/10.1016/j.scitotenv.2021.148625>.
- [12] A. Khursheed, M. A. Rather, V. Jain, et al., "Plant Based Natural Products as Potential Ecofriendly and Safer Biopesticides: A Comprehensive Overview of Their Advantages over Conventional Pesticides, Limitations and Regulatory Aspects," *Microbial Pathogenesis* 173 (2022): <https://doi.org/10.1016/j.micpath.2022.105854>.
- [13] M. Massaro, S. Pieraccini, S. Guernelli, et al., "Photostability Assessment of Natural Pyrethrins Using Halloysite Nanotube Carrier System," *Applied Clay Science* 230 (2022): <https://doi.org/10.1016/j.clay.2022.106719>.
- [14] B. L. Atkinson, A. J. Blackman, and H. Faber, "The Degradation of the Natural Pyrethrins in Crop Storage," *Journal of Agricultural and Food Chemistry* 52, no. 2 (2004): 280–287, <https://doi.org/10.1021/jf0304425>.
- [15] S. Singh, A. Mukherjee, D. K. Jaiswal, et al., "Advances and Future Prospects of Pyrethroids: Toxicity and Microbial Degradation," *Science of the Total Environment* 829 (2022): <https://doi.org/10.1016/j.scitotenv.2022.154561>.
- [16] C. L. Cantrell, F. E. Dayan, and S. O. Duke, "Natural Products as Sources for New Pesticides," *Journal of Natural Products* 75, no. 6 (2012): 1231–1242, <https://doi.org/10.1021/np300024u>.
- [17] N. Möhring, K. Ingold, P. Kudsk, et al., "Pathways for Advancing Pesticide Policies," *Nature Food* 1, no. 9 (2020): 535–540, <https://doi.org/10.1038/s43016-020-00141-4>.
- [18] W. M. Jarman and K. Ballschmiter, "From Coal to DDT: the History of the Development of the Pesticide DDT from Synthetic Dyes till Silent Spring," *Endeavour* 36, no. 4 (2012): 131–142, <https://doi.org/10.1016/j.endeavour.2012.10.003>.
- [19] H. Gay, "Before and after Silent Spring: From Chemical Pesticides to Biological Control and Integrated Pest Management-Britain," *Ambix* 59, no. 2 (2012): 88–108, <https://doi.org/10.1179/174582312x13345259995930>.
- [20] P. Juma, N. Njau, F. W. W, et al., "Trends in Neem (*Azadirachta indica*)-Based Botanical Pesticides," in *New and Future Development in Biopesticide Research: Biotechnological Exploration*, ed. S. D. Mandal, G. Ramkumar, S. Karthi, and F. Jin (Springer Nature Singapore, 2022), 137–156.
- [21] E. Assadpour, A. Can Karaç, M. Fasamanesh, et al., "Application of Essential Oils as Natural Biopesticides; Recent Advances," *Critical Reviews in Food Science and Nutrition* 64, no. 19 (2024): 6477–6497, <https://doi.org/10.1080/10408398.2023.2170317>.
- [22] F. R. Davis, "Pesticides and the Paradox of the Anthropocene: From Natural to Synthetic to Synthesised Nature," *Global Environment* 10 (2017): 114–137.
- [23] C. S. Barfield and M. E. Swisher, "Integrated Pest Management: Ready for Export?" *Food Reviews International* 10, no. 2 (1994): 215–267, <https://doi.org/10.1080/87559129409540999>.
- [24] J. A. Anderson, P. C. Ellsworth, J. C. Faria, et al., "Genetically Engineered Crops: Importance of Diversified Integrated Pest Management for Agricultural Sustainability," *Frontiers in Bioengineering and Biotechnology* 7 (2019): <https://doi.org/10.3389/fbioe.2019.00024>.
- [25] F. Konradsen, W. van der Hoek, D. C. Cole, et al., "Reducing Acute Poisoning in Developing Countries—Options for Restricting the Availability of Pesticides," *Toxicology* 192, no. 2–3 (2003): 249–261, [https://doi.org/10.1016/s0300-483x\(03\)00339-1](https://doi.org/10.1016/s0300-483x(03)00339-1).
- [26] G. M. W. Lengai, J. W. Muthomi, and E. R. Mbega, "Phytochemical Activity and Role of Botanical Pesticides in Pest Management for Sustainable Agricultural Crop Production," *Scientific African* 7 (2020): <https://doi.org/10.1016/j.sciaf.2019.e00239>.
- [27] Y. Zheng, J. Wang, J. Wang, Y. Li, and Z. Jiang, "Insect Cuticle: A Source of Inspiration for Biomimetic Interface Material Design," *Colloid and Interface Science*

*Communications* 64 (2025): <https://doi.org/10.1016/j.colcom.2025.100818>.

[28] Y. Segall, "Biomimetic Chemistry as a Useful Tool for Studying Reactive Metabolites of Pesticides," *Journal of Agricultural and Food Chemistry* 59, no. 7 (2011): 2845–2856, <https://doi.org/10.1021/jf102262p>.

[29] S. Chakraborty, D. Bera, L. Roy, and C. K. Ghosh, "Biomimetic and Bioinspired Nanostructures," *Bioinspired and Green Synthesis of Nanostructures* (2023): 353–404, <https://doi.org/10.1002/9781394174928.ch15>.

[30] S. Chatterjee, S. Bag, D. Biswal, et al., "Neem-based Products as Potential Eco-Friendly Mosquito Control Agents over Conventional Eco-Toxic Chemical Pesticides-A Review," *Acta Tropica* 240 (2023): <https://doi.org/10.1016/j.actatropica.2023.106858>.

[31] C. Kamaraj, P. R. Gandhi, G. Elango, S. Karthi, I.-M. Chung, and G. Rajakumar, "Novel and Environmental Friendly Approach; Impact of Neem (Azadirachta indica) Gum Nano Formulation (NGNF) on Helicoverpa Armigera (Hub.) and Spodoptera Litura (Fab.)," *International Journal of Biological Macromolecules* 107 (2018): 59–69, <https://doi.org/10.1016/j.ijbiomac.2017.08.145>.

[32] A. Chrustek, I. Hołyńska-Iwan, I. Dziembowska, et al., "Current Research on the Safety of Pyrethroids Used as Insecticides," *Medicina* 54, no. 4 (2018): 61, <https://doi.org/10.3390/medicina54040061>.

[33] S. M. Ensley, "Chapter 39-Pyrethrins and Pyrethroids," *Veterinary Toxicology*, ed. R. C. Gupta (Academic Press 2018), 515–520.

[34] A. Nagar, A. Chatterjee, L. Ur Rehman, A. Ahmad, and S. Tandon, "Comparative Extraction and Enrichment Techniques for Pyrethrins from Flowers of Chrysanthemum Cinerariaefolium," *Industrial Crops and Products* 76 (2015): 955–960, <https://doi.org/10.1016/j.indcrop.2015.07.043>.

[35] R. Garg, A. Bhatt, A. Kumar, Y. C. Tripathi, and R. Kant, "Assessment of Seed and Biochemical Traits in Neem Germplasm for Sustainable Agriculture and Industrial Applications," *Industrial Crops and Products* 222 (2024): <https://doi.org/10.1016/j.indcrop.2024.120018>.

[36] S. Kilani-Morakchi, H. Morakchi-Goudjil, and K. Sifi, "Azadirachtin-Based Insecticide: Overview, Risk Assessments, and Future Directions," *Frontiers in Agronomy* 3 (2021): <https://doi.org/10.3389/fagro.2021.676208>.

[37] S. K. Dara, "The New Integrated Pest Management Paradigm for the Modern Age," *Journal of Integrated Pest Management* 10, no. 1 (2019): 12, <https://doi.org/10.1093/jipm/pmw010>.

[38] K. Bhardwaj, R. Sharma, J. Abraham, and P. Sharma, "Pyrethroids: A Natural Product for Crop Protection," in *Natural Bioactive Products in Sustainable Agriculture*, ed. J. Singh and A. N. Yadav (Springer Singapore, 2020), 113–130.

[39] D. B. Lybrand, H. Xu, R. L. Last, and E. Pichersky, "How Plants Synthesize Pyrethrins: Safe and Biodegradable Insecticides," *Trends in Plant Science* 25, no. 12 (2020): 1240–1251, <https://doi.org/10.1016/j.tplants.2020.06.012>.

[40] M. Stojanovic, "Biomimicry in Agriculture: Is the Ecological System-Design Model the Future Agricultural Paradigm?" *Journal of Agricultural and Environmental Ethics* 32, no. 5–6 (2019): 789–804, <https://doi.org/10.1007/s10806-017-9702-7>.

[41] J. E. Casida and K. A. Durkin, "Pesticide Chemical Research in Toxicology: Lessons from Nature," *Chemical Research in Toxicology* 30, no. 1 (2017): 94–104, <https://doi.org/10.1021/acs.chemrestox.6b00303>.

[42] B. Shu, H. Yu, Y. Li, et al., "Identification of Azadirachtin Responsive Genes in Spodoptera Frugiperda Larvae Based on RNA-Seq," *Pesticide Biochemistry and Physiology* 172 (2021): <https://doi.org/10.1016/j.pestbp.2020.104745>.

[43] X. Huang, X. Tang, A. Liao, W. Sun, L. Lei, and J. Wu, "Application of Cyclopropane with Triangular Stable Structure in Pesticides," *Journal of Molecular Structure* 1326 (2025): <https://doi.org/10.1016/j.molstruc.2024.141171>.

[44] J. Gressel, "Perspective: Present Pesticide Discovery Paradigms Promote the Evolution of Resistance – Learn from Nature and Prioritize Multi-Target Site Inhibitor Design," *Pest Management Science* 76, no. 2 (2020): 421–425, <https://doi.org/10.1002/ps.5649>.

[45] M. C. Gentz, G. Murdoch, and G. F. King, "Tandem Use of Selective Insecticides and Natural Enemies for Effective, Reduced-Risk Pest Management," *Biological Control* 52, no. 3 (2010): 208–215, <https://doi.org/10.1016/j.biocntrol.2009.07.012>.

[46] P. M. Ngegba, G. Cui, M. Z. Khalid, and G. Zhong, "Use of Botanical Pesticides in Agriculture as an Alternative to Synthetic Pesticides," *Agriculture* 12, no. 5 (2022): 600, <https://doi.org/10.3390/agriculture12050600>.

[47] E. O. Fenibo, G. N. Ijoma, and T. Matambo, "Biopesticides in Sustainable Agriculture: A Critical Sustainable Development Driver Governed by Green Chemistry Principles," *Frontiers in Sustainable Food Systems* 5 (2021): <https://doi.org/10.3389/fsufs.2021.619058>.

[48] T. C. Sparks, D. R. Hahn, and N. V. Garizi, "Natural Products, Their Derivatives, Mimics and Synthetic Equivalents: Role in Agrochemical Discovery," *Pest Management Science* 73, no. 4 (2017): 700–715, <https://doi.org/10.1002/ps.4458>.

[49] B. Hofmann, K. Ingold, C. Stamm, et al., "Barriers to Evidence Use for Sustainability: Insights from Pesticide Policy and Practice," *Ambio* 52, no. 2 (2023): 425–439, <https://doi.org/10.1007/s13280-022-01790-4>.

[50] D. T. Agbor, T. T. Oben, L. T. Afoh, et al., "Comparative Study of Botanicals and Synthetic Insecticide on the Control of Insect Pests and Diseases of Cowpea," *International Journal of Agriculture and Environmental Research* 8 (2022): 368–387.

[51] V. Stejskal, T. Vendl, R. Aulicky, and C. Athanassiou, "Synthetic and Natural Insecticides: Gas, Liquid, Gel and Solid Formulations for Stored-Product and Food-Industry Pest Control," *Insects* 12, no. 7 (2021): 590, <https://doi.org/10.3390/insects12070590>.

[52] A. Wasim, H. Bushra, R. Rakhi, and V. Ashish, "Comprehensive Review of the Neem Plant's Attributes and Applications," *International Journal of Research Development and Technology* 1 (2023).

[53] S. J. Boeke, M. G. Boersma, G. M. Alink, et al., "Safety Evaluation of Neem (Azadirachta indica) Derived Pesticides," *Journal of Ethnopharmacology* 94, no. 1 (2004): 25–41, <https://doi.org/10.1016/j.jep.2004.05.011>.

[54] S. Panizzi, N. A. Suciu, and M. Trevisan, "Combined Eco-toxicological Risk Assessment in the Frame of European Authorization of Pesticides," *Science of The Total Environment* 580 (2017): 136–146, <https://doi.org/10.1016/j.scitotenv.2016.10.154>.

[55] S. J. Maund, P. J. Campbell, J. M. Giddings, et al., "Eco-toxicology of Synthetic Pyrethroids," in *Pyrethroids: From Chrysanthemum to Modern Industrial Insecticide*, ed. N. Matsuo and T. Mori (Springer Berlin Heidelberg, 2012), 137–165.

[56] A. De Bernardi, E. Marini, C. Casucci, et al., "Ecotoxicological Effects of a Synthetic and a Natural Insecticide on Earthworms and Soil Bacterial Community," *Environmental Advances* 8 (2022): <https://doi.org/10.1016/j.envadv.2022.100225>.

[57] E. Carazo-Rojas, G. Pérez-Rojas, M. Pérez-Villanueva, et al., "Pesticide Monitoring and Ecotoxicological Risk Assessment in Surface Water Bodies and Sediments of a Tropical Agro-Ecosystem," *Environmental Pollution* 241 (2018): 800–809, <https://doi.org/10.1016/j.envpol.2018.06.020>.

[58] G. M. Gray and J. K. Hammitt, "Risk/Risk Trade-Offs in Pesticide Regulation: An Exploratory Analysis of the Public Health Effects of a Ban on Organophosphate and Carbamate Pesticides," *Risk Analysis* 20, no. 5 (2000): 665–680, <https://doi.org/10.1111/0272-4332.205060>.

[59] C. Grovermann, P. Schreinemachers, S. Riwthong, and T. Berger, "Smart Policies to Reduce Pesticide Use and Avoid Income Trade-Offs: An Agent-Based Model Applied to Thai Agriculture," *Ecological Economics* 132 (2017): 91–103, <https://doi.org/10.1016/j.ecolecon.2016.09.031>.

[60] J. Rosa-Schleich, J. Loos, O. Mußhoff, and T. Tscharntke, "Ecological-economic Trade-Offs of Diversified Farming Systems-A Review," *Ecological Economics* 160 (2019): 251–263, <https://doi.org/10.1016/j.ecolecon.2019.03.002>.

[61] E. G. Allahverdiev, M. Baysaeva, and I. Chigvintseva, "Impact of Biomimicry on the Economics of Green Construction: Cost Reductions and Increased Sustainability," in *International Scientific and Practical Conference "Sustainable Development of the Environment and Agricultural Sector: Innovative and Ecological Technologies"* (SDEA2024) (April 2024).

[62] X. Pan, X. Guo, T. Zhai, et al., "Nanobiopesticides in Sustainable Agriculture: Developments, Challenges, and Perspectives," *Environmental Science: Nano* 10, no. 1 (2023): 41–61, <https://doi.org/10.1039/d2en00605g>.

[63] S. Ali, N. Ahmad, M. A. Dar, et al., "Nano-Agrochemicals as Substitutes for Pesticides: Prospects and Risks," *Plants* 13, no. 1 (2023): 109, <https://doi.org/10.3390/plants13010109>.

[64] P. Baweja, S. Kumar, and G. Kumar, "Fertilizers and Pesticides: Their Impact on Soil Health and Environment," in *Soil Health*, ed. B. Giri and A. Varma (Springer International Publishing, 2020), 265–285.

[65] J. X. F. Sim, B. Drigo, C. L. Doolette, S. Vasileiadis, D. G. Karpouzas, and E. Lombi, "Impact of Twenty Pesticides on Soil Carbon Microbial Functions and Community Composition," *Chemosphere* 307 (2022): <https://doi.org/10.1016/j.chemosphere.2022.135820>.

[66] S. Tripathi, P. Srivastava, R. S. Devi, and R. Bhadouria, "Chapter 2-Influence of Synthetic Fertilizers and Pesticides on Soil Health and Soil Microbiology," *Agrochemicals Detection, Treatment and Remediation*, ed. M. N. V. Prasad (Butterworth-Heinemann2020), 25–54.

[67] M. Shahid and M. S. Khan, "Ecotoxicological Implications of Residual Pesticides to Beneficial Soil Bacteria: A Review," *Pesticide Biochemistry and Physiology* 188 (2022): <https://doi.org/10.1016/j.pestbp.2022.105272>.

[68] I. Goktepe, R. Portier, and M. Ahmedna, "Ecological Risk Assessment of Neem-Based Pesticides," *Journal of Environmental Science and Health, Part B* 39, no. 2 (2004): 311–320, <https://doi.org/10.1081/pfc-120030244>.

[69] A. A. Romeh, "Integrated Pest Management for Sustainable Agriculture," in *Sustainability of Agricultural Environment in Egypt: Part II: Soil-Water-Plant Nexus*, ed. A. M. Negm and M. Abu-hashim (Cham: Springer International Publishing, 2019), 215–234.

[70] A. Awad Fahad, "Modern Techniques in Integrated Pest Management to Achieve Sustainable Agricultural Development," *International Journal of Family Studies, Food Science and Nutrition Health* 4 (2023): 1–14, <https://doi.org/10.21608/ijfsnh.2024.293410.1010>.

[71] F. M. Shah and M. Razaq, "From Agriculture to Sustainable Agriculture: Prospects for Improving Pest Management in Industrial Revolution 4.0," in *Handbook of Smart Materials, Technologies, and Devices: Applications of Industry 4.0*, ed. C. M. Hussain and P. Di Sia (Springer International Publishing, 2020), 1–18.

[72] C. Viegas, A. B. Patrício, J. M. Prata, A. Nadhman, P. K. Chintamaneni, and P. Fonte, "Solid Lipid Nanoparticles vs. Nanostructured Lipid Carriers: A Comparative Review," *Pharmaceutics* 15, no. 6 (2023): 1593, <https://doi.org/10.3390/pharmaceutics15061593>.

[73] R. Saberi Riseh, M. Vatankhah, M. Hassanisaadi, and J. F. Kennedy, "Macromolecules-based Encapsulation of Pesticides with Carriers: A Promising Approach for Safe and Effective Delivery," *International Journal of Biological Macromolecules* 269 (2024): <https://doi.org/10.1016/j.ijbiomac.2024.132079>.

[74] M. Mondéjar-López, M. P. García-Simarro, P. Navarro-Simarro, L. Gómez-Gómez, O. Ahrazem, and E. Niza, "A Review on the Encapsulation of "Eco-friendly" Compounds in Natural Polymer-Based Nanoparticles as Next Generation Nano-Agrochemicals for Sustainable Agriculture and Crop Management," *International Journal of Biological Macromolecules* 280 (2024): <https://doi.org/10.1016/j.ijbiomac.2024.136030>.

[75] Q. Xiong, W. Liang, W. Shang, et al., "Bidirectional Uptake, Transfer, and Transport of Dextran-Based Nanoparticles in Plants for Multidimensional Enhancement of Pesticide Utilization," *Small* 20, no. 8 (2024): e2305693, <https://doi.org/10.1002/smll.202305693>.

[76] A. Singh, N. Dhiman, A. K. Kar, et al., "Advances in Controlled Release Pesticide Formulations: Prospects to Safer Integrated Pest Management and Sustainable Agriculture," *Journal of Hazardous Materials* 385 (2020): <https://doi.org/10.1016/j.jhazmat.2019.121525>.

[77] D. Xiao, H. Wu, Y. Zhang, J. Kang, A. Dong, and W. Liang, "Advances in Stimuli-Responsive Systems for Pesticides Delivery: Recent Efforts and Future Outlook," *Journal of Controlled Release* 352 (2022): 288–312, <https://doi.org/10.1016/j.jconrel.2022.10.028>.

[78] A. Singh, N. Shraogi, R. Verma, et al., "Challenges in Current Pest Management Practices: Navigating Problems and a Way Forward by Integrating Controlled Release System Approach," *Chemical Engineering Journal* 498 (2024): <https://doi.org/10.1016/j.cej.2024.154989>.

[79] Y. Zhao, Y. Zhang, Y. Yan, et al., "pH-Responsive Pesticide-Loaded Hollow Mesoporous Silica Nanoparticles with ZnO Quantum Dots as a Gatekeeper for Control of Rice Blast Disease," *Materials* 17, no. 6 (2024): 1344, <https://doi.org/10.3390/ma17061344>.

[80] W. Zhou, Y. Arcot, R. F. Medina, J. Bernal, L. Cisneros-Zevallos, and M. E. S. Akbulut, "Integrated Pest Management: An Update on the Sustainability Approach to Crop Protection," *ACS Omega* 9, no. 40 (2024): 41130–41147, <https://doi.org/10.1021/acsomega.4c06628>.

[81] R. Chaudhary, A. Nawaz, Z. Khattak, et al., "Microbial Bio-Control Agents: A Comprehensive Analysis on Sustainable

Pest Management in Agriculture," *Journal of Agriculture and Food Research* 18 (2024): <https://doi.org/10.1016/j.jafr.2024.101421>.

[82] S. Kumar, M. Nehra, N. Dilbaghi, G. Marrazza, A. A. Hassan, and K.-H. Kim, "Nano-based Smart Pesticide Formulations: Emerging Opportunities for Agriculture," *Journal of Controlled Release* 294 (2019): 131–153, <https://doi.org/10.1016/j.jconrel.2018.12.012>.

[83] X. Jiang, F. Yang, W. Jia, et al., "Nanomaterials and Nanotechnology in Agricultural Pesticide Delivery: A Review," *Langmuir* 40, no. 36 (2024): 18806–18820, <https://doi.org/10.1021/acs.langmuir.4c01842>.

[84] X. Zhao, H. Cui, Y. Wang, C. Sun, B. Cui, and Z. Zeng, "Development Strategies and Prospects of Nano-Based Smart Pesticide Formulation," *Journal of Agricultural and Food Chemistry* 66, no. 26 (2018): 6504–6512, <https://doi.org/10.1021/acs.jafc.7b02004>.

[85] O. Hamlyn, "Sustainability and the Failure of Ambition in European Pesticides Regulation," *Journal of Environmental Law* 27 (2015): 405–429.

[86] V. Piñeiro, J. Arias, J. Dürr, et al., "A Scoping Review on Incentives for Adoption of Sustainable Agricultural Practices and Their Outcomes," *Nature Sustainability* 3, no. 10 (2020): 809–820, <https://doi.org/10.1038/s41893-020-00617-y>.

[87] T. M. Santos, N. P. Costa, A. L. Torres, and A. L. Boiça Júnior, "Effect of Neem Extract on the Cotton Aphid," *Pesquisa Agropecuária Brasileira* 39, no. 11 (2004): 1071–1076, <https://doi.org/10.1590/s0100-204x2004001100003>.

[88] M. Pathania, J. Kaur, and B. Singh, "Efficacy of Neem Based Formulations against Wheat Aphids under Semi-arid Irrigated Conditions in South-West Punjab," *Indian Journal of Entomology* 85 (2022): 1–4, <https://doi.org/10.55446/ije.2021.134>.

[89] H. S. Shannag, J. L. Capinera, and N. M. Freihat, "Efficacy of Different Neem-Based Biopesticides against Green Peach Aphid, *Myzus persicae* (Hemiptera: Aphididae)," *International Journal of Agricultural Policy and Research* (2014).

[90] O. L. Tobing, Y. Mulyaningsih, and A. D. Safitri, "The Effect of Concentration and Frequency of Neem Leaf Extract on Aphid Attacks on Chili Plants," *Indonesian Journal of Applied Research (IJAR)* 4, no. 2 (2023): 146–158, <https://doi.org/10.30997/ijar.v4i2.329>.

[91] T. Ahmad, R. Khan, T. N. Khattak, I. Ullah, A. Khan, and S. Khan, "Effect of Neem Based Bio-Pesticide on the Aphids, Potato Leafhopper Control and Yield of Potato Crop," *Pakistan Journal of Zoology* 4 (2012): 313–320.

[92] S. K. Ghosh, T. Mandal, and K. Chakraborty, "Efficacy of Chemical Insecticides and Neem Oil against White Fly (*Bemisia Tabaci* Genn.) Infesting Ladysfinger (*Abelmoschus Esculentus* L.)," *International journal of Bio-resource and Stress Management* 4 (2013): 348–351.

[93] G. S. Mann, G. S. Dhaliwal, and A. K. Dhawan, "Field Efficacy of Neem-Based Insecticides against Whitefly and Their Impact on Insect Pest Complex of Cotton," *Pesticide Research Journal* 13 (2001): 79–85.

[94] N. Aggarwal and D. S. Brar, "Effects of Different Neem Preparations in Comparison to Synthetic Insecticides on the Whitefly Parasitoid Encarsia Sophia (Hymenoptera: Aphelinidae) and the Predator Chrysoperla Carnea (Neuroptera: Chrysopidae) on Cotton under Laboratory Conditions," *Journal of Pest Science* 79, no. 4 (2006): 201–207, <https://doi.org/10.1007/s10340-006-0134-9>.

[95] R. Hafeez ur, M. Nadeem, M. Ayyaz, and H. A. Begum, "Comparative Efficacy of Neem Oil and Lambdacyhalothrin against Whitefly (*Bemisia Tabaci*) and Jassid (*Amrasca Devastans* Dist.) in Okra Field," *Russian Agricultural Sciences* 41, no. 2-3 (2015): 138–145, <https://doi.org/10.3103/s1068367415020238>.

[96] R. Kumar, S. Kranthi, V. S. Nagrare, et al., "Insecticidal Activity of Botanical Oils and Other Neem-Based Derivatives against Whitefly, *Bemisia Tabaci* (Gennadius) (Homoptera: Aleyrodidae) on Cotton," *International Journal of Tropical Insect Science* 39, no. 3 (2019): 203–210, <https://doi.org/10.1007/s42690-019-00027-4>.

[97] M. Mamoon-Ur-Rashid, K. Abdullah, H. Ali, M. Tariq, A. N. Shah, and S. Ali, "Response of Cotton Mealybug, *Phenacoccus Solenopsis* Tinsley (Sternorrhyncha: Pseudococcidae) to Predators, Neem Oil, and Synthetic Insecticide under Semi-field and Field Conditions," *International Journal of Tropical Insect Science* 44, no. 4 (2024): 1919–1930, <https://doi.org/10.1007/s42690-024-01294-6>.

[98] H. Aliakbarpour, M. R. Che Salmah, and O. Dzolkhifli, "Efficacy of Neem Oil against Thrips (Thysanoptera) on Mango Panicles and its Compatibility with Mango Pollinators," *Journal of Pest Science* 84, no. 4 (2011): 503–512, <https://doi.org/10.1007/s10340-011-0372-3>.

[99] O. L. Reynolds, T. J. Osborne, and I. Barchia, "Efficacy of Chemicals for the Potential Management of the Queensland Fruit Fly Bactrocera Tryoni (Froggatt) (Diptera: Tephritidae)," *Insects* 8, no. 2 (2017): 49, <https://doi.org/10.3390/insects8020049>.

[100] D. Goh, A. F. Abdull Razis, N. A. Yusof, N. Mazlan, N. Nordin, and C. Y. Yu, "A Review of Emerging Techniques for Pyrethroid Residue Detection in Agricultural Commodities," *Heliyon* 11, no. 1 (2025): <https://doi.org/10.1016/j.heliyon.2024.e41154>.

[101] S. N. Mohd Nizam, N. S. Haji Baharudin, and H. Ahmad, "Application of Pesticide in Paddy Fields: a Southeast Asia Case Study Review," *Environmental Geochemistry and Health* 45, no. 8 (2023): 5557–5577, <https://doi.org/10.1007/s10653-023-01668-8>.

[102] A. Gupta, V. Kumar, S. J. Borah, P. K. Sahu, and N. Dheer, "Science through the Lens of Nature: Recent Advances in Biomimetic Approaches towards Pesticide Degradation," *SynOpen* 07, no. 01 (2023): 33–42, <https://doi.org/10.1055/a-2004-7289>.

[103] A. Weiss, J. E. Dripps, and J. Funderburk, "Assessment of Implementation and Sustainability of Integrated Pest Management Programs," *Florida Entomologist* 92, no. 1 (2009): 24–28, <https://doi.org/10.1653/024.092.0105>.

[104] C. S. F. Souza, L. C. P. Silveira, R. M. Pitta, J. M. Waquil, E. J. G. Pereira, and S. M. Mendes, "Response of Field Populations and Cry-Resistant Strains of Fall Armyworm to Bt Maize Hybrids and Bt-Based Bioinsecticides," *Crop Protection* 120 (2019): 1–6, <https://doi.org/10.1016/j.cropro.2019.01.001>.

[105] P. Witzgall, P. Kirsch, and A. Cork, "Sex Pheromones and Their Impact on Pest Management," *Journal of Chemical Ecology* 36, no. 1 (2010): 80–100, <https://doi.org/10.1007/s10886-009-9737-y>.

[106] I. Pertot, T. Caffi, V. Rossi, et al., "A Critical Review of Plant Protection Tools for Reducing Pesticide Use on Grapevine and New Perspectives for the Implementation of IPM in Viticulture," *Crop Protection* 97 (2017): 70–84, <https://doi.org/10.1016/j.cropro.2016.11.025>.

[107] A. Lucchi and G. Benelli, "Towards Pesticide-free Farming? Sharing Needs and Knowledge Promotes Integrated Pest Management," *Environmental Science and Pollution Research* 25, no. 14 (2018): 13439–13445, <https://doi.org/10.1007/s11356-018-1919-0>.

[108] S. Shakarami, A. Heidari, and M. Arbabi, "Efficacy of the EC 1.28% Formulation of Neem, *Azadirachta indica*, on Two-Spotted Spider Mite, *Tetranychus Urticae* (Acar: Tetranychidae), in Laboratory and Field Conditions," *Journal of Entomological Society of Iran* 34 (2014): 85–93.

[109] L. Kumar and B. S. Parmar, "Effect of Emulsion Size and Shelf Life of Azadirachtin A on the Bioefficacy of Neem (*Azadirachta indica* A. Juss) Emulsifiable Concentrates," *Journal of Agricultural and Food Chemistry* 48, no. 8 (2000): 3666–3672, <https://doi.org/10.1021/jf9911141>.

[110] M. B. Isman, "Chapter 2-Commercialization and Regulation of Botanical Biopesticides: a Global Perspective," *Development and Commercialization of Biopesticides*, ed. O. Koul (Academic Press2023), 25–36.

[111] P. Sola, B. M. Mvumi, J. O. Ogendo, et al., "Botanical Pesticide Production, Trade and Regulatory Mechanisms in Sub-saharan Africa: Making a Case for Plant-Based Pesticidal Products," *Food Security* 6, no. 3 (2014): 369–384, <https://doi.org/10.1007/s12571-014-0343-7>.

[112] O. Koul and S. Wahab, "Neem Biotechnology-A Synthesis," in *Neem: Today and in the New Millennium*, ed. O. Koul and S. Wahab (Dordrecht: Springer Netherlands, 2004), 243–259.

[113] A. R. Ravula and S. Yenugu, "Pyrethroid Based Pesticides – Chemical and Biological Aspects," *Critical Reviews in Toxicology* 51, no. 2 (2021): 117–140, <https://doi.org/10.1080/10408444.2021.1879007>.

[114] M. Galadima, S. Singh, A. Pawar, et al., "Toxicity, Microbial Degradation and Analytical Detection of Pyrethroids: A Review," *Environmental Advances* 5 (2021): <https://doi.org/10.1016/j.envadv.2021.100105>.

[115] V. Pelaez, L. R. da Silva, and E. B. Araujo, "Regulation of Pesticides: A Comparative Analysis," *Science and Public Policy* 40, no. 5 (2013): 644–656, <https://doi.org/10.1093/scipol/sct020>.

[116] S. Chowdhury, K. Kar, and R. Mazumder, "Exploration of Different Strategies of Nanoencapsulation of Bioactive Compounds and Their Ensuing Approaches," *Future Journal of Pharmaceutical Sciences* 10, no. 1 (2024): 72, <https://doi.org/10.1186/s43094-024-00644-y>.

[117] W. A. Khattak, M. W. Ullah, S. Manan, S. U. Islam, W. A. Khattak, and M. Ul-Islam, "Emerging Applications and Future Trends of Agri-Nanotechnology," in *Revolutionizing Agriculture: A Comprehensive Exploration of Agri-Nanotechnology*, ed. R. Shahzad, S. Fiaz, A. Qayyum, M. Ul Islam, and I.-J. Lee (Springer Nature Switzerland, 2024), 429–458.

[118] N. Li, C. Sun, J. Jiang, et al., "Advances in Controlled-Release Pesticide Formulations with Improved Efficacy and Targetability," *Journal of Agricultural and Food Chemistry* 69, no. 43 (2021): 12579–12597, <https://doi.org/10.1021/acs.jafc.0c05431>.

[119] P. Fincheira, N. Hoffmann, G. Tortella, et al., "Eco-Efficient Systems Based on Nanocarriers for the Controlled Release of Fertilizers and Pesticides: Toward Smart Agriculture," *Nanomaterials* 13, no. 13 (2023): 1978, <https://doi.org/10.3390/nano13131978>.

[120] T. Wu, K. Zhao, C. Zhang, et al., "Promising Delivery Platform for Smart Pest Control with High Water-Retaining Capacity," *ACS Applied Materials & Interfaces* 14, no. 49 (2022): 55062–55074, <https://doi.org/10.1021/acsami.2c15737>.

[121] A. S. Baghel, A. S. Baghel, A. Bhardwaj, and W. Ibrahim, "Optimization of Pesticides Spray on Crops in Agriculture Using Machine Learning," *Computational Intelligence and Neuroscience* 2022 (2022): 1–10, <https://doi.org/10.1155/2022/9408535>.

[122] J.-L. Cui, H. Li, Q. He, et al., "Integrating Classic AI and Agriculture: A Novel Model for Predicting Insecticide-Likeness to Enhance Efficiency in Insecticide Development," *Computational Biology and Chemistry* 112 (2024): <https://doi.org/10.1016/j.compbiochem.2024.108113>.

[123] M. W. Mullowney, K. R. Duncan, S. S. Elsayed, et al., "Artificial Intelligence for Natural Product Drug Discovery," *Nature Reviews Drug Discovery* 22, no. 11 (2023): 895–916, <https://doi.org/10.1038/s41573-023-00774-7>.

[124] P. Han, C. Rodriguez-Saona, M. P. Zalucki, S.-s. Liu, and N. Desneux, "A Theoretical Framework to Improve the Adoption of Green Integrated Pest Management Tactics," *Communications Biology* 7, no. 1 (2024): 337, <https://doi.org/10.1038/s42003-024-06027-6>.

[125] K. Chojnacka, "Sustainable Chemistry in Adaptive Agriculture: A Review," *Current Opinion in Green and Sustainable Chemistry* 46 (2024): <https://doi.org/10.1016/j.cogsc.2024.100898>.

[126] A. Raihan, M. Ridwan, and M. S. Rahman, "An Exploration of the Latest Developments, Obstacles, and Potential Future Pathways for Climate-Smart Agriculture," *Climate Smart Agriculture* 1, no. 2 (2024): <https://doi.org/10.1016/j.csag.2024.100020>.

[127] B. D. Gossen and M. R. McDonald, "New Technologies Could Enhance Natural Biological Control and Disease Management and Reduce Reliance on Synthetic Pesticides," *Canadian Journal of Plant Pathology* 42, no. 1 (2020): 30–40, <https://doi.org/10.1080/07060661.2019.1697370>.

[128] R. Nicastro, M. Papale, G. M. Fusco, A. Capone, B. Morrone, and P. Carillo, "Legal Barriers in Sustainable Agriculture: Valorization of Agri-Food Waste and Pesticide Use Reduction," *Sustainability* 16, no. 19 (2024): 8677, <https://doi.org/10.3390/su16198677>.

Copyright © 2025 Mohammad Harun-Ur-Rashid and Abu Bin Imran. Journal of Chemistry published by John Wiley & Sons Ltd. This is an open access article under the terms of the Creative Commons Attribution License (the “License”), which permits use, distribution and reproduction in any medium, provided the original work is properly cited. Notwithstanding the ProQuest Terms and Conditions, you may use this content in accordance with the terms of the License. <https://creativecommons.org/licenses/by/4.0/>