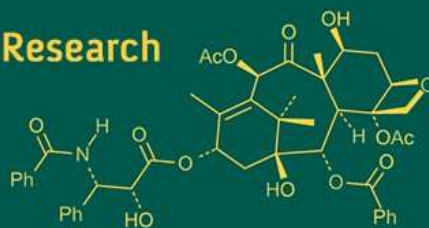
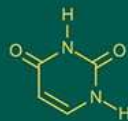
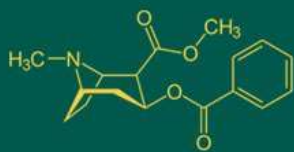


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Antimicrobial resistance in agriculture: Emergence, impact, and sustainable strategies for disease management

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Abstract

Antimicrobial resistance (AMR) has become a major challenge to sustainable agriculture by reducing the effectiveness of conventional plant disease management and threatening food security, environmental health, and public well-being. The indiscriminate use of fungicides, antibiotics, and other antimicrobial agents in crop production has accelerated the emergence of resistant phytopathogens through mechanisms such as target-site mutations, efflux pumps, enzymatic inactivation, biofilm formation, quorum sensing, and horizontal gene transfer. These processes have led to multidrug-resistant pathogen populations, increased disease outbreaks, higher production costs, and greater reliance on chemical inputs. Agricultural ecosystems also serve as important reservoirs of antimicrobial-resistant microorganisms and resistance genes, facilitating their dissemination across plants, animals, humans, and the environment under the One Health framework. This review summarizes the molecular mechanisms, drivers, and agricultural impacts of AMR while highlighting recent advances in sustainable disease management, including antimicrobial stewardship, integrated disease management, biological control, plant-derived antimicrobials, nanotechnology, microbiome engineering, and precision agriculture. Emerging approaches such as RNA interference (RNAi)-based disease control, bacteriophage therapy, genome-edited resistant crops, smart nanoformulations, artificial intelligence-assisted disease forecasting, and One Health surveillance are discussed as promising strategies to reduce antimicrobial dependence and combat resistance.

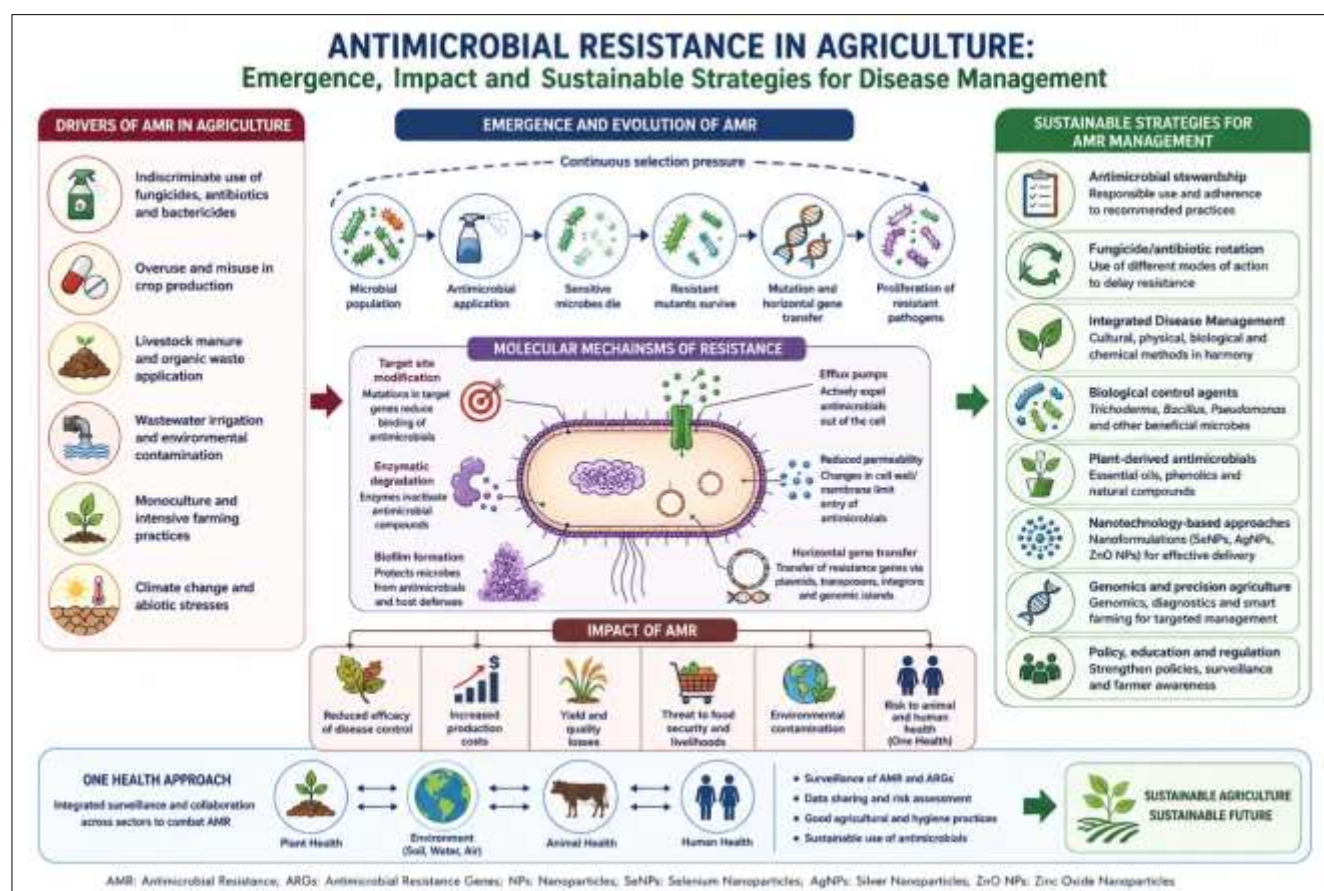
Keywords: Antimicrobial resistance (AMR), Plant disease management, Fungicide resistance, Antibiotic resistance, One Health approach, biological control, Nanotechnology, Precision agriculture

1. Introduction

Antimicrobial resistance (AMR) is one of the major global threats to human, animal, plant, and environmental health (Velazquez-Meza *et al.*, 2022) ^[113]. It refers to the ability of microorganisms, including bacteria and fungi, to survive or proliferate despite exposure to antimicrobial agents that were previously effective against them (Temesgen and Shiferaw, 2025) ^[105]. Resistance can arise through spontaneous genetic mutations or acquisition of resistance determinants through horizontal gene transfer (Temesgen and Shiferaw, 2025) ^[105]. The increasing emergence and dissemination of AMR have reduced the effectiveness of antibiotics, fungicides, and other antimicrobial compounds, resulting in persistent diseases, increased production losses, and substantial economic impacts (Oliveira *et al.*, 2024) ^[81]. Agriculture is an important component of the global AMR problem because antimicrobial agents are widely used to manage bacterial and fungal diseases and maintain crop productivity. Antibiotics such as streptomycin, oxytetracycline, and kasugamycin, and fungicides including azoles, strobilurins (QoIs), benzimidazoles, and succinate dehydrogenase inhibitors (SDHIs), are commonly used for plant disease management (Kilari and Oroszi, 2024) ^[50]. Repeated and inappropriate application of these compounds creates strong selection pressure, allowing resistant microorganisms to survive, multiply, and spread (Endale *et al.*, 2023) ^[29]. Resistance mechanisms include target-site mutations, alteration or overexpression of target proteins, reduced intracellular accumulation, and enhanced efflux of antimicrobial compounds. Consequently, resistance to multiple antimicrobial classes has been reported in economically important phytopathogens, reducing the reliability of conventional disease-control strategies (Shafiq *et al.*, 2025) ^[94].

The agricultural dimension of AMR is closely connected with human, animal, and environmental health and is therefore best understood through a One Health framework (Al-Khalaifah *et al.*, 2025) [2]. Antimicrobial-resistant microorganisms and resistance genes can move between agricultural and other ecosystems through soil, water, food, livestock manure, wildlife, crop residues, and contaminated

environmental reservoirs (Serwecinska, 2020) [93]. Irrigation with contaminated water, antimicrobial residues in agricultural soils, and the application of organic amendments containing resistant microorganisms can contribute to the persistence and dissemination of resistance within Agroecosystems (Iwu *et al.*, 2020) [41].



Plant-associated microbial communities may also act as reservoirs of antimicrobial resistance genes, highlighting the need for coordinated surveillance across plant, animal, human, and environmental sectors (Ifedinezi *et al.*, 2024) [40]. The increasing prevalence of resistant phytopathogens poses a significant threat to sustainable agriculture and global food security (Fones *et al.*, 2020) [31]. Resistance can increase disease incidence and severity, reduce crop yield and quality, raise production and disease-management costs, and limit the availability of effective antimicrobial options (Miller *et al.*, 2022) [72]. The problem is further complicated by climate change, agricultural intensification, and global movement of crops, planting materials, and other agricultural commodities, which can facilitate the emergence and spread of resistant pathogens (EFSA Panel on biological Hazards (BIOHAZ) *et al.*, 2021) [26].

Addressing AMR in agriculture therefore requires a shift from excessive dependence on chemical antimicrobials toward integrated and sustainable disease management. Biological control agents, beneficial microorganisms, antimicrobial peptides, bacteriophages, resistant crop varieties, nanotechnology-based approaches, precision agriculture, and integrated disease management offer promising alternatives for reducing antimicrobial use (Beyari, 2025) [13]. Alongside these approaches, antimicrobial stewardship, resistance surveillance,

appropriate regulation, farmer awareness, and interdisciplinary research are essential for slowing resistance development (Altevogt *et al.*, 2025) [5]. A coordinated One Health approach that integrates plant, animal, human, and environmental health is critical for limiting the emergence and spread of AMR, preserving the effectiveness of existing antimicrobial agents, and ensuring sustainable crop production, environmental protection, and global food security (Altevogt *et al.*, 2025) [5].

Therefore, this review discusses the emergence, mechanisms, and impacts of AMR in agriculture, its implications for crop productivity and food security, and its interconnectedness with human, animal, and environmental health under the One Health framework. It also highlights sustainable strategies, current challenges, and future approaches for effective AMR management in agriculture.

2. Emergence and evolution of antimicrobial resistance in agricultural ecosystems

Agricultural ecosystems provide an ideal environment for the emergence, persistence, and dissemination of antimicrobial resistance (AMR) (Sassi *et al.*, 2025a) [92]. Continuous exposure of microorganisms to antibiotics, fungicides, heavy metals, pesticides, and other environmental contaminants creates strong selective pressure that promotes the survival of resistant microbial

populations (Sonkar *et al.*, 2025) ^[100]. Soil, plant rhizospheres, irrigation water, livestock manure, compost, and agricultural wastewater serve as interconnected reservoirs where antimicrobial-resistant bacteria (ARB) and antimicrobial resistance genes (ARGs) accumulate and circulate (Sassi *et al.*, 2025b) ^[92]. Recent studies emphasize that agricultural environments represent an important component of the global resistome and significantly contribute to the spread of resistance through environmental and food-chain transmission pathways (Ifedinezi *et al.*, 2024) ^[40].

2.1 Evolutionary origins of antimicrobial resistance: The evolutionary origins of antimicrobial resistance (AMR) in agroecosystems can be broadly classified into two categories based on whether resistance traits are inherently present or acquired in response to antimicrobial selection pressure. Intrinsic resistance is a naturally occurring, genetically encoded characteristic of a microbial species that exists prior to antimicrobial exposure (Belay *et al.*, 2024) ^[11]. It results from inherent structural, physiological, or metabolic features, including the absence or modification of antimicrobial targets, low cell-envelope permeability, constitutive multidrug efflux pumps, enzymatic inactivation of antimicrobial compounds, and alternative metabolic pathways. These traits confer natural insensitivity to specific antibiotics or fungicides (Belay *et al.*, 2024) ^[11].

Acquired resistance develops when previously susceptible microorganisms adapt under sustained antimicrobial selection pressure (Temesgen *et al.*, 2025) ^[105]. It arises through two primary mechanisms: (i) spontaneous chromosomal mutations (e.g., mutations in *rpsL* conferring streptomycin resistance or *CYP51* reducing azole sensitivity) and (ii) horizontal gene transfer (HGT), whereby resistance genes are exchanged via plasmids, transposons, integrons, integrative conjugative elements (ICEs), or bacteriophages. Such gene transfer within the soil, rhizosphere, phyllosphere, and irrigation water accelerates the dissemination of resistance across diverse microbial communities (Temesgen *et al.*, 2025) ^[105].

2.2 Selection dynamics and environmental drivers in agroecosystems: Selection pressure is the primary evolutionary force driving the emergence and persistence of antimicrobial resistance (AMR) in agroecosystems. Repeated exposure to antibiotics and fungicides eliminates susceptible microorganisms while favoring resistant variants, enabling their proliferation and eventual dominance within microbial communities (Temesgen *et al.*, 2025) ^[105].

In agricultural systems, selective pressure arises from multiple interconnected sources, including therapeutic and prophylactic antibiotic use in livestock and poultry, application of antibiotics such as streptomycin and oxytetracycline for plant disease management, intensive use of fungicides, including azoles, benzimidazoles, strobilurins (QoIs), and succinate dehydrogenase inhibitors (SDHIs), and the persistence of antimicrobial residues in manure, compost, soil, irrigation water, and agricultural runoff (Enshaie *et al.*, 2025; Miller *et al.*, 2022; Singh *et al.*, 2022) ^[30, 72, 99].

In addition to antimicrobial compounds, non-antibiotic pollutants such as heavy metals (e.g., copper, zinc, cadmium, and mercury), pesticides, and microplastics

contribute to co-selection and cross-resistance, promoting the maintenance and spread of antimicrobial resistance even in the absence of direct antibiotic exposure (Bharadava *et al.*, 2026) ^[14]. These selective pressures facilitate the accumulation of multiple resistance genes on mobile genetic elements, including plasmids and integrons, thereby enhancing horizontal gene transfer and the dissemination of multidrug resistance (Hossain *et al.*, 2026) ^[36]. Consequently, agricultural soils and associated environments serve as persistent reservoirs for antimicrobial resistance genes, contributing to their long-term environmental persistence and spread.

2.3 Mutation as a driver of resistance evolution: Spontaneous mutations are a major driver of antimicrobial resistance evolution. Genetic alterations, including single-nucleotide polymorphisms (SNPs), insertions, deletions, chromosomal rearrangements, and gene amplification, can modify antimicrobial targets, reduce drug uptake, enhance efflux activity, or alter metabolic pathways, thereby decreasing antimicrobial susceptibility (Izydorczyk and church, 2026) ^[42]. For example, mutations in *rpsL* confer streptomycin resistance, while alterations or copy number variations in *CYP51* reduce azole sensitivity. Although these mutations arise at low frequencies, antimicrobial exposure strongly selects for resistant variants, accelerating the evolution and persistence of resistance.

2.4 Horizontal gene transfer: Horizontal gene transfer (HGT) is the primary mechanism driving the rapid dissemination of antimicrobial resistance genes (ARGs) among microorganisms in agricultural ecosystems. Unlike vertical inheritance, HGT enables the direct exchange of genetic material between unrelated microorganisms through transformation, transduction, and conjugation (Michaelis and Grohmann, 2023) ^[71]. Agricultural environments such as manure-amended soils, compost, wastewater, irrigation systems, and root-associated biofilms provide ideal conditions for HGT by supporting high microbial densities and frequent cell-to-cell interactions. Mobile genetic elements, including plasmids, transposons, integrons, and integrative conjugative elements (ICEs), facilitate the acquisition and spread of multiple resistance genes across diverse microbial populations (Ullah *et al.*, 2025a) ^[109]. Recent evidence indicates that biofilms, microplastics, and sub-lethal agrochemical exposure enhance plasmid transfer and stimulate bacterial stress responses, thereby accelerating HGT. Notably, microplastics in the plastisphere have been reported to increase conjugative transfer frequencies by up to 200-fold, while polyethylene microplastics and PVC plastic leachates enhance plasmid conjugation by 8.9-fold and 44.6-fold, respectively (Yang *et al.*, 2025, Ma *et al.*, 2025; Chen *et al.*, 2026) ^[117, 63, 20]. Consequently, agricultural ecosystems act as long-term reservoirs for ARGs, promoting their persistence and dissemination across environmental, plant-, and animal-associated microbiomes.

2.5 Mobile genetic elements: Mobile genetic elements (MGEs) are the principal vehicles for the acquisition and dissemination of antimicrobial resistance genes (ARGs) within and between microbial genomes, playing a central role in the evolution of multidrug-resistant microorganisms (Tokuda and Shintani, 2024) ^[108]. Major MGEs include plasmids, which frequently carry multiple ARGs together

with heavy metal and disinfectant resistance genes; transposons, which mobilize resistance determinants between chromosomes and plasmids; and integrons, particularly Class 1 integrons, which capture, rearrange, and express diverse resistance gene cassettes. Recent advances in metagenomics and long-read sequencing have further identified insertion sequences (ISs), integrative and conjugative elements (ICEs), genomic islands, and bacteriophages as important contributors to ARG dissemination, revealing highly interconnected genetic networks that facilitate resistance exchange across diverse microbial communities (Hossain *et al.*, 2026) [36].

Notably, more than 77% of identified ARGs are associated with MGEs, emphasizing their dominant role in shaping the global resistome. Environmental selective pressures, including antibiotics, heavy metals, pesticides, microplastics, and other contaminants, promote the mobilization and horizontal transfer of these elements, accelerating microbial adaptation and the emergence, persistence, and widespread dissemination of multidrug-resistant populations in Agroecosystems (Zarean *et al.*, 2026) [119].

3. Agricultural practices and environmental factors promoting antimicrobial resistance

Agricultural ecosystems are major reservoirs and transmission hubs for antimicrobial resistance (AMR), where diverse agricultural practices and environmental stressors promote the emergence, persistence, and dissemination of antimicrobial-resistant bacteria (ARB) and antimicrobial resistance genes (ARGs) (Ifedinezi *et al.*, 2024) [40]. The intensive use of fungicides, antibiotics, copper-based bactericides, livestock manure, and wastewater irrigation, together with environmental contaminants such as heavy metals and pesticides, exerts continuous selective pressure on microbial communities, accelerating resistance evolution and horizontal gene transfer (Sui *et al.*, 2026) [101]. Recent metagenomic studies further reveal that manure amended soils, wastewater irrigated fields, and the rhizosphere act as AMR hotspots, while hydrological networks facilitate the movement of resistant microorganisms and ARGs across agricultural landscapes. Consequently, agroecosystems function as interconnected reservoirs linking soil, plants, animals, water, and humans, emphasizing the importance of addressing AMR through an integrated One Health approach.

3.1 Indiscriminate use of fungicides: The intensive and repeated application of fungicides has become a major factor driving the evolution of resistant fungal populations in agricultural systems. Prolonged exposure imposes strong selection pressure, allowing resistant phytopathogens to survive, proliferate, and eventually dominate field populations, thereby reducing fungicide efficacy and increasing the frequency of disease-control failures (Hahn, 2014) [33]. Recent surveillance studies have documented widespread resistance in economically important pathogens, including *Botrytis cinerea*, *Fusarium graminearum*, *Alternaria alternata*, *Zymoseptoria tritici*, *Venturia inaequalis*, and *Magnaporthe oryzae*. Resistance is primarily mediated through target-site mutations (e.g., CYP51, SdhB/C/D, and cytb), overexpression of ATP-binding cassette (ABC) and major facilitator superfamily (MFS) efflux pumps, metabolic detoxification, and biofilm

formation (Javawardana and Fernando, 2024) [45]. A major One Health concern is the extensive use of agricultural demethylation inhibitor (DMI) azoles, which are structurally similar to medical triazoles (Roohi *et al.*, 2026) [88]. Environmental exposure to these fungicides has been linked to the selection of azole-resistant *Aspergillus fumigatus* strains carrying mutations such as TR34/L98H and TR46/Y121F/T289A, compromising the efficacy of clinically important antifungal drugs, including voriconazole and itraconazole (Chowdhary *et al.*, 2013) [22]. Consequently, fungicide resistance has emerged as a significant challenge to both sustainable crop protection and human health.

3.2 Routine application of antibiotics in crop production:

Although antibiotic use in crop production is considerably lower than in livestock, their repeated application for the management of bacterial plant diseases contributes significantly to the emergence and dissemination of antimicrobial resistance (AMR). Antibiotics such as streptomycin, oxytetracycline, kasugamycin, and oxolinic acid are widely used to control pathogens including *Erwinia amylovora*, *Xanthomonas* spp., *Pseudomonas syringae*, and *Candidatus liberibacter* spp. Repeated applications expose environmental microbial communities to sub-lethal antibiotic concentrations, promoting the selection of resistant bacteria and facilitating horizontal transfer of antimicrobial resistance genes (ARGs) (Verhaegen *et al.*, 2023) [114]. Residual antibiotics may persist on plant surfaces, soils, irrigation water, and harvested produce, creating long-term reservoirs for resistance evolution. Recent metagenomic studies further demonstrate that orchard and horticultural systems can enrich the environmental resistome by promoting the exchange of ARGs among soil bacteria, epiphytes, plant-associated microorganisms, and clinically relevant bacteria (Al-Khalaifah *et al.*, 2025) [2]. Moreover, sub-inhibitory antibiotic concentrations and wastewater irrigation enhance bacterial stress responses and horizontal gene transfer, accelerating the emergence of multidrug-resistant populations. These findings highlight the need for responsible antibiotic use in plant agriculture and the adoption of sustainable alternatives to reduce selection pressure while maintaining effective disease management.

3.3 Repeated use of single-site fungicides: Single-site fungicides provide highly effective disease control by targeting specific biochemical pathways in fungal pathogens; however, their site-specific mode of action makes them highly vulnerable to resistance development. Repeated application imposes strong selection pressure, favoring resistant populations carrying mutations in target genes such as cytb (quinone outside inhibitors, QoIs), sdhB/C/D (succinate dehydrogenase inhibitors, SDHIs), β -tubulin (benzimidazoles), and CesA3 (phenylamides), thereby reducing fungicide efficacy (Yin *et al.*, 2023) [118]. In addition, enhanced expression of multidrug efflux pumps contributes to cross-resistance and multidrug resistance in several phytopathogens. Recent resistance monitoring emphasizes that integrated fungicide resistance management, including rotation of fungicides with different modes of action, biological control agents, and cultural practices, is essential to delay resistance evolution and preserve long-term disease control (Hahn, 2014) [33].

3.4 Copper-based bactericides: Copper compounds, including copper hydroxide, copper oxychloride, copper sulfate, and Bordeaux mixture, have been extensively used for more than a century to manage bacterial and fungal diseases (Lamichhane *et al.*, 2018) ^[53]. Their prolonged use has selected copper-resistant populations of plant pathogenic bacteria such as *Xanthomonas*, *Pseudomonas syringae*, and *Erwinia amylovora*. Copper resistance is primarily mediated by plasmid-borne *cop*, *cus*, and *pco* gene clusters encoding copper efflux systems, sequestration proteins, and detoxification mechanisms (Kaur *et al.*, 2024; Husseini *et al.*, 2020) ^[46, 38]. These resistance genes frequently coexist with antibiotic resistance genes on the same plasmids, allowing co-selection, whereby copper exposure indirectly maintains antibiotic resistance even in the absence of antibiotics. Long-term accumulation of copper in agricultural soils also alters microbial diversity, disrupts beneficial soil microbiota, and increases the abundance of mobile genetic elements involved in ARG dissemination. Consequently, copper-based bactericides are now recognized as important environmental drivers of AMR (Hu *et al.*, 2016) ^[37].

3.5 Livestock manure and wastewater irrigation: Livestock manure represents one of the largest environmental reservoirs of antimicrobial-resistant bacteria and resistance genes. Antibiotics administered to food-producing animals are often incompletely metabolized, with substantial proportions excreted in feces and urine together with resistant microorganisms (Endale *et al.*, 2023) ^[29]. A recent farm study revealed that 100% of *E. coli* and 80% of *Klebsiella pneumoniae* isolated from edible leafy vegetables grown in manure-amended soils exhibited severe multi-drug resistance (Abraham *et al.*, 2025) ^[1]. When manure is applied as fertilizer, resistant bacteria, ARGs, antibiotic residues, heavy metals, and mobile genetic elements are introduced into agricultural soils. Wastewater irrigation further amplifies this problem because treated and untreated wastewater frequently contains antibiotics, resistant bacteria, bacteriophages, and residual pharmaceuticals (Jauregi *et al.*, 2021) ^[44]. Research on liquid manure application demonstrated that liquid fertilizer significantly accelerates the vertical migration of a core resistome (comprising 14 ARGs and 5 mobile genetic elements) deep into the soil profile (45-60 cm), subsequently reaching the roots and stems of plants (Li *et al.*, 2025) ^[57]. Traditional on-farm waste treatment practices, such as short-duration composting (under 6 weeks), regularly fail to eliminate antibiotic-resistant bacteria, allowing active drug residues to migrate directly from liquid sludge into solid agricultural fertilizers (Abraham *et al.*, 2025) ^[1]. Metagenomic mapping tracking poultry and cattle manure application confirms a distinct, sequential transmission pathway where 144 unique ARGs successfully migrated across the entire soil-plant continuum moving from bulk soil into the rhizosphere, root endosphere, and ultimately the edible leaf phyllosphere (Liu *et al.*, 2025) ^[61]. Soil exposure studies document that native, non-pathogenic environmental bacteria (such as *Acinetobacter* and *Pseudomonas*) rapidly absorb broad-host-range plasmids (like IncP1) directly from manure microbes. These plasmids serve as highly efficient vectors that transfer resistance against critical clinical antibiotics, including (beta)-lactams, sulfonamides, and tetracyclines (Macedo *et al.*, 2022) ^[64].

3.6 Environmental contamination: Environmental contamination has emerged as a major driver of antimicrobial resistance in agricultural systems. Antibiotic residues, fungicides, pesticides, heavy metals, pharmaceutical effluents, industrial waste, hospital wastewater, and microplastics collectively create complex selective environment that favours resistant microorganisms (Harrelson *et al.*, 2025) ^[34]. Heavy metals such as copper, zinc, mercury, cadmium, and arsenic are particularly important because resistance genes for metals and antibiotics frequently occur on the same mobile genetic elements. This phenomenon, known as co-selection, enables antibiotic resistance to persist even without direct antibiotic exposure (Kumar *et al.*, 2025) ^[51].

Recent studies also identify microplastics as novel ecological niches that facilitate microbial biofilm formation and horizontal gene transfer. These "plastisphere" communities increase microbial interactions and accelerate dissemination of ARGs across agricultural environments. Soil and aquatic ecosystems therefore function as long-term environmental reservoirs that continuously recycle resistance genes between environmental, animal, and human microbial communities (Li *et al.*, 2026) ^[56].

3.7 Climate change and stress-induced adaptation: Climate change accelerates antimicrobial resistance by modifying microbial ecosystems and triggering bacterial survival mechanisms. Rising temperatures directly boost bacterial growth, mutation rates, biofilm formation, and horizontal gene transfer (Kelbrick *et al.*, 2023) ^[48]. At the same time, extreme weather events like floods spread resistance genes across farming landscapes, while droughts select for stress-adapted, resilient microbes. On a cellular level, climate-induced abiotic stress activates bacterial defense pathways such as multidrug efflux pumps and DNA repair systems that promote both transient and stable drug resistance. Consequently, climate change acts as a powerful environmental catalyst for AMR, making climate adaptation vital for agricultural stewardship (Kelbrick *et al.*, 2023) ^[48].

4. Molecular mechanisms of antimicrobial resistance

Antimicrobial resistance (AMR) operates as a highly coordinated, multifactorial defense network rather than a single genetic accident. Driven by continuous exposure to agricultural chemicals like antibiotics, fungicides, and heavy metals, microorganisms survive by combining spontaneous genetic mutations with the rapid uptake of external resistance genes (Salam *et al.*, 2023) ^[90]. Advanced multi-omics technologies show that when confronted with environmental stress, microbes simultaneously activate multiple molecular pathways, adjusting their gene expression, protein structures, and physiological defenses in real time (Nkuna *et al.*, 2026) ^[80]. This sophisticated, multi-layered adaptation accelerates the evolution of highly resilient pathogens, highlighting the urgent need for new disease management strategies that can disrupt these combined bacterial defense systems (Hossain *et al.*, 2025) ^[36].

4.1 Target-site mutations: Target-site modification is one of the most common mechanisms through which microorganisms develop resistance. Most antimicrobial compounds exert their activity by binding to specific proteins or enzymes that are essential for microbial growth

and survival. Mutations within the genes encoding these targets reduce the affinity of the antimicrobial molecule while allowing the target protein to retain its normal biological function (Temesgen *et al.*, 2025) ^[105]. In fungal pathogens, resistance to benzimidazole fungicides frequently results from mutations in the β -tubulin gene, whereas resistance to quinone outside inhibitors (QoIs) is commonly associated with mutations in the mitochondrial cytochrome b (cytb) gene, particularly the G143A substitution. Similarly, mutations in succinate dehydrogenase (sdhB, sdhC, and sdhD) genes confer resistance to succinate dehydrogenase inhibitor (SDHI) fungicides (Yin *et al.*, 2023) ^[118]. In bacterial pathogens, alterations in ribosomal proteins, RNA polymerase, DNA gyrase, and topoisomerase IV reduce susceptibility to several antibiotic classes. Driven by adaptive evolution, microorganisms can accumulate multiple target-site mutations simultaneously, leading to elevated multidrug resistance with minimal fitness costs that allow these resilient populations to persist long-term even in the absence of antimicrobial pressure (Tahmasebi *et al.*, 2025) ^[102].

4.2 Efflux pumps: Efflux pumps are specialized membrane-associated transport proteins that actively expel toxic compounds from microbial cells, reducing intracellular drug concentrations below inhibitory levels to allow pathogen survival (Van Acker and Coenye, 2016) ^[112]. Across several major families including the ATP-binding cassette (ABC) transporters, major facilitator superfamily (MFS) transporters, resistance-nodulation-division (RND) pumps, multidrug and toxic compound extrusion (MATE) transporters, and small multidrug resistance (SMR) proteins. ABC, MFS, RND, MATE, and SMR transporters these pumps serve as a crucial defense mechanism against diverse antimicrobial agents. In major plant-damaging fungi like *Botrytis cinerea*, *Fusarium graminearum*, and *Magnaporthe oryzae*, the overexpression of ABC and MFS transporters drives broad multidrug resistance across multiple fungicide classes (Li, 2017) ^[58]. Controlled by global transcription factors linked to environmental adaptation, efflux pump genes trigger rapidly under antimicrobial stress, and because their broad structural binding pockets recognize unrelated compounds, a single pump system can simultaneously neutralize an array of antibiotics, fungicides, and metabolic toxins (Li and Nikaido, 2009) ^[59].

4.3 Enzymatic degradation and antimicrobial modification: Many microorganisms neutralize antimicrobial agents through enzymatic degradation or chemical modification before the compounds reach their cellular targets (Temesgen *et al.*, 2025) ^[105]. This mechanism is particularly important in bacterial resistance. β -lactamases hydrolyze the β -lactam ring of penicillins and cephalosporins, rendering these antibiotics inactive. Aminoglycoside-modifying enzymes catalyze acetylation, phosphorylation, or adenylation reactions that prevent antibiotic binding to ribosomes. Chloramphenicol acetyltransferases similarly inactivate chloramphenicol through enzymatic acetylation (Elshobary *et al.*, 2025) ^[28]. In agricultural ecosystems, resistance genes encoding these enzymes are frequently located on plasmids, transposons, or integrons, facilitating rapid dissemination through horizontal gene transfer (Avilaran and Kilonzo-Nthenge, 2026) ^[7]. Recent metagenomic studies have identified numerous

previously uncharacterized antimicrobial-inactivating enzymes within agricultural soils, suggesting that environmental microorganisms constitute an extensive reservoir of resistance determinants capable of emerging in pathogenic populations (Lau *et al.*, 2017) ^[54].

4.4 Reduced membrane permeability: Reduced antimicrobial uptake represents another important resistance mechanism. Microorganisms can alter their cell envelope to restrict antimicrobial entry, thereby lowering intracellular drug concentrations (Elshobary *et al.*, 2025) ^[28]. Gram-negative bacteria commonly modify or downregulate outer membrane porins, reducing diffusion of antibiotics into the cell. Alterations in membrane lipid composition, changes in cell wall architecture, and increased production of extracellular polysaccharides further decrease membrane permeability (Zhou *et al.*, 2023) ^[120]. Fungal pathogens likewise modify cell wall components, including chitin, glucans, and melanin, creating physical barriers that reduce fungicide penetration. Recent studies indicate that membrane remodeling often occurs together with enhanced efflux activity, producing synergistic resistance that significantly decreases antimicrobial efficacy (Mohanty *et al.*, 2026) ^[73].

4.5 Biofilm formation: Biofilms are highly organized microbial communities embedded within a self-produced extracellular polymeric matrix composed of polysaccharides, proteins, extracellular DNA, and lipids. Biofilm formation provides microorganisms with enhanced protection against antimicrobial agents, host defenses, and environmental stresses (Sharma *et al.*, 2019) ^[96]. Within biofilms, antimicrobial penetration is limited by the extracellular matrix, while nutrient and oxygen gradients create metabolically inactive persister cells that exhibit increased antimicrobial tolerance (Uruen *et al.*, 2020) ^[111]. Biofilms also facilitate horizontal gene transfer by maintaining close cellular proximity and protecting extracellular DNA from degradation (Lutsenko *et al.*, 2025) ^[62]. Plant pathogenic bacteria including *Pseudomonas syringae*, *Xanthomonas* spp., and *Erwinia amylovora*, as well as several fungal pathogens, rely on biofilm formation for successful colonization of plant surfaces and vascular tissues (Carezzano *et al.*, 2023) ^[17]. Recent microscopic and molecular studies demonstrate that biofilm-associated microorganisms can tolerate antimicrobial concentrations many times higher than planktonic cells, making biofilm disruption an important target for future disease management strategies (Almatroudi, 2025) ^[3].

4.6 Quorum sensing: Quorum sensing (QS) is a cell-density-dependent communication network where microorganisms use small signaling molecules called autoinducers to coordinate population-wide gene expression once a threshold concentration is reached. This synchronized system regulates critical survival mechanisms, including motility, secretion systems, virulence factor production, biofilm development, and direct antimicrobial tolerance pathways (Papaneophytou, 2026) ^[82]. While Gram-negative bacteria primarily communicate using acyl-homoserine lactones (AHLs), Gram-positive bacteria rely on peptide-based autoinducers to trigger these changes. Notably, QS networks directly enhance drug defense by activating multidrug efflux pumps, stimulating extracellular

polymer production for biofilms, and upregulating oxidative stress defenses during chemical exposure (Cui and Kim, 2024) ^[24]. Because this system controls virulence rather than basic cell survival, quorum sensing inhibitors have emerged as a promising management strategy to suppress pathogen damage without imposing the strong evolutionary selection pressure that drives traditional drug resistance (Das *et al.*, 2026) ^[25].

4.7 Cross-resistance and multidrug resistance: Cross-resistance and multidrug resistance (MDR) represent distinct genetic and physiological strategies that allow pathogens to survive exposure to multiple chemical treatments. Cross-resistance occurs when a singular defense mechanism such as a specific target-site mutation confers reduced susceptibility to multiple antimicrobial compounds that share the same chemical class or mode of action (Catalano *et al.*, 2022) ^[18]. In contrast, multidrug resistance describes a pathogen's ability to withstand structurally unrelated antimicrobial agents through the simultaneous deployment of distinct mechanisms, including target-site alterations, efflux pump overexpression, reduced membrane permeability, and enzymatic inactivation (Elshobary *et al.*, 2025) ^[28]. In agricultural ecosystems, this problem is compounded by mobile genetic elements such as plasmids, transposons, and integrons that carry tightly clustered resistance genes alongside determinants for disinfectant resistance and heavy metal tolerance (Sanchez-Corona *et al.*, 2025) ^[91].

5. Influence of Antimicrobial Resistance (AMR) on agriculture

AMR has emerged as a major constraint to sustainable agricultural production by reducing the effectiveness of disease management strategies and increasing the prevalence of difficult-to-control plant pathogens (Mehmood *et al.*, 2025) ^[69]. The widespread occurrence of resistant microorganisms threatens crop productivity, food security, environmental health, and the economic sustainability of farming systems (Singh *et al.*, 2023) ^[98]. Recent studies employing genomic surveillance, metagenomics, and resistance monitoring have demonstrated that AMR affects not only individual pathogens but also the broader agricultural ecosystem through alterations in microbial communities and enhanced dissemination of antimicrobial resistance genes (ARGs) (Chigozie *et al.*, 2025) ^[121]. Consequently, AMR is now recognized as a critical component of the One Health framework, linking plant, animal, human, and environmental health.

5.1 Reduced efficacy of fungicides and antibiotics

(A) Loss of disease control: The primary and immediate consequence of antimicrobial resistance is a sharp decline in the effectiveness of fungicides and antibiotics, causing widespread field failures and reduced crop disease control (Miller *et al.*, 2022) ^[72]. When pathogen populations develop resistance, standard recommended doses fail to suppress them, a problem that accelerates rapidly when farmers repeatedly apply single-mode-of-action chemicals. This erosion of efficacy spans major fungicide classes including benzimidazoles, quinone outside inhibitors (QoIs), succinate dehydrogenase inhibitors (SDHIs), demethylation inhibitors (DMIs), and phenylamides as well as critical

bacterial antibiotics like streptomycin, oxytetracycline, and kasugamycin (Muteeb *et al.*, 2023) ^[75]. As these standard chemical options lose their potency, integrated disease management programs are severely compromised, leaving high-value fruits, vegetables, and ornamental crops vulnerable to catastrophic disease outbreaks when environmental conditions favor the pathogens.

(B) Increased survival of resistant pathogens: Antimicrobial-resistant pathogens survive chemical treatments that normally eliminate susceptible populations, allowing them to reproduce, colonize host tissues, and rapidly spread across agricultural fields (Endale *et al.*, 2023) ^[29]. Because routine antimicrobial applications preferentially eliminate susceptible competitors while selecting for these hardy variants, resistant strains quickly become the dominant population over time. This high survival rate spikes inoculum levels between growing seasons, which severely complicates future disease control by ensuring fields are heavily infested before a new crop is even planted. Long-term monitoring studies demonstrate that these resistant populations can remain highly stable for many years even after a specific antimicrobial compound is completely withdrawn particularly when the underlying resistance mechanisms impose minimal fitness costs on the pathogen (Endale *et al.*, 2023) ^[29].

5.2 Difficulties in plant disease management

(A) Higher application rates: When antimicrobial sensitivity declines, farmers often respond by increasing fungicide or antibiotic dosages to restore disease control, but this strategy rarely eliminates highly resistant strains and instead intensifies selection pressure to accelerate further resistance evolution (Manyi-Loh *et al.*, 2018) ^[66]. While higher application rates might temporarily suppress partially resistant populations, the practice ultimately fails against highly resilient mutants while dramatically escalating overall farm production costs. Furthermore, this excessive chemical use drives severe environmental contamination and leads to the dangerous accumulation of pesticide residues within local agricultural ecosystems (Manyi-Loh *et al.*, 2018) ^[66].

(B) Increased frequency of spraying: To compensate for declining product efficacy, growers frequently shorten their application schedules and increase the frequency of antimicrobial sprays throughout the cropping season raising operational costs and environmental chemical exposure. However, repeated applications intensify selection pressure, promoting resistant pathogen populations and creating a self-reinforcing cycle that progressively reduces disease control effectiveness. For example, azole fungicides target the single CYP51 enzyme, and repeated applications can intensify selection pressure, favoring resistant fungal populations and further reducing disease control efficacy (Rai *et al.*, 2025) ^[84].

(C) Shortened lifespan of antimicrobial products: Resistance can rapidly reduce the useful lifespan of fungicides and antibiotics as resistant pathogen populations spread. For example, azole fungicides may lose effectiveness when resistant fungi with altered CYP51 accumulate. Developing new antimicrobial compounds requires extensive research, regulatory approval, and

substantial investment, often allowing resistance to emerge faster than new disease-control products can reach farmers (Rai *et al.*, 2025) ^[84].

(D) Increased production costs: Antimicrobial resistance significantly drives up agricultural production costs by forcing farmers to spend more on expensive pesticides, repeated spray applications, intensive disease monitoring, resistant cultivar development, extra labor, and complex integrated disease management practices (Miller *et al.*, 2022) ^[72]. It also causes economic losses through reduced crop yields, poor produce quality, and post-harvest decay. Smallholder farmers are particularly affected, as rising production costs reduce farm profitability and threaten rural livelihoods (Miller *et al.*, 2022) ^[72].

5.3 Emergence of multidrug-resistant plant pathogens

One of the most concerning consequences of AMR is the emergence of multidrug-resistant (MDR) plant pathogens that exhibit reduced sensitivity to multiple antimicrobial compounds with different modes of action (Salam *et al.*, 2023) ^[90]. These pathogens often possess combinations of target-site mutations, multidrug efflux pumps, enzymatic detoxification systems, reduced membrane permeability, and resistance genes carried on mobile genetic elements (Salam *et al.*, 2023) ^[90].

(A) *Botrytis cinerea*: *Botrytis cinerea*, the causal agent of gray mold, has developed resistance to numerous fungicide classes, including benzimidazoles, dicarboximides, anilinopyrimidines, hydroxylanilides, QoIs, SDHIs, and DMIs (Thind, 2022) ^[107]. Many field populations exhibit multidrug resistance associated with enhanced expression of ATP-binding cassette (ABC) and major facilitator superfamily (MFS) efflux transporters, making disease control increasingly difficult in fruits, vegetables, and ornamentals.

(B) *Magnaporthe oryzae*: *Magnaporthe oryzae*, the rice blast pathogen, is one of the most destructive fungal pathogens affecting global rice production. Resistance

to QoI fungicides, tricyclazole, and several other fungicides has been associated with mutations in target genes and adaptive stress-response mechanisms (Tan *et al.*, 2023) ^[103]. The continual evolution of resistant populations threatens the long-term sustainability of rice disease management, particularly in regions with intensive fungicide use.

(C) *Rhizoctonia solani*: *Rhizoctonia solani* causes sheath blight, damping-off, and root rot in numerous crops. Resistance has been documented against several SDHI fungicides and other site-specific compounds following repeated field applications. Because *R. solani* survives for extended periods as sclerotia in soil, resistant populations may persist between cropping seasons, increasing disease pressure (Nizamani *et al.*, 2025) ^[79].

(D) *Fusarium spp.*: Species of *Fusarium* are responsible for vascular wilts, root rots, ear rot, and mycotoxin contamination in many crops. Resistance to benzimidazoles, DMIs, and other fungicide groups has been reported in several species. Their genetic diversity, broad host range, and ability to survive in soil and crop residues facilitate the persistence and spread of resistant populations (Neves *et al.*, 2026) ^[78].

(E) *Xanthomonas spp.*: Several species of *Xanthomonas* have evolved resistance to streptomycin and copper-based bactericides through the acquisition of plasmid-borne resistance genes. The coexistence of copper and antibiotic resistance determinants on mobile genetic elements contributes to co-selection, complicating disease management in citrus, tomato, pepper, rice, and numerous horticultural crops (Bhosale *et al.*, 2025) ^[15].

(F) *Pseudomonas syringae*: *Pseudomonas syringae* has developed resistance to streptomycin, oxytetracycline, and copper compounds in several agricultural production systems. Resistance genes carried on conjugative plasmids enable rapid dissemination among bacterial populations, reducing the effectiveness of conventional bacterial disease control strategies (Behlau *et al.*, 2012) ^[10].

Table 1: Major multidrug-resistant plant pathogens and their resistance characteristics

Plant pathogen	Major diseases	Antimicrobial/fungicide resistance reported	Major resistance mechanisms	Critical impact	References
<i>Botrytis cinerea</i>	Gray mold	Benzimidazoles, dicarboximides, anilinopyrimidines, hydroxylanilides, QoIs, SDHIs and DMIs	Target-site mutations; ABC and MFS efflux pumps	Multidrug resistance complicates control in fruits, vegetables and ornamentals	Calidonio <i>et al.</i> , 2025; Leroux <i>et al.</i> , 2010; Raorane <i>et al.</i> , 2022
<i>Magnaporthe oryzae</i>	Rice blast	QoI fungicides, tricyclazole and other fungicides	Target-gene mutations and adaptive stress-response mechanisms	Threatens sustainable rice disease management	Ceresini <i>et al.</i> , 2024; Peng <i>et al.</i> , 2022
<i>Rhizoctonia solani</i>	Sheath blight, damping-off and root rot	SDHI fungicides and other site-specific fungicides	Resistance selection following repeated applications; persistence through sclerotia	Resistant populations may survive between cropping seasons	Nizamani <i>et al.</i> , 2022
<i>Fusarium spp.</i>	Vascular wilt, root rot, ear rot and mycotoxin contamination	Benzimidazoles, DMIs and other fungicide groups	Genetic diversity and adaptation; survival in soil and crop residues	Promotes persistence and spread of resistant populations	Naqvi <i>et al.</i> , 2025; Neves <i>et al.</i> , 2026
<i>Xanthomonas spp.</i>	Diseases of citrus, tomato, pepper, rice and other crops	Streptomycin and copper-based bactericides	Plasmid-borne resistance genes; mobile genetic elements and co-selection	Copper and antibiotic resistance can spread together	Bhosale <i>et al.</i> , 2025; Lingaraj <i>et al.</i> , 2025
<i>Pseudomonas syringae</i>	Bacterial diseases in diverse crops	Streptomycin, oxytetracycline and copper compounds	Resistance genes carried on conjugative plasmids	Rapid dissemination reduces effectiveness of conventional bactericides	Cordova <i>et al.</i> , 2023; Sharma <i>et al.</i> , 2022

QoIs: Quinone outside inhibitors; SDHIs: Succinate dehydrogenase inhibitors; DMIs: Demethylation inhibitors

5.4 Crop yield and quality losses

(A) Reduced productivity: Ineffective control of antimicrobial-resistant (AMR) pathogens increases disease incidence and severity, resulting in reduced plant growth, impaired photosynthesis, poor nutrient uptake, and yield losses (Miller *et al.*, 2022) ^[72].

(B) Economic losses: AMR increases disease management costs while reducing marketable yield and product quality. It also increases the need for alternative control measures and places additional financial burdens on farmers and plant protection programs (Hinchliffe *et al.*, 2018) ^[35].

(C) Food security implications: Resistant plant pathogens threaten food security by reducing crop production, increasing food prices, and disrupting agricultural supply chains. Effective disease management is therefore essential for sustainable and secure food production (Rizzo *et al.*, 2021) ^[87].

5.5 Environmental and public health consequences

(A) Dissemination of antimicrobial resistance genes: Agricultural environments have become important reservoirs of antimicrobial resistance genes (ARGs). Soil, irrigation water, livestock manure, compost, crop residues, and wastewater facilitate the movement of resistant microorganisms between environmental, plant-associated, animal-associated, and human-associated microbial communities. Horizontal gene transfer mediated by plasmids, transposons, integrons, bacteriophages, and other mobile genetic elements accelerates the dissemination of ARGs across diverse microbial populations (Ibekwe *et al.*, 2023) ^[39].

(B) Soil microbiome disruption: Repeated application of antimicrobial compounds alters soil microbial diversity by suppressing beneficial microorganisms involved in nutrient cycling, nitrogen fixation, phosphorus solubilization, organic matter decomposition, and biological control of pathogens (Ullah *et al.*, 2025a) ^[109]. Disturbances in microbial community structure may reduce soil fertility, ecosystem resilience, and the natural suppression of plant diseases. Long-term ecological imbalance can therefore decrease both agricultural productivity and environmental sustainability (Ullah *et al.*, 2025b) ^[110].

(C) Transfer of resistance genes through the food chain: Resistant bacteria and antimicrobial resistance genes may move from agricultural environments to humans through contaminated vegetables, fruits, irrigation water, soil particles, livestock products, and environmental exposure (Wang *et al.*, 2025) ^[115]. Plant-associated microorganisms can serve as intermediate reservoirs that facilitate the exchange of resistance genes with human and animal pathogens. Although direct transfer frequencies vary among production systems, increasing evidence indicates that agricultural ecosystems contribute to the environmental circulation of resistance determinants (Wang *et al.*, 2025) ^[115].

(D) One health implications: The influence of AMR extends far beyond crop production. Human health, veterinary medicine, environmental quality, and agricultural sustainability are closely interconnected through the movement of resistant microorganisms and antimicrobial resistance genes. Resistant pathogens originating in one sector may ultimately affect the others through shared environmental reservoirs, food systems, and water resources (Al-Khalaifah *et al.*, 2025) ^[2]. Therefore, effective

management of AMR requires coordinated surveillance, antimicrobial stewardship, integrated disease management, environmental monitoring, and international collaboration under the One Health framework (Al-Khalaifah *et al.*, 2025) ^[2]. Such multidisciplinary approaches are essential for preserving antimicrobial efficacy, protecting ecosystem health, and ensuring sustainable agricultural production for future generations.

6. Why treatments are becoming increasingly ineffective

The effectiveness of agricultural antimicrobial compounds has declined due to the rapid evolution and spread of antimicrobial resistance (AMR) (Muteeb *et al.*, 2023) ^[75]. Repeated and indiscriminate use of fungicides and antibiotics creates strong selection pressure, allowing resistant pathogens to survive, multiply, and spread (Muteeb *et al.*, 2023) ^[75]. Genetic mutations, horizontal gene transfer, and intensive agricultural practices further accelerate resistance, making disease management increasingly difficult.

6.1 Continuous exposure creates strong selection pressure:

Repeated application of fungicides and antibiotics eliminates susceptible microorganisms while allowing naturally resistant individuals to survive (Kelbrick *et al.*, 2026) ^[47]. These survivors reproduce and gradually increase in frequency. Frequent spraying, prophylactic treatments, monocropping, and repeated use of compounds with similar modes of action further intensify selection pressure and accelerate resistance development (Kelbrick *et al.*, 2026) ^[47].

6.2 Elimination of susceptible microorganisms and survival of resistant strains:

Antimicrobial treatments generally do not eliminate all pathogens. Resistant variants survive treatment, continue to infect plants, reproduce, and spread. Over successive cropping seasons, their proportion increases, eventually making previously effective fungicides or antibiotics less effective (Elbaiomy *et al.*, 2025) ^[27].

6.3 Expansion and dominance of resistant populations:

Resistant pathogens gain a competitive advantage after antimicrobial application and can rapidly increase through repeated cycles of survival and reproduction (Bengtsson-Palme *et al.*, 2018) ^[12]. High reproductive capacity, spore production, environmental persistence, and dispersal through soil, crop residues, water, seeds, and agricultural activities facilitate their establishment and spread across fields and regions (Bengtsson-Palme *et al.*, 2018) ^[12].

6.4 Accumulation of new mutations:

Spontaneous mutations can alter antimicrobial targets, regulatory pathways, membrane properties, or stress-response mechanisms, reducing susceptibility. Under antimicrobial selection, beneficial mutations are retained and may accumulate, producing progressively higher levels of resistance. Multiple mutations and genomic changes can contribute to multidrug resistance (Muteeb *et al.*, 2023) ^[75].

6.5 Horizontal gene transfer accelerates resistance spread:

Microorganisms can acquire resistance genes through horizontal gene transfer (HGT), including transformation, transduction, and conjugation. Resistance determinants carried by plasmids, transposons, and

integrons can spread rapidly among microbial populations in soil, plant surfaces, irrigation water, manure, wastewater, and biofilms (Wu *et al.*, 2025) ^[116]. HGT can also transfer multiple resistance genes simultaneously, promoting multidrug resistance (Tao *et al.*, 2022) ^[104].

6.6 Declining effectiveness of antimicrobial compounds:

The combined effects of selection pressure, survival of resistant strains, mutation, and HGT progressively reduce antimicrobial efficacy, resulting in inconsistent disease control and increased crop losses (Miller *et al.*, 2022) ^[72]. Increasing application rates or spray frequency may provide temporary control but can further accelerate resistance. Therefore, integrated disease management, biological control, resistant cultivars, precision agriculture, antimicrobial stewardship, and resistance monitoring are essential for maintaining the effectiveness of available antimicrobial compounds (Oliveira *et al.*, 2024) ^[81].

7. Sustainable strategies to overcome Antimicrobial Resistance

The increasing prevalence of antimicrobial resistance (AMR) highlights the need for sustainable disease management strategies that reduce dependence on chemical antimicrobials while maintaining crop productivity (Baweja *et al.*, 2025) ^[8]. No single approach can effectively manage resistant pathogens; therefore, integrated strategies combining antimicrobial stewardship, biological control, microbiome engineering, RNAi-based disease control, bacteriophage therapy, genome-edited resistant crops, smart nanoformulations, AI-assisted disease forecasting, precision agriculture, and One Health surveillance are essential. Together with genomics, resistance monitoring, and supportive regulatory policies, these approaches can reduce antimicrobial use, slow resistance evolution, and promote sustainable agriculture (Jacobowski *et al.*, 2025) ^[43].

7.1 Antimicrobial stewardship in agriculture:

Antimicrobial stewardship promotes the judicious use of fungicides and antibiotics based on accurate diagnosis, disease thresholds, and appropriate dose, timing, and application methods. Resistance monitoring and adherence to recommended guidelines help minimize unnecessary selection pressure (McKernan *et al.*, 2021) ^[68].

7.2 Fungicide and antibiotic rotation: Rotating antimicrobials with different modes of action reduces selection for resistant pathogens. Consecutive use of the same chemical group should be avoided. Alternating different FRAC groups and combining single-site fungicides with multi-site protectants, where appropriate, can help preserve antimicrobial efficacy (Beckie *et al.*, 2021) ^[9].

7.3 Integrated Disease Management (IDM): IDM combines cultural, biological, genetic, and chemical approaches, including crop rotation, field sanitation, disease-free planting material, resistant cultivars, balanced nutrition, proper irrigation, and disease monitoring. This reduces pathogen pressure and dependence on antimicrobials (Zhou *et al.*, 2024) ^[121].

7.4 Biological control agents: Beneficial microorganisms such as *Trichoderma*, *Bacillus*, *Pseudomonas*, and *Streptomyces* suppress pathogens through antibiosis, competition, mycoparasitism, lytic enzymes, biofilm

disruption, and induction of systemic resistance. Their multiple modes of action can reduce the risk of resistance development (Lahlali *et al.*, 2022) ^[52].

7.5 Plant derived antimicrobials: Essential oils, phenolics, flavonoids, alkaloids, tannins, terpenoids, and antimicrobial peptides possess broad-spectrum activity against plant pathogens. Their action on multiple cellular targets may reduce resistance development, while nano-formulations can improve their stability and efficacy (McClements *et al.*, 2021) ^[67].

7.6 Nanotechnology based disease management:

Nanoparticles such as selenium, silver, zinc oxide, and chitosan nanoparticles exhibit antimicrobial activity through reactive oxygen species generation, membrane disruption, metabolic interference, and biofilm inhibition (Baweja *et al.*, 2025) ^[8]. Controlled-release formulations can improve delivery, reduce application frequency, and minimize environmental exposure (AlQurashi *et al.*, 2025) ^[4].

7.7 Microbiome engineering:

Manipulation of beneficial rhizosphere and endophytic microbial communities through microbial inoculants, synthetic consortia, and soil microbiome management can enhance nutrient acquisition, pathogen competition, plant immunity, and disease resistance while reducing antimicrobial dependence (Mahmud *et al.*, 2021) ^[65].

7.8 Genomics and precision agriculture:

Whole-genome sequencing and metagenomics enable detection and monitoring of resistance mutations and antimicrobial resistance genes. CRISPR-based diagnostics, artificial intelligence, remote sensing, drones, and precision agriculture can support early disease detection and targeted antimicrobial application, reducing unnecessary chemical use (Sherry *et al.*, 2025) ^[97].

7.9 RNA Interference (RNAi)-based disease control:

RNA interference (RNAi) is a sequence-specific approach for controlling plant pathogens and pests through the use of double-stranded RNA (dsRNA). After uptake by the target organism, dsRNA is processed into small interfering RNAs (siRNAs), which recognize complementary messenger RNA (mRNA) sequences and promote their degradation. Silencing essential genes can thereby disrupt pathogen growth, virulence, or survival without modifying the target organism's genome (Morozov *et al.*, 2019) ^[74]. Because RNAi can be designed against highly specific gene sequences, it has the potential to minimize effects on non-target and beneficial organisms. Its biodegradable and targeted nature also makes RNAi a promising alternative for reducing dependence on conventional chemical antimicrobials (Morozov *et al.*, 2019) ^[74].

7.10 Bacteriophage therapy:

Bacteriophages are viruses that specifically infect bacteria and can be exploited as biological agents against bacterial plant and animal pathogens (Sahu *et al.*, 2023) ^[89]. Following attachment to susceptible bacterial cells, lytic phages replicate within the host and eventually cause cell lysis, releasing progeny phages that can infect additional bacteria. Their narrow host range enables selective suppression of pathogens while potentially causing less disruption to beneficial microbial communities than broad-spectrum antibiotics. Phage-based approaches may therefore provide an alternative strategy for

bacterial disease management and help reduce antibiotic use in agriculture and livestock systems (Sahu *et al.*, 2023) ^[89].

7.11 Genome-edited resistant crops: Genome editing provides an opportunity to develop crops with improved resistance to pathogens through precise modification of specific plant genes. Technologies such as CRISPR-Cas systems can be used to alter susceptibility genes or modify regulatory pathways involved in plant defense. Unlike conventional approaches that may involve introducing foreign genetic material, some genome-editing strategies generate targeted changes within the plant's existing genome (Thakur *et al.*, 2026) ^[106]. Developing crops with enhanced inherent resistance could reduce disease occurrence and decrease reliance on repeated antimicrobial and pesticide applications, thereby contributing to more sustainable disease management.

7.12 Smart Nanoformulations: Smart nanoformulations employ nanoscale carriers to improve the stability, delivery, and controlled release of antimicrobial compounds or biological molecules such as dsRNA. Nanocarriers can protect active ingredients from degradation and enhance their transport to target sites. In some systems, cargo release can be regulated by environmental or biological stimuli, allowing more controlled application. Improved delivery efficiency may reduce the amount and frequency of antimicrobial application while maintaining effective disease suppression. Thus, smart nanoformulations represent a potential strategy for minimizing chemical losses, environmental exposure, and unnecessary selection pressure for resistance (Gressler *et al.*, 2025) ^[32].

7.13 Artificial Intelligence-Assisted disease forecasting: Artificial intelligence (AI)-based disease forecasting uses machine learning and data-driven models to identify

conditions associated with disease development and predict potential outbreaks. These systems can integrate information from weather records, humidity, temperature, remote sensing, crop characteristics, and field observations (Michael *et al.*, 2026) ^[70]. Early prediction enables growers to implement timely and location-specific management practices rather than relying on routine or indiscriminate chemical applications. By supporting more precise decision-making, AI-assisted forecasting can reduce unnecessary antimicrobial use and contribute to strategies aimed at limiting resistance development (Michael *et al.*, 2026) ^[70].

7.14 One Health Surveillance: One Health surveillance recognizes the interconnected nature of human, animal, plant, and environmental health in the emergence and dissemination of antimicrobial resistance. Integrated monitoring of resistant microorganisms and antimicrobial resistance genes across agricultural soils, water, crops, animals, food systems, and human populations can improve the detection of emerging resistance patterns (Al-Khalaifah *et al.*, 2025) ^[2]. Such coordinated surveillance may help identify important reservoirs and transmission pathways and support timely intervention. Combining information across sectors is therefore essential for developing effective AMR management strategies and preserving the long-term effectiveness of antimicrobial agents.

7.9 Regulatory and policy measures: Effective AMR management requires resistance surveillance, responsible antimicrobial use, farmer education, good agricultural practices, and strong regulatory frameworks. One Health-based national and international policies integrating plant, animal, human, and environmental health are essential for coordinated AMR management and sustainable antimicrobial use (Endale *et al.*, 2023) ^[29].

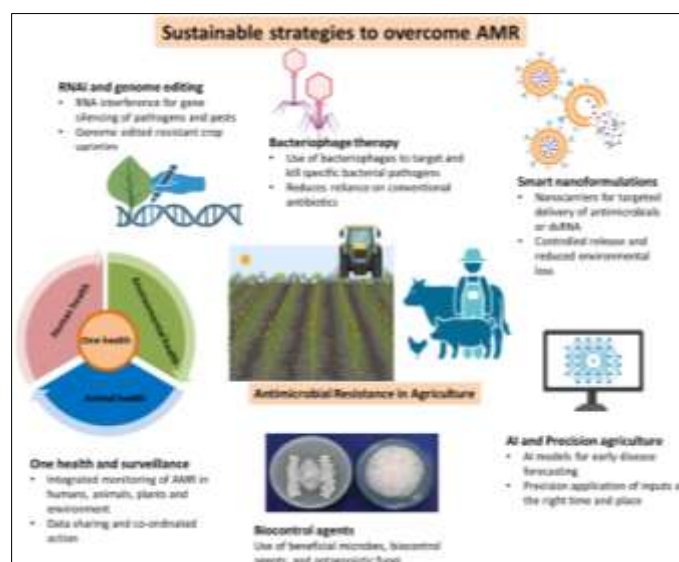


Fig 1: Sustainable strategies for mitigating Antimicrobial Resistance in Agriculture

8. Future perspectives

Antimicrobial resistance (AMR) is rapidly evolving and poses a major challenge to sustainable agriculture and global food security (Aslam *et al.*, 2024) ^[6]. Future disease management should reduce dependence on conventional fungicides and antibiotics through innovations in biotechnology, genomics, artificial intelligence, nanotechnology, and microbiome research. The

development of novel antimicrobials, natural products, antimicrobial peptides, RNA interference (RNAi)-based technologies, bacteriophages, beneficial microbial consortia, and CRISPR/Cas-based genome editing offers promising alternatives for targeted pathogen control and the development of disease-resistant crops (Nazir *et al.*, 2025) ^[77]. Nanotechnology, artificial intelligence, remote sensing, precision agriculture, whole-genome sequencing, and

metagenomics can further support targeted delivery, early disease prediction, resistance monitoring, and detection of ARGs across agricultural ecosystems (Keykhasaber *et al.*, 2026)^[49]. Importantly, these advances should be integrated within a One Health framework through coordinated AMR surveillance, responsible antimicrobial use, regulatory measures, farmer education, data sharing, and interdisciplinary collaboration to protect crop productivity, environmental health, and global food security (Keykhasaber *et al.*, 2026)^[49].

9. Conclusions

Antimicrobial resistance (AMR) has become a major challenge to sustainable agriculture by reducing the effectiveness of conventional fungicides and antibiotics and compromising plant disease management. The indiscriminate and repeated use of antimicrobial agents accelerates the emergence and spread of resistant pathogens, leading to increased disease incidence, reduced crop productivity, and greater economic losses. Addressing this challenge requires an integrated approach that combines antimicrobial stewardship, integrated disease management, biological control agents, resistant cultivars, nanotechnology, microbiome-based strategies, and precision agriculture. Furthermore, continuous resistance surveillance, multidisciplinary research, supportive regulatory policies, and the implementation of the One Health framework are essential to preserve antimicrobial efficacy, protect environmental and public health, and ensure sustainable agricultural productivity and global food security.

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