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Review Article

The Future of Post-Harvest Disease Control: CRISPR, RNA Interference, and Host-Induced Gene Silencing

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Abstract | Post-harvest diseases cause substantial agricultural losses, threatening global food security and economic stability. While traditional fungicides face resistance and environmental concerns, emerging biotechnologies CRISPR-Cas9 genome editing, RNA interference, and Host-Induced Gene Silencing offer targeted, sustainable alternatives. This review examines their mechanisms, applications, and challenges in post-harvest disease control. CRISPR enables precise modification of host or pathogen genomes to enhance resistance, RNAi silences critical pathogen genes through sprayable or host-induced dsRNA, and HIGS provides continuous protection via transgenic RNAi production. Despite their promise, challenges such as off-target effects, RNA instability, and regulatory barriers require resolution. We highlight synergistic integration with AI, nanotechnology, and synthetic biology to optimize efficacy and scalability. The paper concludes with a call for collaborative action among researchers, policymakers, and agricultural stakeholders to accelerate adoption, ensuring equitable access and alignment with sustainability goals. By leveraging these innovations, the agricultural sector can mitigate post-harvest losses by 30–50%, advancing food security while reducing reliance on chemical controls.

Keywords | *R*Post-harvest diseases, Sustainable agriculture, Genome editing, Fungal pathogens, Biopesticides, Food security

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INTRODUCTION

Post-harvest diseases are a major threat to global food security, causing significant losses in fruits, vegetables, and grains each year (Hajji-Hedfi *et al.*, 2023). These losses, which can exceed 30–50% in developing countries, are primarily caused by fungal and bacterial pathogens such as *Botrytis cinerea*, *Penicillium* spp., *Aspergillus* spp., *Alternaria* spp., and *Erwinia carotovora*. Traditional methods of controlling post-harvest diseases rely heavily on synthetic fungicides and chemical treatments (Wen *et al.*, 2024). However, the overuse of these chemicals has led to the emergence of resistant pathogen strains, environmental contamination, and concerns over human health risks due to pesticide residues. Additionally, increasing regulatory restrictions and consumer demand for chemical-free food have driven the search for sustainable, eco-friendly alternatives (Rancāne *et al.*, 2023).

In recent years, biotechnological advancements have introduced innovative strategies for disease management, offering precise and targeted approaches to combat post-harvest pathogens. Among these, CRISPR-based genome editing, RNA interference (RNAi), and Host-Induced Gene Silencing (HIGS) have emerged as promising tools (Wytinck *et al.*, 2020). CRISPR-Cas9 allows for the direct modification of host plant genes to enhance disease resistance, either by knocking out susceptibility factors or by introducing defense-related genes (Debbarma *et al.*, 2023). RNAi technology utilizes small RNA molecules to

silence essential genes in pathogens, effectively inhibiting their growth and virulence (Abdellatef *et al*., 2021). HIGS extends this concept by genetically engineering crops to produce RNAi molecules that specifically target invading pathogens upon infection (Cheng *et al*., 2023).

These technologies present several advantages over conventional methods, including reduced chemical dependency, lower environmental impact, and the potential for durable resistance (Yu *et al*., 2022). However, their widespread adoption faces challenges such as regulatory hurdles, public acceptance of genetically modified organisms (GMOs), and technical limitations in delivery and stability (Akbar *et al*., 2022). This review explores the mechanisms, current applications, and future prospects of CRISPR, RNAi, and HIGS in post-harvest disease control, while addressing the scientific, ethical, and practical considerations that will shape their implementation in agriculture. By integrating these cutting-edge approaches, the agricultural sector may soon transition toward more sustainable and resilient post-harvest management systems, ensuring food safety and security in the face of growing global demand.

CRISPR-CAS9 FOR POST-HARVEST DISEASE RESISTANCE

CRISPR-Cas9 (Clustered Regularly Interspaced Short Palindromic Repeats-associated protein 9) is a revolutionary genome-editing tool that enables precise modifications in the DNA of plants and pathogens (Mascarenhas *et al*., 2024a, b). The system consists of two key components: the Cas9 endonuclease, which cuts DNA, and a guide RNA (gRNA), which directs Cas9 to a specific target sequence. Once the target gene is identified, Cas9 induces a double-strand break (DSB), triggering the cell's natural repair mechanisms either non-homologous end joining (NHEJ), which often results in gene knockouts, or homology-directed repair (HDR), which allows for precise gene insertions or replacements (Liu *et al*., 2022). In the context of post-harvest disease control, CRISPR can be employed in two primary ways: (1) editing host plant genes to enhance resistance by disrupting susceptibility (S) genes or introducing resistance (R) genes, and (2) directly targeting pathogen genomes to disable virulence factors (Fizikova *et al*., 2021; Jacobson *et al*., 2023). For example, knocking out fungal genes responsible for toxin production or cell wall degradation can render pathogens less aggressive, thereby reducing spoilage (Shawky *et al*., 2024).

CRISPR-Cas9 has been successfully applied to improve resistance against several post-harvest pathogens (Zhan *et al*., 2024). In tomatoes, researchers have used CRISPR to knock out the DMR6 gene, which enhances salicylic acid-mediated defense against *B. cinerea*, a major cause of gray mold (Zhu *et al*., 2024). Similarly, in bananas, CRISPR has been used to target the MaPG gene in *Fusarium oxysporum*, reducing fungal colonization and extending shelf life. Another promising approach involves editing ethylene biosynthesis genes in climacteric fruits (e.g., apples, avocados) to delay ripening and reduce susceptibility to opportunistic pathogens (Ijaz *et al*., 2023). Beyond crop improvement, CRISPR can be deployed in pathogen-directed strategies, such as disrupting CYP51 (a key enzyme in fungal ergosterol biosynthesis) in *P. digitatum*, the causative agent of citrus green mold (Erdoğan *et al*., 2023). Additionally, transient CRISPR delivery systems, including virus-induced genome editing (VIGE) or nanoparticle-based methods, allow for non-transgenic modifications, bypassing some regulatory hurdles associated with GMOs (Wan *et al*., 2021; Ijaz *et al*., 2023).

Despite its potential, CRISPR-Cas9 faces several obstacles in post-harvest applications. Off-target effects, where unintended genomic regions are edited, remain a concern, particularly in non-model crops with complex genomes (Le *et al*., 2022). Delivery efficiency is another hurdle, as many post-harvest products are perishable and may not tolerate prolonged transformation protocols (Pramanik *et al*., 2021). Regulatory frameworks for CRISPR-edited crops vary globally, with some regions (e.g., the EU) subjecting them to strict GMO regulations, while others (e.g., the U.S., Argentina) adopt more lenient policies (Farinati *et al*., 2024). Public perception and consumer acceptance of gene-edited foods also pose challenges, necessitating transparent communication about safety and benefits (Daniel *et al*., 2023). Furthermore, pathogen evolution could lead to CRISPR-resistant strains, necessitating continuous refinement of target sequences (Kumari *et al*., 2022). Addressing these limitations will require advances in precision editing tools (e.g., base or prime editing), improved delivery systems (e.g., biodegradable nanoparticles), and harmonized international regulations to facilitate commercialization (Chen *et al*., 2024; Thiruppathi *et al*., 2024).

Ongoing research aims to expand CRISPR's utility through multiplex editing (targeting multiple genes simultaneously) and CRISPR-based antimicrobial strategies (e.g., CRISPR-Cas13 for RNA virus targeting) (Zhou *et al*., 2024). Integrating CRISPR with other technologies, such as RNAi or HIGS, could provide synergistic effects, offering durable and broad-spectrum resistance against post-harvest pathogens (Massa *et al*., 2025).

RNA INTERFERENCE IN POST-HARVEST PROTECTION

RNA interference is a naturally occurring eukaryotic gene regulation mechanism that has been repurposed as a powerful biotechnological tool for post-harvest disease

management (Gebremichael *et al*., 2021). The process involves the introduction of double-stranded RNA (dsRNA) molecules that are processed by the host cell's Dicer enzyme into small interfering RNAs (siRNAs) of 21-24 nucleotides in length (Islam *et al*., 2025). These siRNAs are then incorporated into the RNA-induced silencing complex, which guides the sequence-specific degradation of complementary messenger RNA (mRNA) in the target pathogen (Hernández-Soto and Chacón-Cerdas, 2021). In post-harvest applications, RNAi can be deployed through two primary strategies: (1) host-mediated RNAi, where transgenic plants are engineered to express pathogen-targeting dsRNAs, and (2) exogenous application, where formulated dsRNAs are directly applied to harvested produce (Hoang *et al*., 2022; Koeppe *et al*., 2023). The latter approach, known as spray-induced gene silencing (SIGS), has gained particular attention for its ability to bypass genetic modification requirements while still achieving effective pathogen control (Fajardo *et al*., 2024). The specificity of RNAi allows for precise targeting of essential pathogen genes, such as those involved in cell wall biosynthesis, virulence factor production, or toxin synthesis, without affecting non-target organisms (Bragg and Rieske, 2022).

RNAi technology has demonstrated remarkable success against diverse post-harvest pathogens. In citrus fruits, dsRNA targeting the β-tubulin gene of *P. digitatum* has shown significant reduction in green mold incidence, while similar approaches against *B. cinerea* in strawberries have achieved up to 80% disease suppression (Hernández-Soto and Chacón-Cerdas, 2021; Gebremichael *et al*., 2021; Alexandrova *et al*., 2022; Islam *et al*., 2025). A particularly innovative application involves embedding dsRNAs in edible coatings or nanoparticles, which not only protects the RNA molecules from degradation but also provides controlled release and prolonged activity (Hernández-Soto and Chacón-Cerdas, 2021; Gebremichael *et al*., 2021; Alexandrova *et al*., 2022; Samarskaya *et al*., 2022; Zhang *et al*., 2022a, b, c). For instance, chitosan-based nanoparticles carrying dsRNA against *F. graminearum* have effectively reduced mycotoxin contamination in stored wheat (Spada *et al*., 2024). The technology has also proven effective against bacterial pathogens, with dsRNAs targeting quorum-sensing genes in *E. amylovora* reducing fire blight in apples (Hernández-Soto and Chacón-Cerdas, 2021; Gebremichael *et al*., 2021; Alexandrova *et al*., 2022; Samarskaya *et al*., 2022; Zhang *et al*., 2022a, b, c). Recent advances include the development of "RNAi triggers" - designer small RNAs that can simultaneously target multiple pathogen genes or even different pathogen species, offering broad-spectrum protection (Zhang *et al*., 2022a, b, c). Field trials with SIGS formulations have shown promising results, with some products already in the commercialization pipeline, particularly for high-value crops where post-harvest losses are most economically damaging (Delgado-Martín *et al*., 2022).

Despite its potential, several significant challenges hinder the widespread adoption of RNAi for post-harvest protection (Nityagovsky *et al*., 2022). The instability of naked dsRNA in environmental conditions necessitates sophisticated formulation technologies, increasing production costs and complicating application protocols (Villegas-Estrada *et al*., 2022). While nanoparticle carriers can enhance stability, they raise additional regulatory and safety concerns regarding their composition and environmental fate (Zhang *et al*., 2022a, b, c). Another major limitation is the variable uptake efficiency of dsRNAs among different pathogen species, with some fungi demonstrating natural barriers to RNA uptake that reduce treatment efficacy (Bocos-Asenjo *et al*., 2022). The potential for off-target effects, though generally lower than chemical pesticides, still requires careful evaluation, particularly regarding impacts on beneficial microbiota associated with produce (Hoang *et al*., 2022). Regulatory frameworks for RNAi-based products remain uncertain in many jurisdictions, with ongoing debates about whether they should be classified as pesticides or biostimulants (Mourenets *et al*., 2023). Furthermore, the possibility of pathogen resistance development through mutations in target sequences or enhanced RNA degradation mechanisms necessitates the development of resistance management strategies, such as using multiple target genes or rotating different dsRNA formulations (Akbar *et al*., 2022). Addressing these challenges will require continued research into more efficient and cost-effective production methods, improved delivery systems, and the establishment of clear regulatory pathways to facilitate commercialization (Gebremichael *et al*., 2021).

Host-induced gene silencing in post-harvest protection

Host-Induced Gene Silencing (HIGS) represents an advanced application of RNA interference (RNAi) technology where the host plant is genetically engineered to produce silencing molecules that target specific genes in attacking pathogens (Su *et al*., 2020; Mann *et al*., 2023). This innovative approach leverages the plant's own cellular machinery to generate double-stranded RNA (dsRNA) molecules designed to complement and silence essential genes in invading fungi, oomycetes, or other pathogens (Islam *et al*., 2018). The mechanism begins when the engineered plant transcribes the dsRNA, which is then processed into small interfering RNAs (siRNAs) by the plant's RNAi machinery (Dubrovina and Kiselev, 2019). These siRNAs can move intracellularly or be transported to the infection site through the plant's vascular system

(Qiao *et al*., 2024). Remarkably, recent research has shown that these silencing molecules can cross kingdom boundaries, being taken up by the pathogen during infection and subsequently incorporated into its RNA-induced silencing complex (RISC) (Bakhat *et al*., 2023). This leads to the degradation of complementary mRNA in the pathogen, effectively silencing genes critical for its virulence, growth, or survival (Ivanov and Golubeva, 2023). The HIGS approach is particularly valuable because it provides continuous, systemic protection throughout the plant's tissues, including harvested organs like fruits and tubers that are vulnerable to post-harvest pathogens (Cheng *et al*., 2020; Ashapkin *et al*., 2023). The technology's specificity stems from careful selection of target genes that are essential to the pathogen but absent or divergent in the host plant and non-target organisms, minimizing ecological impacts (Lobo and Boto, 2022).

HIGS technology has shown remarkable success in controlling various devastating post-harvest diseases across multiple crop systems (Wytinck *et al*., 2020). In cereal crops, wheat engineered to produce siRNAs targeting the CYP51 gene in *F. graminearum* demonstrated significantly reduced *Fusarium* head blight and mycotoxin contamination in grains during storage (Okubara *et al*., 2019; Omolehin *et al*., 2021). Similarly, potato plants expressing RNAi constructs against *P. infestans* effector genes showed enhanced resistance to late blight, with tubers maintaining better quality during long-term storage (Samarskaya *et al*., 2023). Fruit crops have also benefited from HIGS approaches, with apple and pear trees expressing silencing RNAs against fire blight (*E. amylovora*) exhibiting reduced disease incidence in harvested fruits. Perhaps most impressively, HIGS has been successfully applied to control aflatoxin-producing *Aspergillus* species in nuts and maize, where the engineered plants silence fungal genes involved in aflatoxin biosynthesis (Chang, 2024). Recent innovations include the development of "inducible HIGS" systems, where the production of silencing RNAs is triggered only upon pathogen detection, and "multi-target HIGS" constructs that simultaneously silence several pathogen genes to prevent resistance development (Qi *et al*., 2019). The technology has also been adapted for use in non-transgenic formats through viral vectors or transient expression systems, offering potential solutions for crops where genetic transformation is challenging or where GMO regulations are restrictive (Murai and Mochizuki, 2022). These applications demonstrate HIGS' versatility in addressing diverse post-harvest challenges while maintaining produce quality and safety (Cheng *et al*., 2023).

Despite its considerable promise, HIGS technology faces several significant challenges that must be addressed for widespread commercial adoption (Omolehin *et al*., 2025). One major limitation is the variable efficiency of cross-kingdom RNAi, as some pathogens have developed mechanisms to degrade or exclude foreign RNAs, while others show differential uptake capabilities of silencing molecules (Prasad *et al*., 2023). The stability and mobility of silencing signals within plant tissues can also be inconsistent, particularly in harvested organs that may have reduced metabolic activity (Zhu *et al*., 2021). Regulatory hurdles present another substantial barrier, as HIGS-engineered crops are typically classified as GMOs, subjecting them to stringent and costly approval processes in many countries (Zhang *et al*., 2025). Public perception and acceptance of GMO-derived foods remain polarized, potentially limiting market opportunities for HIGS-protected produce (Su *et al*., 2020). Additionally, the potential for pathogens to evolve resistance to HIGS through mutations in target sequences or enhanced RNA degradation mechanisms necessitates careful design of constructs targeting multiple essential genes (Ouyang *et al*., 2025). Future research directions include optimizing RNA stability and transport within plants, developing non-transgenic delivery methods such as root absorption or nanoparticle-mediated transfer, and creating "smart" HIGS systems that activate only when pathogens are detected (Tian *et al*., 2024). Combining HIGS with other emerging technologies like CRISPR-based genome editing or conventional resistance breeding may provide more durable and comprehensive protection (Spada *et al*., 2025; Zhang *et al*., 2025). As our understanding of RNA trafficking mechanisms improves and genetic transformation techniques advance, HIGS is poised to become an increasingly important tool in sustainable post-harvest disease management, potentially revolutionizing how we protect food crops from field to fork (Zhu *et al*., 2017; Niño-Sánchez *et al*., 2021).

Comparative advantages and limitations of emerging biotechnologies for post-harvest disease control

The three leading biotechnological approaches CRISPR-Cas9 genome editing, RNA interference, and host-induced gene silencing each offer distinct advantages and face unique challenges in post-harvest disease management. Understanding their comparative strengths and limitations is crucial for determining their optimal applications and guiding future research and commercialization efforts (Wytinck *et al*., 2020).

CRISPR-Cas9 stands out for its unparalleled precision in genome editing, allowing for targeted modifications of either host plant genes (to enhance resistance) or pathogen genomes (to disrupt virulence). Unlike broad-spectrum fungicides, CRISPR can be designed to avoid off-target effects through careful guide RNA selection,

though the risk remains higher than with RNAi-based methods (Tavakoli *et al.*, 2021; Spada *et al.*, 2025). RNAi and HIGS, by contrast, operate at the transcriptional level, using sequence-specific silencing to knock down pathogen genes without altering the host genome (Wytinck *et al.*, 2020; Atabekova *et al.*, 2023; Fan *et al.*, 2024). While RNAi is highly specific, its efficacy depends on efficient dsRNA uptake by pathogens a process that varies across fungal and bacterial species (Hashiro and Yasueda, 2022). HIGS combines the precision of RNAi with the added advantage of being continuously expressed by the host plant, providing systemic and long-lasting protection even in harvested produce (Lucena-Leandro *et al.*, 2022; Spada *et al.*, 2024; Stakheev *et al.*, 2024). However, HIGS requires stable genetic transformation, which may limit its use in crops with regulatory or public acceptance barriers (Wang *et al.*, 2023) (Table 1).

One of the most significant advantages of CRISPR is its potential for durable resistance, particularly when targeting multiple susceptibility (S) genes or introducing stacked resistance (R) genes (Mascarenhas *et al.*, 2024a, b). However, pathogens may still evolve around edited host defenses, especially if a single gene is targeted (Samarskaya *et al.*, 2023). RNAi and HIGS face similar resistance risks, as point mutations in the target pathogen genes can render silencing ineffective (Bocos-Asenjo *et al.*, 2022; Koeppe *et al.*, 2023). To mitigate this, researchers are developing multiplex RNAi constructs that simultaneously target several essential pathogen genes, reducing the likelihood of evasion (Padilla-Roji *et al.*, 2023). HIGS has an edge in durability over spray-based RNAi because the host plant continuously produces silencing molecules, but its effectiveness can wane if the pathogen evolves RNA-degrading enzymes (Abdellatef *et al.*, 2021) (Table 1).

From a regulatory standpoint, non-transgenic CRISPR-edited crops (those without foreign DNA integration) are gaining faster approval in countries like the U.S. and Japan, offering a smoother path to market compared to GMO-dependent HIGS (Debbarma *et al.*, 2023). RNAi-based sprays may face fewer regulatory hurdles as they are externally applied and degrade naturally, but their classification as biopesticides still requires extensive safety testing (Zhang *et al.*, 2022a, b, c). HIGS, being a transgenic technology, encounters the most stringent regulations and public skepticism, particularly in the EU and organic markets (Ruiz-Jiménez *et al.*, 2021). Economically, RNAi sprays are currently costly to produce at scale, though advances in fermentation-based dsRNA synthesis could lower prices (Spada *et al.*, 2023; Vatanparast *et al.*, 2024). CRISPR-edited crops involve high initial R&D costs but may offer long-term savings by reducing fungicide use (Erdoğan *et al.*, 2023). HIGS, while potentially cost-effective over time, demands significant investment in transformation and breeding programs for each crop-pathogen system (Yin *et al.*, 2020; Shahriar *et al.*, 2021; Rukavtsova *et al.*, 2023) (Table 1).

For immediate post-harvest applications, SIGS and CRISPR-enhanced produce are the most feasible (Fizikova *et al.*, 2024). RNAi can be applied directly to stored fruits or grains, similar to conventional fungicides, without the need for genetic modification (Spada *et al.*, 2025). CRISPR-edited crops, once developed, require no additional treatment but are limited to diseases with known host resistance mechanisms (Li *et al.*, 2023). HIGS is best suited for perennial crops or staple foods with long

Table 1: Comparative analysis of biotechnological approaches for post-harvest disease management.

Feature	CRISPR-Cas9	RNAi/SIGS	HIGS
Mechanism	Edits host/pathogen DNA to disrupt genes	Silences pathogen mRNA via delivered dsRNA	Host produces dsRNA to silence pathogen genes
Precision	High (gene-specific)	High (sequence-specific)	High (sequence-specific)
Durability	Long-term (heritable edits)	Short-term (requires reapplication)	Long-term (host-driven)
Resistance risk	Moderate (pathogen evolution possible)	High (single-target vulnerability)	Moderate (pathogen may degrade RNA)
Regulatory status	Non-GMO edits favored in some regions	Less regulated (biodegradable sprays)	Strict GMO regulations apply
Cost	High R&D, low long-term costs	High production costs (dsRNA synthesis)	High (transformation + breeding)
Scalability	Crop-specific (requires transformation)	Broad-spectrum (spray applications)	Limited to transformable crops
Best for	Editing host resistance traits	Rapid, flexible pathogen control	Systemic protection in stored produce
Key limitation	Off-target effects, GMO perception	RNA stability, pathogen uptake issues	GMO restrictions, variable efficiency

storage periods, where continuous protection is critical (Tretiakova *et al.*, 2022). However, its reliance on genetic engineering restricts its use to crops with established transformation protocols (Ou *et al.*, 2024) (Table 1).

The future of post-harvest disease control may lie in integrating these technologies. For example, CRISPR could be used to knock out host susceptibility genes while HIGS provides ongoing RNAi-mediated defense against evolving pathogens (Wang *et al.*, 2022). RNAi sprays could serve as a flexible, on-demand supplement for high-risk periods. Overcoming the limitations of each approach will require advances in delivery systems (e.g., nanoparticle carriers for RNAi), pathogen genomics (to identify optimal CRISPR and RNAi targets), and regulatory harmonization to accelerate commercialization (Rasheed *et al.*, 2021; Menezes *et al.*, 2022; Nie *et al.*, 2024; Spada *et al.*, 2025). By leveraging their complementary strengths, these biotechnologies could collectively reduce post-harvest losses by 50% or more, ushering in a new era of sustainable agriculture (Wang *et al.*, 2024) (Table 1).

Future perspectives in post-harvest disease control: Integrating biotechnology for sustainable solutions

The future of post-harvest disease management lies in the strategic integration of CRISPR, RNAi, and HIGS technologies with emerging innovations to create robust, sustainable solutions (Su *et al.*, 2020). One promising direction is the convergence of nanotechnology and RNAi delivery systems, where lipid or chitosan-based nanoparticles could protect dsRNA from degradation while enhancing its uptake by pathogens (Goodfellow *et al.*, 2019). These "smart nanocarriers" could be engineered to respond to environmental triggers (e.g., pH changes in rotting fruit) for targeted release, minimizing waste and maximizing efficacy (Motorina *et al.*, 2024). Similarly, CRISPR multiplexing simultaneously editing multiple host susceptibility genes or pathogen virulence factors could provide durable, broad-spectrum resistance (Rukavtsova *et al.*, 2023). Advances in base and prime editing further refine precision, enabling single-nucleotide modifications without double-strand breaks, thereby reducing unintended genomic effects (Spada *et al.*, 2025).

Another transformative avenue is the development of pathogen-inducible systems, where HIGS or CRISPR defenses activate only upon pathogen detection (Spada *et al.*, 2025). Synthetic biology tools could engineer crops with "sense-and-respond" circuits, such as promoters activated by fungal effector proteins, ensuring silencing occurs precisely when and where needed (Cheng *et al.*, 2023). This approach would conserve plant energy and reduce the risk of off-target effects. Additionally, cross-kingdom RNA trafficking research may unlock ways to enhance siRNA mobility from host plants to pathogens, addressing current limitations in HIGS efficiency (Niño-Sánchez *et al.*, 2021).

To combat resistance evolution, combination strategies will be critical. For example, rotating RNAi targets (akin to antibiotic cycling) or pairing CRISPR-edited host resistance with RNAi sprays could delay pathogen adaptation (Marques *et al.*, 2021). Integrating these tools with traditional methods such as biocontrol agents (e.g., *Bacillus* spp.) or physical treatments (UV-C light) may offer synergistic benefits. For instance, RNAi could weaken fungal cell walls, enhancing the efficacy of antagonistic microbes (Spada *et al.*, 2025).

Regulatory and commercial adoption will require global harmonization of policies, especially for gene-edited crops. Public-private partnerships could accelerate this by funding large-scale trials and addressing consumer concerns through transparent communication (Mat Jalaluddin *et al.*, 2023). Meanwhile, breakthroughs in cell-free dsRNA production or in planta RNA amplification systems could slash costs, making RNAi sprays viable for staple crops (Nerva *et al.*, 2020).

Ultimately, the future envisions modular, precision solutions: CRISPR for permanent host traits, HIGS for high-value crops, and RNAi sprays for flexible, on-demand use all monitored by AI-driven pathogen surveillance systems (Joshi *et al.*, 2024). This integrated framework could reduce post-harvest losses by >50%, transforming global food security while aligning with sustainable agriculture goals (Ali *et al.*, 2020; Spada *et al.*, 2025).

Conclusion: Towards a sustainable paradigm in post-harvest disease management

The escalating challenges of global food security demand transformative solutions to combat post-harvest diseases, which continue to account for staggering losses of up to 50% in perishable crops worldwide. Traditional reliance on chemical fungicides has proven unsustainable, driving the urgent need for precision-based, eco-friendly alternatives. The emergence of CRISPR-Cas9 genome editing, RNAi, and HIGS represents a revolutionary shift in post-harvest disease control, offering targeted, effective, and sustainable strategies that align with the principles of agricultural sustainability and food safety.

CRISPR-Cas9 stands out for its unparalleled precision in enhancing host resistance through genome editing, whether by disrupting pathogen susceptibility genes or introducing durable defense traits. While challenges such as off-target effects and regulatory hurdles persist,

ongoing advancements in base editing and multiplex gene targeting promise to overcome these limitations. RNAi technology, particularly through SIGS, provides a flexible and biodegradable solution that can be tailored to specific pathogens without genetic modification. However, its widespread adoption hinges on improving RNA stability and reducing production costs through innovations like microbial fermentation and nanotechnology-based delivery systems. HIGS, though constrained by GMO regulations, offers long-term protection by enabling crops to continuously produce silencing RNAs, making it particularly valuable for staple foods requiring extended storage.

The future of post-harvest disease management lies in the strategic integration of these technologies with cutting-edge advancements in synthetic biology, artificial intelligence, and nanotechnology. AI-driven pathogen surveillance and automated treatment systems could enable real-time responses to disease outbreaks, while engineered genetic circuits in crops could allow for conditional activation of defense mechanisms. Furthermore, the convergence of these tools with traditional methods such as biocontrol agents and physical treatments holds promise for synergistic effects that enhance efficacy and delay resistance evolution.

However, realizing this vision requires addressing critical ethical, regulatory, and economic barriers. International collaboration is essential to harmonize policies and ensure equitable access to these technologies, particularly for smallholder farmers in developing nations. Public acceptance and transparent communication about the safety and benefits of these innovations will be equally crucial to their adoption.

In conclusion, CRISPR, RNAi, and HIGS are poised to redefine post-harvest disease control, moving agriculture toward a future where food waste is minimized, chemical inputs are reduced, and food security is strengthened. By embracing these technologies within a framework of responsible innovation and global cooperation, we can transform post-harvest systems to meet the demands of a growing population while safeguarding planetary health. The journey ahead will require sustained investment in research, cross-sector partnerships, and policy reforms but the potential rewards a world with abundant, safe, and sustainably preserved food are well worth the effort.

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NOVELTY STATEMENT

This paper presents several key novel contributions that advance the field of post-harvest disease management. First, it offers the first comprehensive comparative analysis of three cutting-edge biotechnologies - CRISPR-Cas9 genome editing, RNA interference, and Host-Induced Gene Silencing - specifically tailored for post-harvest applications, bridging an important gap between agricultural biotechnology and food preservation science. Beyond simply reviewing these technologies, we propose an innovative synergistic framework that integrates them with emerging approaches like AI-driven pathogen monitoring and nanotechnology-based delivery systems, representing a significant advance over conventional siloed approaches. The work identifies several underexplored but promising applications, including non-transgenic CRISPR for transient protection of stored produce, edible RNAi coatings with tunable release kinetics, and pathogen-inducible HIGS systems that activate only during infection. Our analysis addresses critical research gaps by presenting concrete strategies to overcome major challenges such as pathogen resistance evolution through multiplexed targeting, cost reduction via microbial biofactories for dsRNA production, and clearer regulatory roadmaps distinguishing GMO and non-GMO classifications. The paper makes an original contribution by introducing and elaborating the novel concept of "precision post-harvest management" a paradigm shift from reactive fungicide use to pre-programmed, pathogen-specific interventions. Importantly, we move beyond technical analysis to propose a global action plan advocating for standardized AI protocols for early disease detection and open-access biotech platforms to ensure equitable technology access. These collective innovations position our work as a foundational reference that not only synthesizes current knowledge but also charts a transformative course for future research and implementation at the intersection of biotechnology, food science, and sustainable agriculture.

Conflict of interest

The authors have declared no conflict of interest.

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