Review Article

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A review on RNA interference (RNAi)-based treatment in corn plant to fight against pests

Abstract

RNA interference (RNAi) is the process of a biological response to double-stranded RNA (dsRNA) that mediates resistance to both endogenous parasitic and exogenous pathogenic nucleic acids, and controls the expression of protein-coding genes. This natural mechanism for sequence specific gene silencing promises to revolutionize biology and have potential practical applications in functional genomics, therapeutic intervention, agriculture and other areas. RNA interference (RNAi) represents a revolutionary advancement in agricultural biotechnology, which has a precise strength in gene silencing for pest control in crops. This paper focuses on applications to target Diabrotica *virgifera virgifera* (Western corn rootworm-WCR)- "a billion-dollar bug", using RNA interference (RNAi), a major pest responsible for substantial economic losses in maize crop production. This pest causes over $1 billion annually in the USA alone in crop damages and control expenses, while in all over the continent of North America the number has surpassed $2 billion. Yield losses from root pruning can reach up to 15% per damaged node, making the development of durable, precise control methods critical. This paper includes the approach to control a dangerous pest in corn plants through RNAi, which will further describe the mechanism of this process in insects, development and commercialization of the product. Moreover, the paper also includes a gene selection in insects, resistance mechanism and practical implication along with environmental safety and regulations and future market opportunities.

Keywords: RNA interference (RNAi), western corn rootworm (WCR), SmartStax PRO, Snf7 gene, dsRNA, sustainable agriculture, pest management biotechnology, genetically modified maize

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Abbreviations: RNAi, RNA interference; WCR, western corn rootworm; USA, The United States of America; FONSI, finding of no significant impact; USDA, United States department of agriculture; EPA, environmental protection agency; dsRNA, double-stranded RNA; mRNA, messenger RNA; siRNAs, small interfering RNAs; RISC, RNA-induced silencing complex; Bt, *Bacillus thuringiensis*; PIPs, plant-incorporated protectants; IRM, integrated risk management; qPCR, quantitative polymerase chain reaction; CRISPR, clustered regularly interspaced short pelindromic repeats

Introduction

Corn (*Zea mays*) is one of the most essential cereal crops in the world, and it is utilised for food, feed and biofuel production.[1] However,crop production is always harmed by different types of pest insects, in which the Western corn rootworm (WCR) is the most destructive in terms of damage to the crop and it increases the use of synthetic fertilizers and pesticides which increases the production cost.[2] This pest is immune to conventional pest controls like, Bt crops or use of chemical pesticides due to the resistance mechanism.[3] RNA interference (RNAi) is a biological process that generates naturally and it provides a target specific mechanism by attacking specific pest survival genes.[4]

RNA interference (RNAi)

RNA interference (RNAi) provides the most selective suppression mechanism by interrupting important genes, particularly Snf7 which is a part of cellular transport.[5] This critical move for the development of the technology for plant protection, improves the use of traditional pesticides with high specificity and environmentally positive alternatives.[6]

RNA interference for corn is basically available in the market as SmartStax PRO hybrids and it has been popular for superior field results, highly advanced and enhanced resistance mechanism, and the least ecological disturbance.[7]

SmartStax PRO

As a leader in agricultural innovation, Bayer Crop Science was the first to introduce RNAi technology, the first new mode of action to protect against corn rootworm in over a decade.[8] SmartStax PRO with RNAi Technology is the corn rootworm fighter for farmers dealing with the highest pressure. It combines the proven benefits of SmartStax technology with the breakthrough RNAi Technology to provide more than double the root node protection against competitor products.[8]

Mechanism of RNA interference in insects

RNAi is a highly conserved biological mechanism in eukaryotic organisms, where double-stranded RNA (dsRNA) triggers the degradation of complementary messenger RNA (mRNA), thus inhibiting gene expression.[4,7]

Uptake and processing of dsRNA in insect

The process of the mechanism begins with the cellular uptake of dsRNA of dsRNA, followed by its processing by the enzyme dices into small interfering RNAs (siRNAs). These siRNAs are incorporated into the RNA-induced silencing complex (RISC), which then identifies and cleaves the target mRNA.[4,7,8] In insect systems such as the Western corn rootworm, RNAi has shown to be a potent means of silencing genes critical to survival, development or reproduction.[4,5,7] For example, silencing genes critically interferes with endosomal sorting pathways, resulting in cell death.[9,10] The mechanism is systemic in some insects, allowing the RNAi signal to spread throughout the body, though variability exists among insect orders to their sensitivity to RNAi.[7,11,12] Figure 1 shows a two step model for the mechanism of gene silencing induced by double stranded RNA.

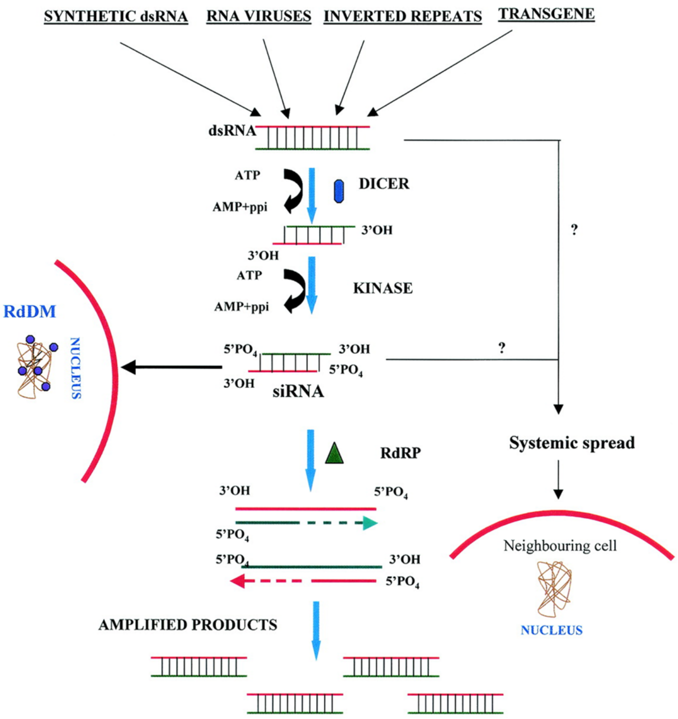

Figure 1 Two-step model for the mechanism of gene silencing induced by double-stranded RNA.

The image shows the complete mechanism of gene silencing by double stranded RNA, in which dsRNA is cleaved by the Dicer enzyme to produce siRNAs which bind to RISC and are activated by helicase. This leads to a silencing of genes.[26]

Snf7 gene selection

In addition to Snf7, other gene targets include V-ATPase (for cellular energy), chitin synthase (for exoskeleton formation) and trehalose for metabolism of sugar, all selected for their crucial roles in insect physiology and their minimal similarity to non-target organisms.[7,13,14] Western corn rootworm exhibits a systemic RNAi response allowing the gene-silencing effect to disseminate throughout the insect's body following localized dsRNA exposure, thereby increasing the potency and persistence of RNAi-mediated control.[6,9,15]

Development and commercialization of RNAi maize (SmartStax PRO)

The commercial utilisation of RNAi in corn indicates a major achievement in pest control in the area of biotechnology.[11] SmartStax PRO is the first genetically engineered hybrid maize to integrate with RNAi-based approach with multiple traits of *Bacillus thuringiensis* (Bt).[7,11]

Engineering of MON 87411 trait

SmartStax PRO, based on the MON 87411, expresses a dsRNA targeting the Snf7 gene of *Diabrotica virgifera virgifera.*[8] This dsRNA is transcribed specifically on the feeding site of corn rootworm larvae in the root tissues, ensuring efficient oral delivery. The gene cassette was carefully designed to include[7]:

To limit expression where required a root specific promoter

Inverted repeats to form dsRNA structures

Selective gene sequences to minimize off-target effects[7]

Agrobacterium mediated transformation was used to introduce the construct into the maize genome.[8] Its insertion site, molecular stability and expression profile were thoroughly characterized during regulatory evaluation.[16]

Trait combination with Bt toxin

SmartStax PRO combines RNAi and six Bt proteins to target both Lepidopteran and Coleopteran pests.[7,10,17] (14)(33)(34). This trait combination broadens the spectrum of control and enhances durability and efficiency, as pests are likely to develop resistance to multiple traits with distinct mechanisms of action. The RNAi component acts synergistically with Bt, reducing pest pressure and helping to preserve the efficacy of Bt proteins.[7,12]

Gene target selection, resistance mechanism and practical implications

Effective RNAi pest control depends on choosing genes critical for insect survival and specific to the pest.[9]

Gene targeting: Snf7

The Snf7 gene is critical for cell viability and it is a part of the endosomal sorting complex required for transport (ESCRT). The Snf7 gene is a primary target due to its role in endosomal sorting and cellular mechanism in Western corn rootworm (WCR).[6,9] When dsRNA silence Snf7 gene, it leads to dysfunction and death of cells, which forms the basis for RNAi traits like MON 87411.[6,14] Other genes, including V-ATPase, Chitin synthase and trehalose are being explored for broader control and trait combining.[18]

Resistance mechanism

Resistance remains a key concern. Western corn rootworm (WCR) can develop RNAi resistance through different mechanisms, such as reduced dsRNA uptake, increased degradation by gut nucleases or mutations in core RNAi components like Dicer or SID-1, which can compromise trait effectiveness and spread under selection pressure.[7,19] To manage resistance, Integrated Risk Management (IRM) practices, such as rotating crops, planting refuges and stacking traits with Bt toxins, are crucial to manage resistance in pests.[7] Additionally, tools like quantitative Polymerase Chain Reaction (qPCR) and genetic markers help to track resistance evolution.[20]

Practical results on-field

Field results from SmartStax PRO show significantly reduced root injury, greater production stability, and less use of insecticides.8,21,22 (42)(43)(44). Figure 2 shows the comparison between RNAi technology untreated (top) and treated plant (bottom). Figure 3 shows comparison of the effects on corn roots with different treatments. Sublethal effects such as delayed pest development and reproduction also assist in control.[23] Although benefits are significant, challenges like high trait costs, regulatory complexity and consumer concerns must be addressed.[24] Continued research and outreach are vital for broader acceptance and sustainable use of RNAi in crop protection.[11]

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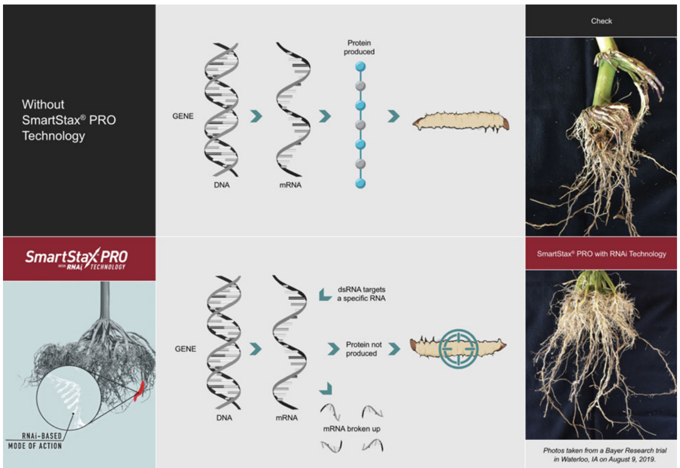

Figure 2 Comparison between RNAi technology untreated plant (top) and treated plant (bottom).

The image shows that required protein is being produced by a rootworm via mRNA protein message (top) and not being produced (bottom) because the rootworm has ingested the RNAi messenger protein which clearly replicates the importance of RNAi for crop protection.[42]

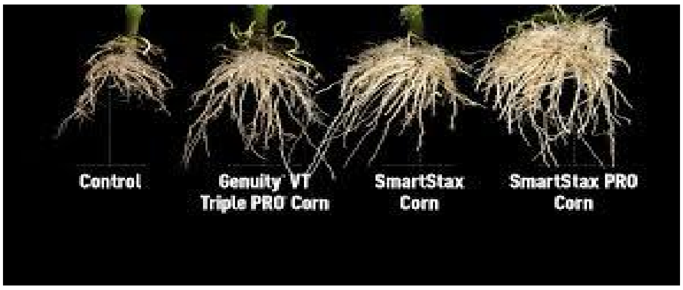

Figure 3 Comparison of the effects on corn roots with different treatment.

The image shows the condition of corn roots when it is treated with different controls.[53]

Environmental safety, regulatory approvals and risk assessment

Environmental safety and regulatory approvals required for all the new products which come in contact directly or indirectly to ecology, where RNA interference (RNAi) based product, SmartStax PRO- a genetically modified corn, has also gone through this process due to its novel approach to fight against pests.[18]

Risk management

Sequence specificity is the most important trait of RNAi technology, which targets only those organisms which are harmful to plants and minimizes impacts on non-target organisms. It is evidented through much practical research and studies that there are no such negative impacts on crop beneficial insects, pollinators, soil invertebrates or mammals because Western corn rootworm has the Snf7 gene which is targeted by dsRNA.[6]

According to bioinformatics analysis and laboratory assays, the homologous gene sequence is generally absent in non-target species and it confirms that off-target effects are highly avoidable.[6] In addition to that, the dsRNA has rapid degradation in soil and water, probably hours to days, depending on microbial and surrounding conditions according to environmental fate studies, which reduces the ecological accumulation and persistence or transfer through food chains to other species or animals.[25]

Regulatory reviews and approvals

Regulatory bodies such as the USDA and EPA have thoroughly evaluated RNAi traits like MON 87411, concluding in 2013 with a Finding of No Significant Impact (FONSI) for SmartStax PRO. The product also passed EPA's review under regulations for Plant-Incorporated Protectants (PIPs).[16] The international market has also accepted this RNAi based technology through corn plants, which includes countries like Canada, Brazil, Argentina, etc.[11] The present research scientists and regulators support RNAi technology as a safe, target specific and environmentally sustainable alternative to traditional chemical insecticides, with the ongoing resistance evolution and essential gene flow.[11]

Market outlook and future prospects

SmartStax PRO has a great ability out of all other similar products and involvement of RNA interference (RNAi) has made it an effective tool against pest resistance.[7] It is estimated, the global market of RNAi technology in agriculture will expand up to $4.5 billion in 2030 from $980 million in 2024.[2] WCR alone causes over $1 billion in annual damage in the USA, making RNAi maize a valuable solution.[11]

Prospective broader applications

RNAi maize technology has been developed primarily to control the Western corn rootworm, but current research expands its utility related pests, which includes:

Northern corn rootworm (*Diabrotica barberi*).[7,26]

Colorado potato beetle (*Leptinotarsa decemlineata*)[26–28]

Brown rice planthopper (*Laodelphax striatellus*)[29,30]

In addition to broader applications, gene targets, V-ATPase, chitin synthase and actin are in observation across multiple insects, opening possible RNAi applications in crops, such as cotton and soybean.[11,31]

Commercial innovations

Commercial biotech organizations like Bayer, Syngenta and Pioneer are working on advancing future RNAi products[8,21] These includes:

Sprayable dsRNA formulations for foliar or soil application[11,32]

Stacking with Clustered Regularly Interspaced Short Pelindromic Repeats (CRISPR) or Bt traits for multi-layered pest protection.[33–41]

In-plant RNAi against fungal and viral pathogens, which expands this technology along with insect targets.[33]

Conclusion

RNA interference (RNAi), a globally accepted transformative technology with its unique mechanism to defeat insect pests in corn production along with the major agriculture sector, offers a target-specific, environmentally safe approach that targets directly important genes in insect pests, which are responsible for the damage to plants with high efficiency.[13] This review report has enlightened functions of RNAi technology when it combines with agriculture, its application as maize hybrid- SmartStax PRO, describing various steps taken to confirm gene target selection, efficacy and environmental safety.[11]

The Western corn rootworm (WCR) is one of the most economically dangerous insect pests in cornfields of the United States, which has evolved resistance to conventional practices like use of Bt traits and chemical pesticides, which created demand for alternative and more effective solution as RNA interference (RNAi).[3] RNAi directly targets specific Snf7 gene, related to cellular functions in rootworm larvae, which is responsible for larvae's death without harming non-target species,[42–45] which is validated by field results and regulatory reviews.[6]

Technical obstacles, such as stability of dsRNA, getting complicated regulatory approvals, obstructing generation of resistance remains, but the market importance of RNAi crops highlights a revolutionary moment in agricultural biotechnology.[20] As this technology continues to evolve, its integration with other pest control tools and potential extension to other crops and pests make RNAi a cornerstone of future pest management strategies.[34]

In this current world, RNAi technology is one of the best options for farmers to protect yield, environment and biodiversity and reduces the excessive use of chemical fertilizers and pesticides, which leads to sustainable agriculture and environmentally positive approach.[46–52]

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Conflict of interest

The author declares that there is no conflict of interest.

Funding sources

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Appendix

Companies:

1a. Bayer Crop Science: https://www.bayer.com/

1b. Syngenta: https://www.syngenta.com/

1c. Pioneer: https://www.pioneer.com/

Products:

1a. SmartStax PRO: https://www.cropscience.bayer.us/brands/dekalb/smartstax

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