

Resistance Management in Cotton: Addressing Bt Cotton Efficacy

Shanjun Zhu, Mengting Luo ✉

Institute of Life Science, Jiyang College of Zhejiang A&F University, Zhuji, 311800, Zhejiang, China

✉ Corresponding email: mengting.luo@jicat.org

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Abstract Bt cotton has revolutionized pest management in cotton cultivation by providing an effective means of controlling major pests, such as the pink bollworm and cotton bollworm. However, the widespread adoption of Bt cotton has also led to the emergence of resistance in target pests, threatening its long-term efficacy. This study explores the development of resistance in cotton pests, the factors contributing to this challenge, and the current strategies implemented to manage resistance, such as refuge strategies and integrated pest management (IPM). A specific case study is presented, detailing the successful application of resistance management techniques in a Bt cotton-growing region. This study also discusses recent advancements in genetic and biotechnological approaches aimed at enhancing Bt cotton's efficacy and addressing resistance issues. It concludes with future perspectives, emphasizing the need for collaborative efforts, continuous monitoring, and the development of policies to sustain the benefits of Bt cotton in global cotton production.

Keywords Bt cotton; Pest resistance; Integrated pest management; Resistance management; Cotton production

1 Introduction

Bt cotton, genetically engineered to produce insecticidal proteins from the bacterium *Bacillus thuringiensis* (Bt), has revolutionized pest management in cotton cultivation. By expressing Bt toxins such as Cry1Ac and Cry2Ab, Bt cotton provides an effective defense against major lepidopteran pests, significantly reducing the need for chemical insecticides and promoting environmentally sustainable agricultural practices (Tabashnik et al., 2013; Gupta et al., 2021). Since its introduction, Bt cotton has been widely adopted in many cotton-growing regions around the world, leading to substantial economic and environmental benefits.

Despite the initial success of Bt cotton, the evolution of resistance in target pests poses a significant threat to its long-term efficacy. Field-evolved resistance has been documented in several pest species, including the pink bollworm (*Pectinophora gossypiella*), which has shown high levels of resistance to both Cry1Ac and Cry2Ab toxins in regions such as central and southern India (Naik et al., 2018). Globally, practical resistance has been observed in populations of 11 pest species, affecting multiple Bt toxins and compromising the effectiveness of Bt crops (Tabashnik et al., 2023). Factors contributing to resistance development include the genetic variability of pest populations, the inheritance patterns of resistance traits, and the management practices employed in Bt crop cultivation (Zafar et al., 2020; Jurat-Fuentes et al., 2021).

This study integrates current knowledge on the mechanisms and patterns of pest resistance development in Bt cotton by examining field data, resistance monitoring studies, and the genetic basis of resistance, providing a comprehensive understanding of the challenges and strategies for managing Bt cotton resistance; insights gained from this study are crucial for developing effective resistance management practices that can sustain the benefits of Bt cotton and ensure its continued role in promoting sustainable cotton production and reducing reliance on chemical insecticides.

2 Bt Cotton and Its Mode of Action

2.1 Description of Bt cotton and its genetic modifications

Bt cotton is a genetically modified organism (GMO) that has been engineered to produce insecticidal proteins derived from the bacterium *Bacillus thuringiensis* (Bt). These proteins, known as Cry toxins, target specific insect pests, providing an effective means of pest control (Bravo et al., 2011). The genetic modifications involve

inserting genes from Bt into the cotton genome, enabling the plant to produce these insecticidal proteins throughout its tissues (Tabashnik et al., 2023). This innovation has significantly reduced the need for chemical insecticides, leading to environmental and economic benefits (Naranjo, 2011; Guan et al., 2020).

2.2 Mechanisms through which Bt cotton controls pests

The primary mechanism through which Bt cotton controls pests is by producing Cry proteins that are toxic to specific insect larvae when ingested. These proteins bind to receptors in the gut cells of the larvae, causing cell lysis and eventually leading to the death of the insect (Yang et al., 2022). This mode of action is highly specific, targeting only certain pests such as the pink bollworm (*Pectinophora gossypiella*) and the cotton bollworm (*Helicoverpa armigera*), while being safe for non-target organisms and humans (Gassmann and Reisig, 2022). The effectiveness of Bt cotton can be enhanced by planting refuges of non-Bt cotton to delay the evolution of resistance in pest populations (Arends et al., 2021).

2.3 Success stories of Bt cotton efficacy in various cotton-growing regions

Bt cotton has demonstrated remarkable success in various cotton-growing regions around the world. In the southwestern United States, a combination of Bt cotton, non-Bt refuges, and sterile insect releases led to the eradication of the pink bollworm. In China, the use of hybrid seeds that mix Bt and non-Bt cotton has effectively managed resistance and maintained the efficacy of Bt cotton (Tabashnik and Carrière, 2019). Australia has also seen long-term success with a proactive resistance management plan that has kept resistance allele frequencies low in pest populations (Figure 1) (Tabashnik et al., 2010). These success stories highlight the importance of integrated pest management strategies and the adaptability of Bt cotton to different agricultural contexts (Knight et al., 2021).

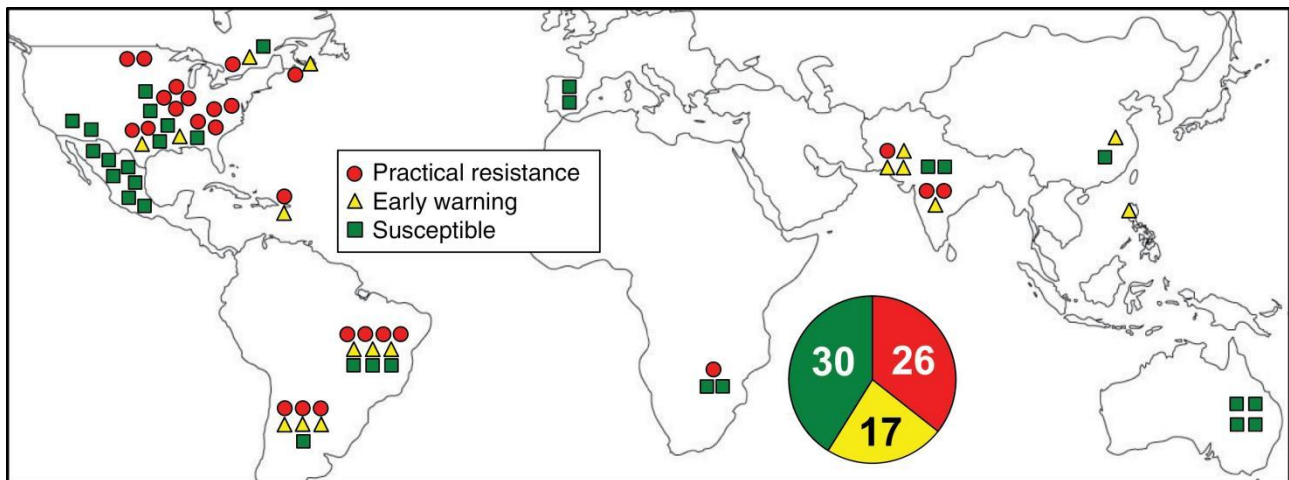


Figure 1 Global status of field-evolved pest resistance to Bt crops. Each symbol represents 1 of 73 cases indicating responses of one pest species in one country to one toxin in Bt corn, cotton, soy, and/or sugarcane (Adopted from Tabashnik et al., 2023)

The global map provides a visual representation of pest resistance to Bt crops, indicating varied responses across different regions. Red circles show areas with practical resistance, while yellow triangles signal early warnings of potential resistance, and green squares mark regions where pests remain susceptible. The data highlight significant cases of resistance in North and South America, India, and China. Additionally, proactive resistance management strategies, such as those implemented in Australia, have proven effective in maintaining pest susceptibility. This map underscores the importance of ongoing monitoring and management to mitigate resistance development globally.

3 Resistance Development in Cotton Pests

3.1 Patterns and mechanisms of resistance in target pests

The development of resistance in cotton pests, particularly the pink bollworm (*Pectinophora gossypiella*) and cotton bollworm (*Helicoverpa armigera*), has been a significant challenge in maintaining the efficacy of Bt cotton (Liu, 2024). The pink bollworm has shown varied resistance patterns across different regions. In India,

field-evolved resistance to Bt cotton expressing Cry1Ac and Cry2Ab toxins has been documented, with resistance ratios (RRs) increasing significantly over time (Naik et al., 2018). The genetic basis of this resistance often involves mutations in the cadherin gene, which is crucial for the binding of Bt toxins (Fabrick et al., 2014). In China, similar resistance mechanisms have been observed, with mutations in the cadherin gene leading to resistance (Wang et al., 2019). The cotton bollworm, on the other hand, has been managed effectively in China through the use of natural refuges and hybrid seed strategies, which have delayed resistance development.

3.2 Factors contributing to resistance development in pests

Several factors contribute to the development of resistance in cotton pests. One major factor is the lack of sufficient non-Bt cotton refuges, which are essential for maintaining a population of susceptible pests that can dilute the resistance genes (Quan and Wu, 2023). In India, the scarcity of non-Bt cotton refuges has been a significant issue, leading to widespread resistance in pink bollworm populations (Tabashnik and Carrière, 2019). Another factor is the genetic makeup of the pests themselves. Mutations in specific genes, such as the cadherin gene in pink bollworm, have been identified as key contributors to resistance (Wang et al., 2022). Additionally, the use of single-toxin Bt cotton varieties has been less effective in managing resistance compared to pyramided varieties that express multiple toxins (Fabrick et al., 2023).

3.3 Case examples of resistance emergence in different regions

The emergence of resistance in cotton pests has been documented in various regions, each with unique contributing factors and outcomes. In the southwestern United States, a combination of non-Bt cotton refuges, sterile moth releases, and other integrated pest management tactics successfully delayed resistance and eventually eradicated the pink bollworm (Tabashnik et al., 2012). In China, the use of hybrid seeds that produce a mix of Bt and non-Bt cotton plants has been effective in managing resistance, with no reported failures in pest control over 25 years (Wan et al., 2017). However, in India, the lack of non-Bt refuges and the widespread planting of Bt cotton expressing Cry1Ac and Cry2Ab toxins have led to significant resistance issues, necessitating the adoption of integrated pest management strategies to mitigate the problem.

4 Current Resistance Management Strategies

4.1 Use of refuge strategies in Bt cotton cultivation

Refuge strategies are a cornerstone in managing resistance to Bt cotton. These strategies involve planting non-Bt crops alongside Bt crops to provide a habitat for susceptible pests, thereby diluting the population of resistant pests. In the United States, the high-dose/refuge strategy has been particularly effective. This approach involves planting non-Bt cotton refuges to delay resistance, as seen in the successful management of pink bollworm in the southwestern United States from 1996 to 2005 (Huang et al., 2011). Similarly, in China, a seed mix refuge strategy, which includes a 25% non-Bt cotton mix, has been employed to manage resistance in pink bollworm effectively (Figure 2) (Quan and Wu, 2023). The natural refuge strategy, involving non-Bt crops like corn, soybeans, and peanuts, has also been used to manage resistance in polyphagous pests such as the cotton bollworm (Arends et al., 2021).

4.2 Integrated pest management (IPM) practices alongside Bt cotton

Integrated pest management (IPM) practices are essential in complementing Bt cotton to manage pest resistance. IPM involves a combination of biological, cultural, and chemical control methods to manage pest populations sustainably. In India, IPM practices such as shortening the cotton season and destroying crop residues have become crucial due to widespread resistance to pyramided Bt cotton (Tabashnik and Carrière, 2019). In the United States, IPM practices have been recommended to prolong the durability of Bt technologies, especially for pests like the western corn rootworm (Martinez and Caprio, 2016). The use of IPM has also been shown to enhance biological control, contributing to the suppression of other key and sporadic pests in cotton (Naranjo, 2011).

4.3 Benefits and limitations of current management strategies

The current resistance management strategies offer several benefits but also come with limitations. The high-dose/refuge strategy has been successful in delaying resistance and maintaining the efficacy of Bt crops in various regions, including North America and Australia (Knight et al., 2021). The use of natural refuges and seed

mix strategies in China has also been effective in managing resistance without any reported failures in lepidopteran pest control. However, these strategies require high compliance from farmers, which can be variable and challenging to enforce (Tabashnik et al., 2010). Additionally, the effectiveness of natural refuges can be influenced by the local abundance of non-Bt crops, as seen in the case of *Helicoverpa zea* in the United States. IPM practices offer a holistic approach to pest management, but their success depends on the integration and proper implementation of various control methods. Despite these challenges, the continuous improvement and adaptation of these strategies are crucial for the sustainable management of pest resistance in Bt cotton.

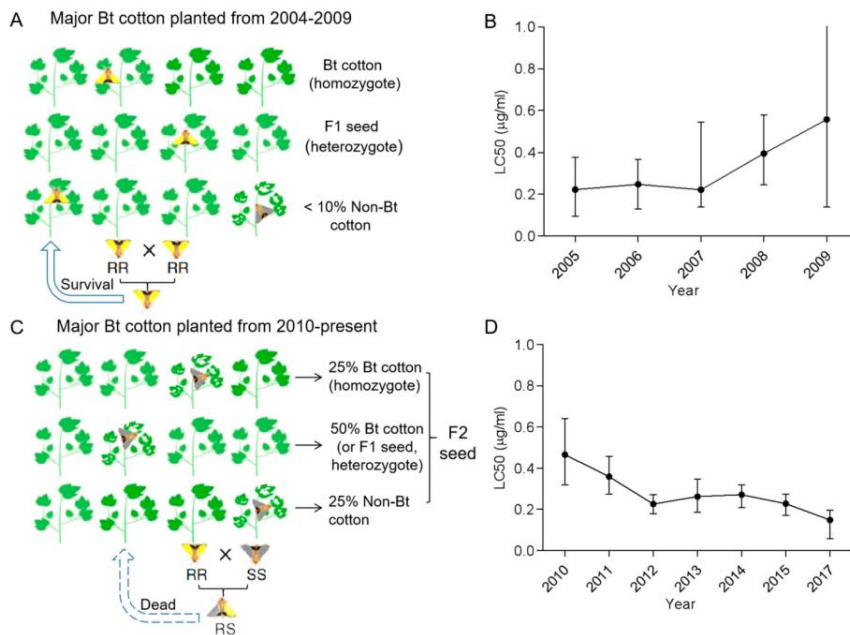


Figure 2 Major Bt cotton planted (A, B) and field monitoring of *Pectinophora gossypiella* Cry1Ac resistance (C,D) in China (Adopted from Quan and Wu, 2023)

Image caption: LC50 represents the median lethal concentration of the Cry1Ac protein to the collected larvae, and error bars stand for the 95% fiducial limits (Adopted from Quan and Wu, 2023)

5 Case Study

5.1 Overview of a specific case study highlighting Bt cotton resistance management

This case study focuses on the successful resistance management of Bt cotton in the southwestern United States, where a comprehensive strategy was implemented to combat the pink bollworm (*Pectinophora gossypiella*). This pest had developed resistance to Bt cotton, posing a significant threat to cotton production in the region.

5.2 Background of the region or field chosen for the case study

The southwestern United States, particularly Arizona, has been a major cotton-producing region. The introduction of Bt cotton in the mid-1990s provided an effective means to control the pink bollworm, a major pest in this area. However, by the early 2000s, there were growing concerns about the pest developing resistance to the Bt toxin, which could undermine the benefits of this genetically engineered crop (Tabashnik and Carrière, 2019).

5.3 Description of the resistance problem and strategies implemented to address it

The resistance problem emerged as pink bollworm populations began to show reduced susceptibility to the Bt toxin Cry1Ac. To address this, a multi-faceted resistance management strategy was implemented. This included the planting of non-Bt cotton refuges to maintain a population of susceptible pests, mass releases of sterile pink bollworm moths to reduce the pest population, and the use of integrated pest management (IPM) practices. These IPM practices included crop rotation, destruction of crop residues, and the use of additional insecticides when necessary (Knight et al., 2021).

5.4 Outcomes of the resistance management strategy and lessons learned

The outcomes of this comprehensive resistance management strategy were highly successful. By 2005, the pink

bollworm was effectively eradicated from the region, and the efficacy of Bt cotton was restored. This case study highlights several key lessons: the importance of a strong science base, broad stakeholder support, rigorous implementation and monitoring, and the need for continuous improvement in resistance management practices. The success in the southwestern United States serves as a model for other regions facing similar challenges with Bt cotton and other transgenic crops (Carrière et al., 2019).

6 Advances in Resistance Management

6.1 Genetic approaches to enhance Bt cotton efficacy

One innovative genetic approach to enhance Bt cotton efficacy involves hybridizing transgenic Bt cotton with non-Bt cotton. This strategy, tested over an 11-year field study in China, involves crossing Bt plants with conventional non-Bt plants and then sowing the second-generation seeds. This method results in a field mixture where three-quarters of the plants produce Bt protein and one-quarter do not. The presence of non-Bt plants promotes the survival of susceptible insects, thereby delaying the evolution of resistance in pests like the pink bollworm (*Pectinophora gossypiella*) (Wan et al., 2017; Tabashnik and Carrière, 2019). Additionally, understanding the genetic basis of resistance, such as identifying mutations in pest genes that confer resistance, can inform the development of more effective Bt crops. For instance, a dominant point mutation in the *tetraspanin* gene of the cotton bollworm (*Helicoverpa armigera*) has been linked to resistance, and tracking such mutations can improve resistance management strategies (Guan et al., 2020).

6.2 Development of new Bt varieties with multiple modes of action

The development of new Bt cotton varieties that incorporate multiple modes of action is crucial for effective resistance management. Next-generation Bt crops often include pyramided traits, which combine multiple Bt toxins to target pests. This approach has shown promise in delaying resistance. For example, Bt cotton varieties producing Cry1Ac, Cry1Fa, and Vip3Aa have been effective against pests like *Helicoverpa zea*, which have developed resistance to other Cry toxins (Head and Greenplate, 2012; Yang et al., 2022). The use of multiple toxins ensures that even if pests develop resistance to one toxin, they are still susceptible to others, thereby maintaining the efficacy of Bt crops (Tabashnik et al., 2023).

6.3 Role of biotechnology in supporting resistance management

Biotechnology plays a pivotal role in supporting resistance management by enabling the development of advanced Bt crops and facilitating the implementation of integrated pest management (IPM) strategies (Zhu and Luo, 2024). The use of biotechnological tools such as CRISPR/Cas9 for gene editing allows for precise modifications in pest genomes to study resistance mechanisms and develop countermeasures (Jin et al., 2018). Additionally, biotechnology supports the creation of structured and unstructured refuges, which are essential components of resistance management plans. For instance, the natural refuge strategy, which relies on the presence of non-Bt crops like soybean and maize, has been shown to be effective in managing resistance in pests like *Helicoverpa zea* (Arends et al., 2021). Moreover, the integration of biotechnological advancements with traditional IPM practices, such as the use of sterile insect techniques and crop rotation, can enhance the sustainability of Bt crops and delay resistance (Knight et al., 2021; Gassmann and Reisig, 2022).

7 Future Perspectives and Recommendations

7.1 Suggestions for improving current resistance management strategies

To enhance the efficacy of current resistance management strategies for Bt cotton, several key improvements can be made. Firstly, integrating multiple Bt toxins with different modes of action can help delay resistance development. For instance, the combination of Cry1Ac and Cry2Ab has shown synergistic effects against resistant strains of *Helicoverpa armigera*, suggesting that pyramiding these toxins could prolong the efficacy of Bt cotton (Wei et al., 2015). Additionally, the use of Vip3Aa in combination with Cry toxins has been effective against *Helicoverpa zea*, indicating that incorporating Vip3Aa could be a valuable strategy (Yang et al., 2022).

Another suggestion is the implementation of structured refuges, which has been successful in delaying resistance in various regions. For example, in the United States, planting non-Bt cotton refuges alongside Bt cotton has been effective in managing pink bollworm resistance. Similarly, in China, the use of natural refuges and seed mix

refuges has successfully delayed resistance in cotton bollworm and pink bollworm. These strategies should be adapted and enforced more rigorously in regions where resistance is emerging rapidly.

7.2 Importance of stakeholder collaboration in resistance management

Effective resistance management requires the collaboration of multiple stakeholders, including farmers, researchers, industry representatives, and government regulators. The success of Bt cotton in Australia, for instance, can be attributed to broad stakeholder support and a strong implementation program that includes auditing and enforced remediation of deviations from the mandated resistance management plan (Knight et al., 2021). Similarly, in the United States, coordinated efforts between farmers and government agencies have been crucial in managing resistance.

A shared understanding of resistance risks among all stakeholders is essential for effective governance. This includes regular communication and education to ensure that all parties are aware of the importance of compliance with resistance management strategies. In Brazil, India, and the United States, strong coordination between actors and direct linkages between the group that appraises resistance risks and growers have enhanced the prospects for effective governance (Carrière et al., 2019).

7.3 Long-term monitoring and policy recommendations

Long-term monitoring of resistance allele frequencies in pest populations is critical for the early detection of resistance and the timely implementation of remedial actions. Continuous monitoring has been a cornerstone of the successful resistance management plan in Australia, where no detectable changes in resistance allele frequency have been observed in field populations of *Helicoverpa* species. Similarly, in China, long-term field monitoring has shown no failures in lepidopteran pest control, indicating the success of their resistance management strategies (Quan and Wu, 2023).

Policy recommendations should focus on mandating the use of refuges, both structured and natural, and ensuring compliance through regular audits and penalties for non-compliance. Additionally, policies should encourage the adoption of integrated pest management (IPM) practices that reduce reliance on Bt crops alone. For instance, in India, integrated pest management strategies that include shortening the cotton season and destroying crop residues are essential for managing pink bollworm resistance (Tabashnik and Carrière, 2019).

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Conflict of Interest Disclosure

The authors affirm that this research was conducted without any commercial or financial relationships that could be construed as a potential conflict of interest.

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