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Economic Impacts of Bt (*Bacillus thuringiensis*) Cotton

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ABSTRACT

In recent years, high-yield production has gained importance due to the decrease in agricultural fields in the world and the rapid increase in the population. Cotton is an important source of income for farmers worldwide and is an important crop, especially for the textile industry. Bt-cotton technology, which entered our lives in 1996, has been quickly adopted in many developed and developing countries. It has been shown to provide advantages in many areas. In particular, the economic growth is gaining importance every year. Additionally, it has also brought an environmentally friendly solution to the crop losses caused by insects and pests over the years, by decreasing chemical spraying. Thus, the cost of farmers was reduced and their health was preserved. It enables farmers to be more profitable by shortening the working hours in the fields and reducing labor force. Moreover, this technology has been shown to increase the yield in cotton production. Fifteen years since the commercialization of Bt-cotton technology was first approved and planted, farmers made profit of million dollars from reduced pesticide use. This study includes detailed information about the contribution of Bt-cotton technology to the leading cotton-producing countries' economies, their commercialization, and explores the current methods used in plants transformation. Although there are some conflicts about whether this technology will provide sustainability and long-term benefits, currently, there are 15 countries that have adopted this technology including India, China and the United States. Also, many more countries are expected to be included in this list in the coming years.

抽象

近年来, 由于世界农业田的减少和人口的迅速增加, 高产成为越来越重要的. 棉花是全世界农民的重要收入来源, 是纺织业的重要作物. Bt-棉花技术于1996年进入我们的生活, 在许多发达国家和发展中国家迅速得到采用. 它已被证明在许多领域具有优势. 特别是, 经济增长每年都在增加重要性. 此外, 它还通过减少化学喷洒, 为多年来昆虫和害虫造成的作物损失带来了一种无害环境的解决方案. 因此, 农民的费用降低了, 他们的健康得到保护. 它通过缩短田间工作时间和减少劳动力, 使农民获得更高的利润. 此外, 该技术已证明可提高棉花产量. Bt-棉花技术首次得到批准并种植15年来, 农民通过减少农药使用赚取了数百万美元的利润. 这项研究包括关于Bt-棉花技术对主要棉花生产国经济的贡献及其商业化的详细资料, 并探讨了目前用于植物转化的方法. 虽然这项技术能否带来可持续性和长期效益存在一些矛盾, 但目前有15个国家采用了这项技术, 包括印度, 中国和美国. 此外, 预计更多的国家将列入这一名单.

KEYWORDS
Production; price; income; import; export; GM crops

关键词
生产; 价格; 收入; 进口; 出口; 作物

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Introduction

In the early 1990s, some growers and researchers had doubts that genetically modified (GM) crops would be effective in agriculture. Especially in developing countries, it was expected that GM technology would be difficult to adopt. However, despite conflicts, the realization of the benefits of GM crops for the world's economy, food security and environment and health issues, has increased the number of cultivated fields, especially by small or resource-poor farmers (James 2010). In addition, in the past few decades, despite the increase in world population, the amount of land suitable for agriculture has decreased and crops are thought to have an average of 11–30% losses due to diseases and pests (Zhang, Wohlhueter, and Zhang 2016). Global issues such as a food crisis, climate change and problems in the economies of countries are promoting the production and the use of GM plants in agriculture (Fedoroff 2010). Genetic modification is mainly adding a specific DNA extension to the genome of the plant and providing new, different traits. Today, in the twenty-fifth anniversary of first commercialization, plenty of economically important crops such as corn, soybean, cotton, canola, tomatoes and potatoes are GM crops (Banfalvi et al. 2020; Danilo et al. 2019; Gelvin 2003; Li et al. 2017). Among them, especially Bt-cotton technology was adopted in northern China shortly after commercialization in 1997 due to its high profitability. During the period between 1990 and 2012, the pesticide cost dropped and the labor use decreased, whereas seed cost and yield increased, as seen in India (Kranthi and Stone 2020; Qaim and De Janvry 2003; Qiao 2015). Controlled pesticide use and reduced crop loss are thought to increase yields (Qaim and De Janvry 2003). The decrease in the time allocated to pesticide spraying can be considered as one of the reasons for the decreased labor use, while the fact that Bt-cotton is more expensive than non-Bt-cotton can be considered as the reason for the increase in seed cost as expected (Qiao 2015) Until 2012, the positive impact of Bt-cotton was at its highest. However, as of 2013, it was observed that spraying and insecticide usage cost per hectare increased and reached to US$23.58 by 2018 which is 37% more than before Bt-cotton was adopted (Kranthi and Stone 2020).

In the early years of the adoption of Bt-cotton, it was observed that farmers' benefits increased by US$261–438 per hectare (Qiao and Huang 2019). Chinese farmers made a profit of US$8.46 billion in the period 1997–2012 only from the use of few pesticides. According to Mr. Maotang Zu, President of the Farmer Technology Association, Bt-cotton has provided great advantages by providing a 10-fold increase in the products of Chinese farmers from 1996 to 2018 (ISAAA 2020).

The U.S. is now leading in Bt-cotton exports, it has been observed that US farmers have received an additional economic gain of between US$50 billion and US$160 billion in the sixteen-year period after adopting GM technology (Carlson 2016). Although there are disagreements about whether Bt and other GM technologies are advantageous today, it is thought to be beneficial in the long term (Kathage and Qaim 2012; Mandal et al. 2020).

Cotton plant

Cotton takes its name from the Arabic word "al qutn." It belongs to the genus *Gossypium* L. including more than 50 species, the Malvaceae family in the Malvales order (Wendel and Grover 2015). There are four species of cotton cultivated; *G. herbaceum, G. arboreum, G. hirsutum* and *G. barbadense*. The *Gossypium* genus has eight diploid genome groups (A-G, K) and 1 alloploid group (AD). Genomic studies show that *G. hirsutum* (AD), an allotetraploid, was formed 6 million years ago by hybridization of two diploid now-extinct ancestor species *G. arboreum* (A) *and G. raimondii* (D) (Yang et al. 2020; Zhao et al. 2017). Besides its economic importance, *G. hirsutum* is used as a model in polyploidization, cell initiation, growth and development researches (Yu and Gervers 2019). *G. arboreum* was native to India and Pakistan and cultivated in southern Asia, in the Persian Gulf and in some parts of North Africa. *G. herbaceum* and *G. arboreum* species were both domesticated in the Old World. However, *G. herbaceum* was grown differently in the plains and forests of Africa. Wild species have long stems and small fruits. *G. hirsutum* and *G. barbadense* species are domesticated in the New World and they were cultivated in Mexico and Peru, respectively (Aslam et al. 2020). They are the species that are responsible for 90% of cotton production worldwide (Yang et al. 2020).

G. hirsutum is native to Mexico and Central America (Khizar et al. 2020). Its fibers are used in textile products, cordage and it is now grown in more than 90 countries in the world (Khan et al. 2020; Malik et al. 2018). Additionally, its seed products such as linters used in industrial cellulose, hulls and oil are valuable (Ozyigit and Gozukirmizi 2009). Cotton seeds are also valuable since its oil can be used for culinary purposes and the oilcake. Its stalks and leaves are used to enrich soil as an organic compound. It is generally grown in warm climates and requires 60–120 cm rain (Khan et al. 2020; Ur Rahman et al. 2018).

As with other plants, cotton has 10% to 30% losses per year due to various biotic stress factors such as insects and pests. Various bacterial, fungal and viral pathogens can cause diseases such as bacterial blight caused by *Xanthomonas citri* pv. *malvacearum*, Fusarium wilt caused by *Fusarium oxysporum* f. sp. *vasinfectum*, cotton leaf curl disease and mosaic disease caused by *Begomovirus* and cotton blue disease caused by *Poleovirus* (Cox et al. 2019; da Silva et al. 2015; Naqvi et al. 2019; Tarazi, Jimenez, and Vaslin 2020). Additionally, *Helicoverpa armigera, Pectinophora gossypiella, Spodoptera frugiperda* and *Tetranychus urticae* are some of the most harmful pests on cotton plants (Allen et al. 2018).

In addition to the biotic stress condition, cotton plant is also affected by abiotic stress like drought, salinity, low or high temperatures and pollutants (heavy metals, polyaromatic hydrocarbons, herbicides, and insecticides etc.) that limit growth and quality (Abdelraheem, Adams, and Zhang 2020; Hocaoglu-Ozyigit et al. 2020). Similarly due to climate change, agricultural fields are affected in many countries, and precipitation or high temperatures cause crop loss and changes in expression of genes (Nakashima and Yamaguchi-Shinozaki 2006). The presence of salt in the environment is also important since the *AtNHX1* gene is expressed in cotton, resulting in more fiber formation (Pasapula et al. 2011). Furthermore, it was found that cotton plants expressing *GhDof1* gene have higher tolerance to cold and salt stress (Su et al. 2017).

In recent years, the decrease in suitable lands for agriculture and the rapid increase in the world population have increased the importance of high-yielding plant production. With biotechnological methods, the yield and variety can be increased, and the desired feature can be transferred to plants by various methods (McGrath and Stevanato 2020). The general logic is to introduce the gene encoding the protein of interest, into the plant genome by direct or indirect methods. Direct or non-biologic methods include physical methods such as biolistics, electroporation, micro-and macroinjection and chemical methods such as calcium phosphate and polyethylene glycol-mediated transfer (PEG). Indirect or biologic methods include the transference of DNA through *Agrobacterium* or viral vectors, conjugation, and transposition (Keshavareddy, Kumar, and Ramu 2018; Ozyigit 2020).

Electroporation, which is one of the direct methods, is based on the principle of introducing DNA into the cell with the use of high voltage electric shock. It is preferred due to its availability in many different cell types and being a low-step process (Ozyigit 2020; Potter and Heller 2018). Macroinjection is a method tried in cereals plants, where hypodermic needles of diameter greater than the cell are used for DNA transfer (De la Pena, Lörz, and Schell 1987). Microinjection is the transfer of DNA directly to the protoplast or nucleus with a glass microcapillary injection pipette with a diameter of 0.5–1.0 μm (Crossway et al. 1986; Ozyigit 2020). Calcium phosphate method is based on the principle that calcium phosphate forms a precipitate with DNA and adheres to the cell surface and then taken into the cell by endocytosis (Guo et al. 2017). The polyethylene glycol-mediated transfer method is based on the principle of soaking and incubating protoplasts in a PEG-containing solution in order to facilitate DNA uptake by endocytosis (Moore, Sheppard, and Sakiyama-Elbert 2009; Yu et al. 2008; Zhao et al. 2016).

Currently, biolistics also known as particle bombardment and gene gun is one of the most frequently used methods especially in cotton cultivation, and is used in studies such as transgenic plant production and inoculation of plants with viral pathogens. In biolistics, a tool like gold beads coated with DNA is being used in order to deliver foreign genes into any tissue types of cotton, which is also an important advantage (Chakraborty et al. 2020; Zhang 2013). Another preferred method in cotton production is pollen tube-pathway-mediated transformation which was first discovered by Zhou and colleagues (Zhou et al. 1983). The method is based on transferring a specific DNA into embryo sacs and implanted into the genome of the plant following self-pollination. During the

pollination process, a long pollen tube pathway is developed by the pollen that germinates and forms a pollen tube until it reaches the ovary (Huang, Dong, and Sun 1999). This method is a genotype-independent and also can be performed by anyone since it does not depend upon expensive equipment (Wang et al. 2019).

Conjugation is an indirect transformation method including the transfer of genetic material by bridge-like connections or directly between cells (Cabezon et al. 2015). Transposition is a transformation method that takes place through transposable elements that can insert and copy itself into the genome rather than inserting bacterial DNA into the genome (Ozyigit 2020; Yan and Rommens 2007). Plant viruses have been used as a vector for various purposes, such as commercial production of proteins of interest. RNA viruses such as *Wheat streak mosaic virus* (WSMV), *Barley stripe mosaic virus* (BSMV), *Tobacco rattle virus* (TRV) and DNA viruses such as *Geminiviruses* are used as vectors in various crops (Lee, Hammond-Kosack, and Kanyuka 2012; Zaidi and Mansoor 2017).

Among the indirect transformation methods, *Agrobacterium*-mediated genetic transformation is the most commonly used as well as the most successful method in cotton transformation (Chen et al. 2017). Many factors play a role in the success of *Agrobacterium*-mediated gene transfer such as using certain strains known to be effective in cotton production, ensuring appropriate temperature conditions, using specific explants to increase *Agrobacterium*'s effect (Wu et al. 2008). Detailed information about this method is given in the next section.

In recent years, a new method of genome editing named as CRISPR/Cas9 (Clustered Regularly Interspaced Short Palindromic Repeats/CRISPR associated system) is widely used in plants (Bortesi and Fischer 2015; Rinaldo and Ayliffe 2015). So far it has been applied on rice, wheat, tobacco, arabidopsis, tomato, and maize (Gao et al. 2017). CRISPR/Cas9 allows us to modify specific DNA sequences by using specific genome targeting technologies. So far, this method has been applied on various plants and crops in order to improve the disease resistance. The previous genome editing systems and tools such as zinc finger nucleases (ZFNs), transcription activator-like effector nuclease (TALENs) have been frequently used in plants. However, CRISPR has more advantages over ZNFs and TALENs. For instance, design of target and vector is flexible and simple, more efficient due to Cas9 protein and guide RNA, the target sequence can be randomly and easily multiplexed (Ma et al. 2015; Ozyigit 2020). Although the entire genome sequencing of cotton was completed in 2015 (Li et al. 2015a) and more genomic information has been known, due to its allopolyploidy, functional genomics research has become more difficult compared to other plants. A study revealed that targeted mutagenesis via CRISPR/Cas9 system is possible in cotton. In the same study, two target genes in cotton protoplasts and transgenic plants were successfully edited (Chen et al. 2017). Moreover, it has been reported that CRISPR method has shown an effective result in studies targeting *MYB25, GFP, GhVP* and *GhCLA1* genes of cotton (Gao et al. 2017). However, more extensive studies on this method are needed in cotton.

Another new method used in cotton plants is RNA interference (RNAi), which is a gene-silencing technique. This technique allows the gene of the desired trait to be more expressed and suppressed in the undesired gene. It has been already used in traits of *Gossypium* sp. such as early maturity and flowering, fertility and embryogenesis, microbial and insect resistance and improved seed and oil quality (Abdurakhmonov et al. 2016, 2014).

The history of *Agrobacterium*-mediated genetic transformation in plants

The journey of this genetic modification technique first began in the 19th century with the investigation of the neoplastic plant disease crown gall (Barton, Fuqua, and Platt 2018). The disease targets the transportation system of plants, prevents substance transport, and causes tumor formation in the crown of woody plants. The causative agent *Agrobacterium tumefaciens* was first isolated from the tumors in 1897 in Italy (Kado 2014). In subsequent studies, it was understood that the disease was caused by the transfer of *A. tumefaciens* T-DNA (transferred DNA) and virulence proteins into the genome of the plant host cells via wound sites. Wound sites of the plant secrete various phenolic

compounds that attract *Agrobacterium*. Thus, with the expression of the encoded oncogenes and the increase in the amount of phytohormone such as auxin and cytokinin, proliferation is stimulated and a tumor is formed (Hwang, Yu, and Lai 2017; Ozyigit 2012). Initially, it was thought that tumor formation was caused by the presence of the bacteria via chemical or mechanical. However, in subsequent serological and cultural studies, bacteria were not detected in the crown gall tumors derived from the secondary tumors. Thus, a new hypothesis has been proposed that there is some kind of genetic transformation from *A. tumefaciens* to the host plant cell (White and Braun 1942). Isolation of octopine and nopaline from crown gall tissue which are used by *A. tumefaciens* as a source of carbon and nitrogen shows that the bacteria transfer to the plant is for its own benefit and they have been found to vary with bacterial strain, but not with plant species (Kado 2014; Ozyigit 2012). Thanks to these properties, *Agrobacterium* has become an important tool in plant breeding. In recombinant *Agrobacterium* strains, transgenic plant species with different properties can be produced by replacing bacterial T-DNA with the gene of interest (Tzfira and Citovsky 2006). It is known that *Agrobacterium* can infect more than 90 families of plants (Gohlke and Deeken 2014).

In addition to current transgenic crops, many more of them are expected to be generated by *Agrobacterium* in the following years. There are various transformation methods but they have low efficiency, limitations on the size of DNA and require more time (Hwang, Yu, and Lai 2017). Therefore, *Agrobacterium*-mediated genetic transformation is frequently used for generation of transgenic crops and plants. As is known, for *Agrobacterium*-mediated genetic transformation, plants should generally be reproduced in tissue culture and genetic transformation should be done in tissue culture at an appropriate stage of plant development.

In the early days, problems were encountered in cotton tissue culture studies such as somatic embryogenesis and direct organogenesis methods that have some long culture period, low rate of conversation of somatic embryos into plantlets and poor rooting (Kumria et al. 2003; Ozyigit and Gozukirmizi 2008). Phenolic oxidation dependent explant browning is another problem that affects the success of tissue culture (Ozyigit 2008; Ozyigit, Kahraman, and Ercan 2007). However, these problems were solved in the following years. Today, successful tissue culture and especially *Agrobacterium*-mediated genetic transformation studies are carried out (Ahmad et al. 2020; Gurusaravanan, Vinoth, and Jayabalan 2020).

On the other hand, none of the transferred genes by these methods had a direct effect on the quality of the fibers, but instead had effects on quantitative traits such as insect resistance, herbicide resistance, and environmental stress (Haigler et al. 2007). Thus, recent researches have focused on improving cotton fiber quality via genetic engineering especially in last two decades (Han et al. 2014; Li et al. 2015b).

Definitions of genetically-modified cotton and Bt-cotton

Breeders cultivated cotton using classical methods for many years but due to increasing demand, climate change and losses due to pests, there is a decrease in growth and yield (Chen et al. 2008; Noman et al. 2016).

Bt-cotton which is also genetically modified cotton, gets its name from an aerobic gram-positive soil bacterium *Bacillus thuringiensis* (Bt) and is the first non-food transgenic crop which serves as an effective tool on lepidopteran and coleopteran insects. In 1901, the bacterium was isolated from dead silkworm larvae during the investigation of sotto disease in silkworms. Bt is also characterized by forming crystal inclusions such as Crystal (Cry) and Cytolytic (Cyt) toxins during sporulation while crystals dissolved in the midgut of insects after ingestion, proteolytically activated by midgut proteases and after binding to special receptors on the insect cell membrane, they induce cell disruption and cause death of the insect (Ibrahim et al. 2010; Raymond et al. 2010; Srikanth, Maxton, and Masih 2019). Another important feature of the Bt-cry protein is that it is nontoxic to humans and animals (Sheikh et al. 2017). All of these advantages make Bt-cotton important in agriculture.

Developments in biotechnology promoted the commercialization of Bt-cotton and it has been widely adopted by farmers, especially in developing countries. In 1997, Bt-cotton varieties containing

Cry1Ac gene were first introduced in the U.S. In the following years, another new version containing *Cry1Ac* and *Cry2Ab* was commercialized in 2003 which is thought to be more effective (Siddiqui et al. 2019). Since the first commercialization of Bt-cotton, plenty of *Cry* genes from many bacterium strains including *Cry1, Cry2, Cry9* and *Cry13* have been found. These *Cry* genes are efficient on lepidopteran insects and *Cry3, Cry7* and *Cry8* proteins are efficient on coleopteran insects. Additionally, *Cry4, Cry10* and *Cry11* proteins were found to be effective on dipterous insects (Singh et al. 2019).

In the last decade, a new class of insecticidal proteins has been identified that differ from *Cry* proteins found in *B. thuringiensis*. These vegetative insecticidal proteins (Vips) are released into the extracellular medium while some strains are in the growth phase. As a result of genetic analysis, Vip proteins are divided into four classes; Vip1, Vip2, Vip3, and Vip4 proteins. Vip1 and Vip2 have coleopteran activity, while *Vip3* toxins have lepidopteran activity. The specificity of the Vip4 protein has not yet been reported (Beard et al. 2008). Studies have found that Vip3 protein is significantly different from Cry proteins phylogenetically; making them an important insecticidal protein as the insecticidal receptor binding sites of Vip3 proteins are distinct from Cry proteins. When the *Vip3a* gene was first applied to cotton, it was applied alone as an insecticidal protein and then it was combined with Cry proteins to protect crops (Chakrabarty et al. 2020; Zheng et al. 2020).

From the past up to date: Bt-cotton cultivation

Currently, cotton is grown commercially in more than 100 countries. Approximately 12 USD billion worth, and twenty-five-million metric tons of cotton can be produced in a year. In 2019/2020 the top cotton-producing countries were and have been India, China, USA, Brazil, Pakistan, Turkey, Uzbekistan, Mexico, Argentina and Greece, respectively. The amounts of cotton produced annually in a thousand metric tons are: 6000, 5800, 4377, 2755, 1350, 815, 641, 369, 358, and 317, respectively (ICAC 2020; Khan et al. 2020).

Among the countries, India produces 26% of the total cotton in the world even though the average yield per hectare is much lower than other cotton-producing countries. Indian farmers were very successful in the production of native desi cotton species (*G. arboreum*) in ancient times. However, difficulties arose with the new hybrid (*G. hirsutum*) in 1990s since their seeds were not resistant to Asian pests. Indian farmers experienced great difficulty since they lacked knowledge and experience; the high cost of insecticides as well as their debts were hindrances for them. Meanwhile, Bt-cotton seeds were developed in the United States in 1995 and introduced to China in 1997. In 1998, Bt-cotton was first tested in India and their seeds including the *Cry1Ac* gene were approved for sale in 2002. The first applications were carried out in southern lndia in 2002 but Bt-cotton containing both *Cry1Ac* and *Cry2Ab* genes, and from 2005 it was accepted in northern India (Kranthi and Stone 2020). As of 2010, cultivation of hybrid species increased to nearly 70% and 90% in 2011 (Mayee and Choudhary 2013). As an advantage, it has been observed that the yields across the country increased significantly after switching to Bt-cotton until 2007. Nonetheless, no improvement has been registered on the yields in the last 13 years whereas farmers are using more insecticides per area than when Bt-cotton began (Kranthi and Stone 2020). As of 2019, the use of 5 Bt-cotton variants in the country has been approved including *Cry1Ac, Cry1Ac/Cry2Ab, CryAc* (belongs to another company), *Cry1Ab/Cry1Ac* and *Cry1C* genes (USDA 2020a).

Cotton is grown mostly in the US states of Arizona, California, Florida, Mississippi, and Texas. The insect-resistant transgenic cotton that Monsanto (an agricultural biotechnology company) offered commercially carried the *Cry1Ac* gene. After the application of Bt-cotton cultivation, the boll weevil was eradicated and the use of insecticides decreased significantly. Later, transgenic cultivars containing both the CP4-EPSPS protein of *A. tumefaciens* and *Cry1Ac* were introduced to the markets (Akbar et al. 2019). The variants carrying the *Cry1Ac* and *Cry2Ab* were released in 2004, and the ones carrying the *Cry1Ac* and *Cry1F* genes released in 2005 (Tabashnik and Carrière 2017; Zhang 2015).

Due to the rapid urbanization, climate change, excessive pesticides and fertilizer use, as well as many other countries China has lost arable lands over the last two decades. As a result, China was

importing large amounts from various crops (Liu et al. 2020). Afterward, with the action of the government, it was aimed to increase agriculture by using agricultural biotechnology. Cotton is the primary crop in China and is cultivated in 24 provinces. Xinjiang Uygur Autonomous region is where the best quality cotton plants have been grown in the 2000s (Li et al. 2020a). So far, nearly 300 insects have been observed in Chinese cotton fields containing cotton bollworm (*Helicoverpa armigera*) and pink bollworm (*Pectinophora gossypiella*). Of these herbivorous insects, especially cotton bollworm caused a large amount of economic loss and excessive use of insecticides (Chen, Huang, and Qiao 2013). The first trial of Bt-cotton including *Cry1Ac* and *Cry1Ab* genes were introduced in 1994, and had an 80% effective rate against cotton bollworm. Since Bt-cotton was commercialized in 1997, planting has increased rapidly and reached nearly 4 million ha. However, due to policy changes in 2017 the cotton planted area has reduced to 2.9 million ha. Currently, Bt-cotton plants in China include *Cry1Ac, Cry1Ab/Ac, Cry1A/CpTl* genes that target lepidopteran pests (Li et al. 2020b).

Brazil has become one of the leading countries in agriculture in the world, especially since 2000s. Brazil is one of the leading countries in the export of sugar, soy, corn, orange juice, coffee, pork, and cotton. One of the reasons for this success can be said to have favorable weather conditions, suitable land, and water resources in the country. In addition, it is an important factor for agricultural centers to use research centers and farmers to work in harmony (Rocha, Gonçalves, and Almeida 2019). While cotton was grown on small farms in Cerrado province and collected by hand in the 1970s and 1980s, cotton production was damaged with the emergence of the boll weevil pest. Since the 1990s, production has moved to large-capacity farms, and has steadily increased. Furthermore, with transgenic technologies emerging in recent years and the increase in cotton, it means there has been an increase in production. The average seed cotton fields are currently the largest in the world (Raphael 2019). Brazil is also ranked 2nd in cotton exports after United States (ICAC 2020). The use of transgenic plants was approved by Comissão Tecnica Nacional de Biossegurança (CTNBio) and transgenic cotton cultivation, which was applied for the first time in 2002, to the 40% of the land (Hoffmann et al. 2019). Currently, traits that are used for cotton are high lint yield, high lint percentage, high fiber quality, resistance to pathogen organisms, and diseases. There were 83 transgenic cotton cultivars registered in 2018 including *Cry1Ac, Cry1F/CryAc, Cry1Ac/Cry2Ab2, Cry2Ae/Cry1Ab/bar* genes against many insects. Recently, studies have been conducted on boll weevil resistant transgenic cotton genotype in Brazil. These genotypes are intended to carry the *Cry1, Cry10Aa* and *Cry1b* genes and be resistant to coleopterans (Raphael 2019).

Pakistan is the 5th most cotton-producing country in the world and cotton is the most important crop of their agriculture. Pakistan is the 7th largest cloth producer and 79% of the cotton is cultivated in Punjab, and secondly in Sindh provinces (Kouser, Spielman, and Qaim 2019). Cotton growing season starts in May when temperature is high, and harvesting starts in September (Shahbaz, Yu, and Naeem 2019). The intensive use of pesticides in agriculture has resulted in the pests becoming resistant to pesticides and annual average losses of 10–15%. Pakistan wanted to bring Bt-cotton in 1998–1999 by the Government of Pakistan, but work was suspended in 1999 when the military coup occurred. However, it was unofficially planted in 2002, and first officially approved in 2009. Bt-cotton is the only transgenic crop in the country with approved commercial cultivation until 2018. In 2013–2014, 16 Bt-cotton varieties were planted on more than 2.8 million hectares in the country (Ali et al. 2018). As of the end of 2018, a total of 30 Bt-cotton varieties were approved and allowed to be used.

The 6th most cotton-producing country is Turkey, and cotton production has been increasing since the 1990s. While cotton fiber has an important place in the country's economy and textile, thousands of people also have the opportunity to work in this industry. Cotton production is carried out in the Aegean, Cukurova, Antalya and southeastern Anatolia region of Turkey. Especially in the Aegean region, the highest quality and maximum amount of cotton is produced. Although there are losses in cotton fiber production every year due to diseases, insects, and pests, transgenic cotton cultivation has not been allowed yet (Baydar, Ciliz, and Mammadov 2015; Gunaydin et al. 2019). Turkey which has not applied Bt technology on its cotton crops is one of the pioneers in natural colored organic and

premium quality cotton worldwide (Burkitbayeva, Qaim, and Swinnen 2016; Khan et al. 2020; Palamutcu et al. 2019).

Uzbekistan, Turkmenistan, and Tajikistan, where 60% of cotton production was made during the Soviet Union, were important countries in cotton production. Cotton has not lost its importance after the collapse of the Soviet Union and is an important export source in Uzbekistan and Tajikistan. Only 3.5 million people work in cotton farming in Uzbekistan. However, in none of these countries has Bt-cotton yet been approved (Burkitbayeva, Qaim, and Swinnen 2016).

Mexico produces many economically important plants such as maize, cotton, and cocoa (Garcia Ruiz, Knapp, and Garcia-Ruiz 2018). Cotton plant is mainly grown in northern Mexico. Before Mexico met GM technology, there was a need for a new strategy to solve the environmental economic costs caused by the use of excess pesticides. GM cotton was first commercialized in 1996 when it was needed against pest attacks. Since 2008, approximately 96% of cotton fields were planted with Bt-cotton. There has been no increase in the number of land cultivated in Bt-cotton in recent years. The main reasons for this are fiber prices, cost, prevalence of pests, and diseases. Two main traits conferred to plants were tolerance to herbicides like glyphosate and dicamba and resistance to lepidopterant pests via *Bt*-genes. Currently, Bt-cotton cultivation is regulated by Biosafety Law of Genetically Modified Organisms in Mexico (Rocha-Munive et al. 2018).

Argentina was the first Latin American country to accept glyphosate-tolerant soybean in 1996 followed by Bt-cotton application. Unlike GM soybeans, it took some time to adopt Bt-cotton technology (Qaim and De Janvry 2003). Three years after the approval, the proportion of Bt-cotton cultivated cotton fields was only 5%. There are two different agriculture subsystems in the country. One of them is the big commercial farmers and others are small or family farms. Bt-cotton has been adopted especially in family farms that traditionally cultivate cotton in North-East of Argentina (Van Zwanenberg and Arza 2013). After switching to Bt technology, the use of pesticides has significantly decreased and the yield has increased. For example, a classic Latin American cotton grower had to spray the field 12–25 times a year before Bt-cotton could be planted. There is no longer any need to use chemicals in spraying (Blanco et al. 2016). As of 2020, currently, the country is one of the global leaders in GM crop production and regulation. However, there are problems in the country due to illegal cultivation and increasing costs (Lapegna and Perelmuter 2020).

Cotton is the national product of Greece and 80% of the cotton production of the European Union (EU) belongs to this country. Cotton is mainly cultivated in central and northern Greece. Bt-cotton has not yet been permitted in Greece and in the EU (Basal et al. 2019; Voloudakis et al. 2018). Therefore, pest control is provided by insecticide applications (Milonas et al. 2016).

Role of Bt-Cotton in the world economy

Cotton is used in a wide variety of fields today. Cotton fiber is the most commonly used natural fiber. Cotton is a natural fiber with good absorbance, air permeability, softness and non-allergic nature for humans. Cotton and cotton industry-based by-products used in making vegetable oil, fishnets, book-binding, food packaging, coffee filters, seedcake, and pillows. Cotton seed is used in margarine, cosmetics, pharmaceuticals, soap, rubber, and plastic production (Munir et al. 2020; Ozyigit, Kahraman, and Ercan 2007; Wegier, Alavez, and Piñero 2016).

Cotton prices are regulated by variety and quality. Properties that determine the grade of cotton are staple length of cotton fibers, fiber fineness and moisture content. Over-ginning of cotton, cotton fibers cause their value to decrease as they can be damaged. With the adoption of Bt-cotton, the use of chemicals and pesticides in agriculture has decreased, so costs have also decreased (Sawan 2018). In addition, it was observed that the harvest yield increased at a remarkable level and provided a profit for the economy (Kouser, Spielman, and Qaim 2019). These applications both provided advantages to large farms in developed countries like the United States and Australia, in labor savings, high yields and to smallholder farmers (Vitale, Vognan, and Vitale 2016).

Cotton production is very important in terms of generating employment in agriculture and industry sector. In addition, cotton covers 85% of the raw material used in textile industry especially in clothing and armor manufacture (Gamanagatti and Dodamani 2016). It is also estimated that the share of cotton in the textiles industry and its contribution to the world economy is 600 USD billion a year. Bt-cotton technology has been used in many cotton-producing countries since the 1990s. Currently, Bt-cotton is the most desired variant in agriculture due to its advantages (Tausif et al. 2018). According to International Service for the Acquisition of Agri-biotech Applications (ISAAA) in 2018, 15 countries planted Bt-cotton worldwide (ISAAA 2019a). While the area planted with Bt-cotton was 24.1 million hectares in 2017, this number increased to 24.9 million hectares in 2018 (Shera et al. 2018). As one of the reasons for this 3% increase, it is thought to be the adaptation in the production of insect resistance and herbicide-tolerant cotton crop with increasing global market value. In 2018, United States, China, Pakistan, and Brazil were the countries with the highest Bt-cotton cultivation, with India being the first in line. The cultivated fields in million hectares were 11.6, 5.06, 2.93, 2.8, and 1 million hectares, respectively. The mega Bt-cotton producing countries were followed by Argentina, Myanmar, Australia, Sudan, Mexico, South Africa, Paraguay, and Colombia (ISAAA 2019b).

Bt-cotton was released in India in 2002, and cotton yield increased across the country substantially in 2003–2004. The adoption of technology took place after 2005 and the yield level reached its peak. In India, crop loss was experienced due to insects and pests, and it was found that Bt-cotton seeds provided a good control (Kranthi and Stone 2020). Bt-cotton is mainly cultivated for clothing, oil extraction for human consumption and animal feed. Until 2015, China was the country that produced the most cotton in the world. However, in the following years, India became the leader. By 2020, Bt-cotton is still the only GM crop approved for commercial cultivation in the country. In 2019/20 marketing year, Bt-cotton was planted in 92% of the cotton fields (USDA 2019a). In 2020, cotton exports in the country decreased to 800.13 USD million from 3379.21 USD million in 2019 (Trading Economics 2020a). India is the third largest cotton exporter after the United States and Brazil. Additionally, a small amount of cottonseed is also exported. At the same time, a significant amount of Bt-cotton is imported to meet the need of the local textile industry for quality cotton (USDA 2020b). However, cotton imports, which increased rapidly until the 2019/20 marketing year, fell sharply in the August 2020/21 period, with a decline of over 50% (USDA 2020c).

In China, it was observed that the yield in the fields planted with Bt-cotton in 2001 was 6% higher than in non-Bt-cotton fields. This showed that Bt-cotton technology was well adapted in the period from 1999 to 2001. After joining the World Trade Organization (WTO), the problems in agriculture in China caused a decrease in cotton production. Then, various policies were followed to increase exports (Tausif et al. 2018). The Chinese Government has invested large budgets for biotech crops and seeds research. In 2008, Key Scientific and Technological Grant of China for Breeding New Biotech Varieties research program has been supported approximately 3.5 USD billion. Cotton fiber and cottonseed are exported in the country and a significant amount is imported in Bt-cotton. Bt-cotton seed import is not allowed for commercial cultivation in the country whereas the only insect-resistant GM crop whose commercial production is allowed is Bt-cotton (Li et al. 2020b; USDA 2019b). Currently, declining demand due to the pandemic caused a decrease in cotton use and import in the 2019/20 marketing year. However, consumption and production are expected to increase in China in the first 6 months of 2020/21 marketing year. Recent data also show that in July 2020, textile exports in China increased to 31.3 USD billion compared to the previous month while total export reached 56.5 USD billion in the first 7 months of the year. Especially the increasing demand for medical personal protective equipment has a large share in the export (USDA 2020d).

The cotton industry in the U.S. provides jobs to over 100,000 employees annually and more than 21 USD billion in products and services (USDA 2020e) As in recent years, the U.S. ranks first in cotton exports in 2019/2020. As of 2020, 88% of the U.S. fields are planted with Bt-cotton which increased from 37% in 2001 (USDA 2020f). On the other hand, in 2018, a dispute was made with major trading partners such as China, India, Mexico, Turkey and the EU, and agricultural exports to China dropped significantly. (Grant et al. 2019). The rising trend in cotton production from 2018 to the end of the

2019 season left its place to decline until August 2020 due to the pandemic. The decrease in production is expected to decrease by approximately 5% in September compared to the previous month (USDA 2020c).

Brazil is one of the leading countries that mostly export soybeans, Bt-cotton and corn. For this reason, the United States and Brazil compete with each other in the third country markets such as China which is the largest destination for Brazil exports. In recent years, despite the decrease in cotton production in many countries, the production in Brazil has increased and cotton need of China has been met by taking advantage of the trade war between China and the United States (Barros et al. 2020). Bt-cotton import from Brazil is mainly made to China and EU countries. As of 2019, the use of 23 Bt-cotton variants has been approved (USDA 2019c). Cotton production and yield increased in 2018/2019 and 2019/20 marketing years whereas there was a 1% decrease in production in August 2020 (USDA 2020c). The increase in cotton exports in Brazil has continued in recent years and reached 2.79 USD billion in 2019/20 marketing year. It is expected to reach a peak point in September 2020/21 marketing year (Trading Economics 2020b; USDA 2020g).

Although it has been legal in Pakistan for the last decade, cotton variants containing different genes are under trial. In 2019, Pakistani farmers cultivated Bt-cotton in an area of 2.5 million hectares in total. In addition, the country exports various products such as cotton yarn, cotton fabric derived from both Bt-cotton and domestic cotton (Ali et al. 2020). In the 2020/21 marketing year, a significant decrease in exports and imports is seen so far compared to the previous year. Cotton exports reached 3.24 USD billion in Pakistan at the 2019/20 marketing year (Trading Economics 2020c). Although the cotton import of the 2019/20 marketing year, which reached its peak, decreased in August 2020/21, it is expected to reach the same level again in September (USDA 2020g). While Bt-cotton has a large share in the economy in Pakistan, textile exports made up 5% of the country's total exports. The Pakistani government is trying to make regulations in the country, especially by tightening trade rules for GM products (USDA 2020h). Besides, there are problems in yield due to factors such as salinity, drought, water logging, and heat stress in the country. So far, 15.0 million hectares of cultivated area have been abandoned due to drought (Babar et al. 2020). There is a decrease in cotton production and yield in Pakistan in 2019/20 compared to the previous marketing year and also a decrease in production is expected in September 2020 compared to the previous month (USDA 2020c).

Bt-cotton technology is not yet approved in Turkey. However, the Turkish textile industry has a big share in the economy as 29.4 USD billion of the total 168 USD billion exports in 2018 belong to the clothing and textile sector (Basal et al. 2019; UPK 2019). In the Cukurova region, which is one of the regions where cotton production is made in the country, citrus orchards fields have been replaced by most cotton areas due to changes in weather conditions and easier export. Cotton yarn exports decreased by 11% in 2019 but an important amount of cotton yarn worth 139,681 USD was exported to the European Union countries, Egypt and Pakistan. Cotton imports are expected to continue in the country in the coming years due to the large textile industry and reduced production (USDA 2020i).

In the cotton production, a decreasing trend is seen today from the 2018/19 marketing year. As of 2020, there is a 20% decrease in production and it is expected that the decline will continue in September 2020 (USDA 2020c).

As of March 2020, the liberalization of the cotton market by the government is an important development in the Uzbekistan cotton industry. Thus, farmers will plant what they want, and the government will not be able to interfere with cotton production and prices. The European Union will provide Uzbekistan with €40 million for the development of agriculture (Timesca 2020). The increase in cotton consumption in the country limits the cotton to be used for export. Bt-cotton has not yet been approved in Uzbekistan. Cotton lints and cotton fabrics are exported to China, Bangladesh, Turkey, and Iran. In the third quarter of 2019, cotton exports of Uzbekistan reached 13677 USD million from 8437 USD million in the second quarter of 2019 (Trading Economics 2020d; USDA 2020j). Cotton production increased compared to the previous year in 2019/20 marketing year, but production decreased in August 2020. No change in cotton production is expected in September 2020 (USDA 2020c).

In Mexico, there has been no progress in agricultural biotechnology in the country since 2018. Since only four Bt-cotton variants have been approved so far, farmers have a hard time finding these outdated seeds. For these reasons, cotton production is expected to drop in the current season. Although Bt-cotton production is for domestic consumption, nearly 130 thousand tons of cotton is exported annually to China, Pakistan, Vietnam, and Indonesia thanks to the increasing production. Since the Bt-cotton production in the country meets about 60% of domestic cotton consumption, all of the total imports are made from the USA. The cotton imported from the United States during 2019 was worth 617.71 USD million (Trading Economics 2020e). Cotton production in Mexico has increased significantly over the last decade as a result of the use of Bt-cotton seeds, correct pesticide use, and investments (USDA 2020k). However, due to pandemic, cotton production in Mexico has decreased by approximately 33% compared to 2019 (USDA 2020c).

Commercial production of six cotton varieties has been approved in Argentina to date and all GM events have been approved primarily in China since 2015. In the 2018/2019 season, stacked event (Bt x TH) was planted to all of the total cotton fields and two new variants have been approved in 2019. Argentina exports cotton to many countries, even to the United States (Brookes and Barfoot 2018; USDA 2020l). Although cotton production increased significantly in Argentina in the 2019/20 season, there has been a decrease of approximately 7% in production as of August 2020 (USDA 2020c).

Due to favorable weather conditions, yield, and the increase of fields for production increase in Greece, a growth of 18.8% is expected in cotton production in the 2019/2020 season compared to the previous year. Greece, where Bt-cotton has not yet been approved, is the country that produces the highest amount of cotton in the European Union (Hundleby and Harwood 2019). According to the United Nations COMTRADE data, Greece exported 636.73 USD million worth of cotton in 2019 (Trading Economics 2020f). However, the economic crisis in the country has negatively affected the cotton market for years. In addition, cotton yarn imports of the country increased to 10.4% in 2019, and cotton was mainly imported from Turkey, Bulgaria, and India (USDA 2020m). Although cotton production in Greece decreased in August 2020, production was higher than 2018–19 marketing year (USDA 2020c).

Before the COVID-19 pandemic, cotton trade was expected to expand significantly in the period 2020/2021 worldwide. Moreover, the United States, Brazil, and India were expected to be the most exporting countries. Given the increasing demand worldwide, cotton imports were expected to increase by 20% in China. However, due to the pandemic, only in May, there was more than a million metric tons of reduction in consumption and a sharp increase in ending stocks (Europeanseed 2020). Besides, travel restrictions and closing the borders of countries in order to control the spread of the disease, will make it difficult to seasonal labors (Kerr 2020; USDA 2020n). During the pandemic, the sales of clothing and textiles around the world have decreased and therefore so has the global cotton demand and cotton economy, severely impacting on the price of cotton (Europeanseed 2020). The effects of a pandemic on the agricultural economy will be better understood in the following months.

Conclusion and future perspectives

Heat-waves, drought, torrential rain, weather, and climate conditions are well documented in negatively affecting agriculture worldwide. This alongside the estimated world population increasing to ten billion by 2050, suggests a possible food crisis. Despite Bt-cotton originally attracting attention to simply solve the insect and pesticide problem, it has proved itself to be even more beneficial than first thought. In the past 24 years, the adoption of Bt-cotton technology has brought many economic benefits. After the adoption, chemical spraying in the field against insects has decreased, therefore it has had positive effects on the environment and health of farmers as well as consumers, and it has also been observed that cost of production and labor use have decreased. Since the adoption of Bt-cotton, farmer pesticide poisoning cases as well as farmer suicides and cancer rates have decreased significantly in China, India, and Pakistan (Kouser, Spielman, and Qaim 2019; Smyth 2020). Especially in developed countries where Bt-cotton technology is adopted, a clear increase in farmer profits and yield

has been observed. Another point of view, some farmers worry that pest resistances or secondary pest outbreaks may occur in the long run, suggesting that these benefits are short term. Even though there are conflicts of opinion regarding the use of Bt-cotton technology, it has been adopted since 1996 in 15 countries; Argentina, Australia, Brazil, Burkina Faso, China, Costa Rica, United States, India, Mexico, Colombia, Paraguay, Burma, Pakistan, South Africa, and Sudan.

In this study, information on commercialization and adoption of Bt-cotton in the countries that produce the most cotton in the world, and the contributions of Bt-cotton to the national/international economies, environment, and health are given in order to provide insights into the current status in the world. Future studies in countries where Bt-cotton is adopted will enable the effects of Bt-cotton on economy to be more clearly demonstrated.

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