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REVIEW
Safety Evaluation of Bt Plants

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Abstract
Bt plants are insect-resistant plants engineered to carry the gene coding the insecticidal protein of a soil bacterium, *Bacillus thuringiensis*. These transgenic plants provide a highly effective method of insect control and reduce dependence on pesticide chemicals. In consequence, they have provided higher yields, reduced crop mycotoxin levels because of the effective lowering of the insect damage, and have decreased the pesticide spraying work and cost. However, there are public concerns about the safety of Bt plants for humans, animals and the environment. This review describes recent research on the safety evaluation of Bt plants, focusing on our results in the toxicological studies of Bt11 corn.

Discipline: Animal health
Additional key words: cattle, genetically modified plant, pig, poultry

Introduction

Transgenic manipulation is a very useful biotechnology that produces new and valuable varieties of organisms for humans by transferring a target gene from one organism to another. Discovery and engineering development for transgenic manipulation in natural science history began with the clarification of the molecular structure of DNA by Watson and Crick in 1953[59]. Zimmerman et al. discovered DNA ligase[63], and Linn et al. described the effect of restriction endonuclease[31]. In 1973, Cohen et al. succeeded in transforming *Escherichia coli* by gene transfer[13]. This success suggested the possibility of artificially creating transgenic organisms that are extremely useful in agriculture, medicine and other natural science sectors. Agricultural researchers were inspired to make new, valuable plants by implanting useful genes from other living creatures. Finally, they had developed a new, valuable plant, the genetically modified plant, and, in 1994, the Flavr Savr tomato that is engineered to resist rotting was approved as the world's first genetically modified food for sale in the USA. The technology is now expected to be a key technology for resolving breadbasket issues and global environmental problems.

However, there are public concerns about the safety of genetically modified plants. For instance, the general public seems to have a vague anxiety about plants expressing insecticidal toxins or indicates a physiological discomfort against implanting the genes derived from bacteria. Considering this, the governments in many countries review and approve genetically modified plants for human consumption or for use in livestock feed based on the global standard of safety evaluation formulated by the Codex Alimentarius Commission in 2003 under the concept of "substantial equivalence." The concept is regarded as fundamental in safety evaulation for genetically modified plants, based on considering the conventional plant as a safe foodstuff or feedstuff. When a new, genetically modified plant is developed, it is first compared with its conventional homologue to assess whether it can be considered to be ''substantially equivalent'' in regard to its fundamental constituents and usage. Substantial equivalence is therefore only the starting point of safety assessment. Safety evaluations for alterations in composition, metabolic and protein profiles, metabolic activity, antinutrients, toxicity, and allergenicity potentially developed by implanting a new gene are needed as next steps.

In Japan, the Ministry of Agriculture, Forestry and Fisheries evaluates the safety of genetically modified

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feed. For the genetically modified food, the Food Safety Commission reviews and the Ministry of Health, Labor and Welfare approves it based on the judgment of the Food Safety Commission. In addition, the Food Safety Commission reviews animal products from livestock fed the genetically modified feed.

Various genetically modified plants have been developed in which traits such as increased resistance to pests or tolerance of herbicides have been transferred or the nutrient composition has been effectively changed. This article focuses on the safety evaluation of Bt plants, which are insect-resistant plants, that are embedded with the gene coding the insecticidal protein, Cry toxin, of *B. thuringiensis*. In this article, we review livestock-feeding and small experimental animal-feeding studies of Bt plants including corn, cotton and rice, in vitro safety evaluations of Cry toxin, and the transfer of Cry toxin and *cry* gene to tissues of animals fed Bt plants, with a central focus on our recent toxicological studies of Bt11 corn that is one variety of Bt corn.

Cry toxin

Cry toxin is an insecticidal protein that is the component of crystalline inclusions produced by *B. thuringiensis* during its sporulation. The toxin can be further categorized into 53 classes based on amino acid identity[14,15]. Figure 1 depicts the mode of action of Cry toxin. After the insect larva ingests the crystalline inclusions, Cry toxin dissolves in the alkaline gut juice of insects, and gut proteases subsequently degrade the toxin's C-terminal extension as well as the small N-terminal fragment. The resulting 'activated toxin' binds to receptors on the membrane of midgut epithelial cells. The fraction of the toxin is then inserted into the membrane after structural rearrangement. The inserted toxin forms pores as oligomers and causes cellular lysis due to the inflow of ions and water through the pores. Eventually, the insect larva dies[16,42]. Owing to such a complicated mode of action, Cry toxin has a narrow specific spectrum and kills only the target insect larvae. Thus, the toxin does not attack non-target insects.

Due to its unique characteristics, Cry toxin has been used as the active element of the environmentally benign microbial pesticide, Bt pesticides, including toxins and/or spores without live *B. thuringiensis* since 1961 in the USA. However, pesticide spraying is very arduous work and, despite this, the superficial spraying of Bt pesticide is not effective against pests invading stalks, such as the European corn borer (*Ostrinia nubilalis*). Farmers demanded a more effective method of insect control. The demand promoted the birth of an innovative genetically modified Bt plant in 1987. Vaeck et al. developed Bt tobacco expressing Cry toxin that protects it from feeding damage by larvae of the tobacco hornworm[57]. At present, Cry toxin is widely used in insect-resistant transgenic plants.

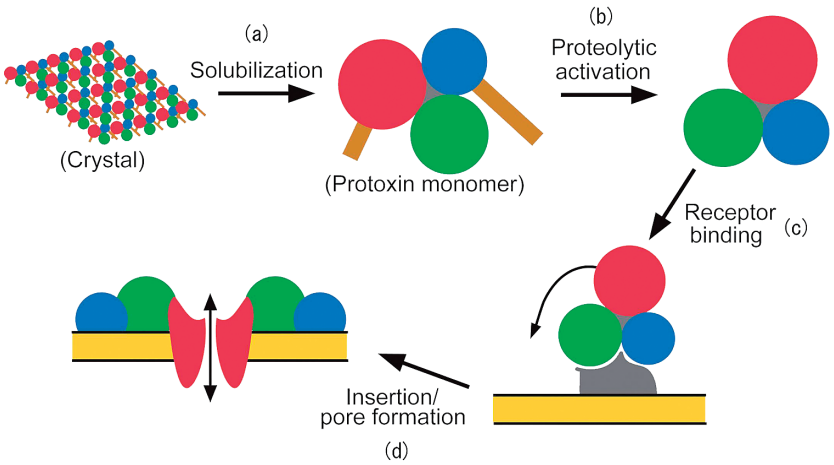

Fig. 1. Mode of action of Cry toxin

(a): After ingestion by the insect larva, crystal solubilizes in the gut juice. (b): Gut proteases subsequently degrade the C- and N-terminal fragments (brown). (c): The resulting 'activated Cry toxin' binds to receptors on the membrane of midgut epithelial cell. (d): The fraction of Cry toxin (red) then inserts itself into the membrane after structural rearrangement, and the inserted toxins form pores as oligomers. Reprinted from Griffitts et al. (© 2005 Wiley Peniodicals, Inc.)[24] with permission of Wiley-Liss, Inc., a subsidiary of John Wiley & Sons, Inc.

In vivo safety evaluation

Since the commercialization of the Flavr Savr tomato in 1994, the global planted area of transgenic plants continued to increase for ten consecutive years (1996 to 2006) at a growth rate of 12 million hectares, reaching 102 million hectares in 2006[28]. However, there are increasing uncertainties about the safety and nutritive value of Bt plants as food or feed. Although we find many reports regarding nutritive evaluation and animal performance (feed intake, daily weight gain, and milk or carcass production) using livestock fed Bt plants and some reports regarding toxicological tests of Bt plants using small experimental animals, there are very few reports on the safety evaluation of Bt plants from the toxicological standpoint using livestock. Therefore, toxicity assays of Bt11 corn, a Bt plant, was performed using calves, pigs and layers following a request by the Japanese government.

1. Cattle

Twelve healthy four-month-old cross-breed calves (Japanese Black × Holstein) were fed 43.3% Bt11 or 43.3% non-genetically modified isoline corn kernels as dry matter for 90 days, according to the feeding experiment procedure for safety assessment of feeds recommended by the Ministry of Agriculture, Forestry and Fisheries of Japan. Samples of peripheral blood and rumen juice were collected every two weeks. At the end of the experiment, tissues from the liver, spleen, kidney, mesenteric lymph nodes, and musculus longissimus were sampled after slaughter. We then examined these tissue samples histopathologically and measured hematological and biochemical parameters, i.e. red blood cells, white blood cells, hematocrit, hemoglobin, aspartate aminotransferase, γ-glutamyltransferase, alkaline phosphatase, total-Bilirubin, total protein, albumin, total cholesterol, triacylglycerol, blood urea nitrogen, creatinine, calcium, inorganic phosphorus, magnesium, glucose, sodium, potassium, and chlorine in peripheral blood and ruminal pH, volatile fatty acid, lactic acid, ammonia nitrogen, and free lipopolysaccharides in rumen juice. As a result, we found no significant gross or histopathological lesions and no discernible clinical, hematological, biochemical, or ruminal abnormalities in calves fed Bt11 corn as compared with control calves fed non-Bt corn[11,47]. To date, there are no reported safety evaluations of Bt plants from the toxicological standpoint using cattle. In that sense, these reports are valuable, and we consider that such research provides scientific knowledge needed to diminish public concerns about the safety of genetically modified plants.

As far as we know, no other toxicity assays of Bt plants from the toxicological standpoint using cattle have been published, although many nutritive evaluations and feeding studies using cattle fed Bt plants have been conducted. Aulrich et al. reported that the results of the analyzed Bt corn samples indicated equivalence to nontransgenic corn in all investigated components, such as crude protein, crude ash, crude fiber, amino acids, fatty acids, minerals, and non-starch polysaccharides. Furthermore, the slaughter results revealed no significant differences between the fattening bulls fed silage made from the Bt or nontransgenic corn[2]. There were no significant differences in fat-corrected milk yield, protein content, fat content, protein fractions, fatty acid composition, or coagulation properties of milk between Bt and conventional isogenic-corn-fed cows[3]. Effects of Bt corn on rumen functions that play an important role in digestion and absorption were also examined, and ruminal pH, acetate: propionate ratio, in situ digestion kinetics of NDF (neutral detergent fiber), efficiency of milk production, and daily body weight gain were unaffected by the transgenic corn[22]. Other feeding studies also demonstrated the equivalence of nutritional value of Bt corn and productivity of animal products from cattle fed Bt corn, compared with its nontransgenic control[18,23,58]. Additionally, the results of some compositional analyses and feeding studies of Bt cotton indicated that transgenic cotton is substantially equivalent to its non-transgenic control, similar to Bt corn[8,25].

2. Pigs

A toxicity test similar to that for calves was also performed using pigs. Ten castrated pigs weighing 42 kg (Large White/Duroc cross) were fed diets containing 60% Bt11 or non-Bt isoline corn kernels for four weeks. At the end of the experiment, the liver, spleen, kidney, heart, lung, lymph nodes, thymus, tonsils, stomach, duodenum, pancreas, jejunum, ileum, ileocecum, cecum, colon, rectum, and spinal cord were sampled after slaughter. These tissue samples were then examined histopathologically. Consequently, there were no significant differences in histopathological observation between Bt and control groups[62].

Although there are no other toxicological tests of Bt plants using pigs, some feeding studies have been conducted to judge the appropriateness as feed for pigs. Aulrich et al. reported that nutrient digestibility and energy content of Bt and non-Bt corn were not affected by genetic modification[2]. This research group also published similar results the following year[39]. In their article, they concluded that the genetically modified corn could be regarded as substantially equivalent to the parental corn line from the view of a nutritional assessment. Yamazaki

et al. conducted nutritive evaluations and feeding studies in addition to the above pathological examination, and they found no significant differences in nutritive value between Bt and control corn, and Bt corn did not influence growth performance in pigs[62].

3. Poultry

In the toxicity study for layers, ten one-week-old male White Leghorns were fed diets containing 61.22% of Bt11 or non-Bt isoline corn for four weeks. At the end of the experiment, the liver, spleen, kidney, heart, lung, thymus, thyroid, glandular stomach, gizzard, duodenum, jejunoileum, and spinal cord were sampled after slaughter. These tissue samples were then examined histopathologically. No significant differences in histopathological observation were found between Bt and control groups[62].

Although there are no other toxicological tests of Bt plants using poultry, many feeding studies using poultry have been published, similar to those on cattle and pigs. The first poultry study with Bt corn was published by Brake et al.[6]. They found Bt corn had no deleterious effects on body weight gain, feed conversion, survival rate, or parts yield. In addition, Brake et al. reported similar results in a feeding study of a different kind of Bt corn[7]. Aulrich et al. confirmed there were no significant adverse effects in feed conversion rate, individual egg mass, and digestibility and energy content of the diet when Bt corn was fed to laying hens and broiler chickens[2]. Tony et al. conducted nutritive evaluations, feeding studies and biochemical tests[55], and Aeschbacher et al. examined the nutrient composition of eggs from laying hens fed Bt corn[1]. In these studies, there were no significant differences between experiment and control groups. Taylor et al. chose rapidly growing broilers as a useful model because of their sensitivity to changes in nutrient quality and exposure to relatively high levels of the test material in the diet. They compared the wholesomeness of 11 kinds of Bt corn with conventional corn[48–53]. They reported no meaningful differences in nutrient composition, broiler performance, carcass yield, or meat composition, and they concluded that Bt corn is nutritionally equivalent to the control or conventional reference corn. Flachowsky et al. carried out a ten-generation study with quails and found feeding of Bt corn did not significantly influence health, animal performance, and quality of meat and eggs[21].

4. Small experiment animals

Cry toxin has been safely used as microbial insecticide for more than 40 years. For the approval of Cry toxin as an active constituent of microbial insecticide, many safety evaluations of Cry toxin have been conducted using laboratory animals. In consequence, no adverse effects of Cry toxin were found on body weight gain, clinical signs and autopsy gross observation in acute, subacute and chronic toxicity tests by oral administration of Cry toxin[4,20,35].

However, surprisingly, there are few toxicological studies with small experiment animals fed Bt plants. Teshima et al. examined growth, food intake, organ weights, and histopathological observations of thymus, spleen, mesenteric lymph nodes, Peyer's patches, small intestines, liver, kidney, and bone marrow from mice fed Bt corn for 13 weeks. In this study, they confirmed there were no toxicologically significant findings in any component of the examination[54]. Hammond et al. found that overall health, body weight gain, food consumption, clinical pathology parameters (hematology, blood chemistry, urinalysis), organ weights, and gross and microscopic appearance of tissues were comparable between rats fed Bt and conventional corn varieties for 90 days[26]. Furthermore, some research groups also reported similar results in their 90−day safety studies using rats[32,33,43].

In addition to these general toxicity tests, a special toxicity test has been published. Using dual-parameter flow cytometry, Brake et al. found that there were no apparent differences in percentages of testicular cell populations (haploid, diploid and tetraploid) between mice fed Bt corn diet and those fed the conventional diet for gestation, lactation and 87 days after birth[5]. Testicular germ cells are highly susceptible to some toxic agents because of the high rate of cell proliferation and extensive differentiation. Therefore, this result suggests that Bt plants are not harmful to mammalian reproductive development.

Considering these enormous numbers of in vivo safety evaluations with various livestock and small experiment animals, Bt plants are considered to be substantially equivalent to conventional nontransgenic plants from the viewpoints of both toxicology and nutritive aptitude.

In vitro safety evaluation

To understand the effects of Cry toxin on mammals in greater detail, we need to clarify the toxicity to mammalian cells and biochemical characteristics of Cry toxin on the in vitro level. For these reasons, various in vitro safety evaluations of Cry toxin have been performed.

1. Effects of Cry toxin on mammalian cells

Cry toxin universally induces morphological changes in the target insect cell, such as ballooning and burst-

Table 1. Research on in vivo safety evaluation

Authors	Bt plant	Animal	Results	Reference No.
Brake et al. (1998)	Corn	Broiler	No adverse effects on survivability, animal performance, or carcass production.	6
Aulrich et al. (2001)	Corn	Cattle, pig, poultry	Substantial equivalence to the nontransgenic corn in slaughter results.	2
Barriere et al. (2001)	Corn	Dairy cow	No adverse effects on milk yield or animal performance.	3
Folmer et al. (2002)	Corn	Beef, dairy cow	No adverse effects on milk production, rumen function, or animal performance.	22
Teshima et al. (2002)	Corn	Mouse	No adverse effects on growth, food intake, organ weights, or microscopic pathology.	54
Reuter et al. (2002)	Corn	Pig	Substantial equivalence to the nontransgenic corn in digestibility and energy content.	39
Brake et al. (2003)	Corn	Broiler	No adverse effects on survivability, animal performance, or carcass production.	7
Chowdhury et al. (2003)	Corn	Calf	No pathological lesions in visceral organs.	11
Donkin et al. (2003)	Corn	Dairy cow	No adverse effects on animal performance, milk production, or ruminal digestibility.	18
Grant et al. (2003)	Corn	Dairy cow	No adverse effects on animal performance or milk production.	23
Tony et al. (2003)	Corn	Broiler	No adverse effects on animal performance and no biochemical abnormalities.	55
Taylor et al. (2003)	Corn	Broiler	No adverse effects on animal performance or carcass production	48,49,50
Yamazaki et al. (2003)	Corn	Pig, layer	No significant differences in energy content, animal performance, or histopatholgical observation.	62
Brake et al. (2004)	Corn	Mouse	No adverse effect on percentages of testicular cell populations.	5
Castillo et al. (2004)	Cotton	Dairy cow	No adverse effects on animal performance or milk production.	8
Hamilton et al. (2004)	Cotton	Dairy cow, quail	No adverse effects on animal performance or milk production.	25
Aeschbacher et al. (2005)	Corn	Layer, broiler	No adverse effects on animal performance or egg production.	1
Flachowsky et al. (2005)	Corn	Quail	No adverse effects on animal performance, or carcass and egg production.	21
Taylor et al. (2005)	Corn	Broiler	No adverse effects on animal performance or carcass production.	51
Vander Pol et al. (2005)	Corn	Beef cattle	No adverse effects on animal performance or carcass characteristics.	58
Hammond et al. (2006)	Corn	Rat	No adverse effects on overall health, animal performance, clinical pathology parameters, organ weights, or pathological observation.	26
Shimada et al. (2006)	Corn	Calf	No clinical, hematological, biochemical, or ruminal abnormalities.	47
MacKenzie et al. (2007)	Corn	Rat	No adverse effects on nutritional performance variables, clinical and neurobehavioral signs, ophthalmology, clinical pathology, organ weights, or pathological observation.	32
Malley et al. (2007)	Corn	Rat	No adverse effects on animal performance, clinical signs, mortality, ophthalmology, neurobehavioral assessments, clinical pathology, organ weights, or pathological observation.	33
Schroder et al. (2007)	Rice	Rat	No adverse effects on behavior, weight gain, hematological and biochemical parameters, organ weight, or pathological observation.	43
Taylor et al. (2007)	Corn	Broiler	No adverse effects on animal performance or carcass production.	52,53

ing after the toxin treatment. However, cells developed from mammalians exhibited no morphological changes at the light and electron microscopic level[36,44].

In addition, there have been no reports that Cry toxin adversely affects cell function. In toxicology, functional toxicity and morphological toxicity complement one another. Functional toxicity potentially detects minimal effects that cannot be identified morphologically or are not intrinsically accompanied by morphological change. However, functional toxicity is not always more sensitive than morphological toxicity because reciprocal vital function may hide slight changes. We should conduct toxicological tests from both functional and morphological viewpoints considering this verity. Based on this background, Sacchi et al. confirmed that Cry toxin did not disturb the absorption of amino acids of brush border membrane vesicles prepared from rabbit jejunum[41], and Shimada et al. reported that there were no significant changes in the secretion of albumin from Cry-toxin-treated primary cultured bovine heapatocytes[44]. Moreover, to examine the mechanical damage of the cell membrane, liberation of UV-absorbing substances[36] or lactate dehydrogenase[44] from the cells into the medium and the membrane potential change of the cells[45], which indicate the membrane unintegrity, were measured, and no serious effects were found.

One of the factors for the insect-oriented selective toxicity of Cry toxin seems to be the receptor. No Cry toxin receptors have been identified on the membrane of mammalian cells[27,46]. Tsuda et al. succeeded in making an unsusceptible mammalian cell susceptible to Cry toxin by transferring the receptor gene derived from silkworm (*Bombyx mori*) to the cell[56]. These results suggest that the receptor is deeply involved in the susceptibility.

Effects of Cry toxin on mammalian cells have been precisely investigated in vitro, and many results supporting the safety of Cry toxin have been accumulated. Although there are reports that some types of Cry toxin, newly discovered ones, exhibit cytocidal activity on mammalian cell lines originating from cancer cells without intrinsic cell functions[30,37,61], no one has reported that Cry toxin exhibits cytocidal activity on normal mammalian cells with intact cell functions.

2. Digestibility of Cry toxin with mammalian digestive fluid

In the insect midgut, a fraction of C-terminal and N-terminal fragments of Cry toxin was clipped off with midgut proteases, but the toxic core is resistant to them. The resulting toxic core, activated Cry toxin, persists without degradation and attacks the midgut epithelial cells. However, Cry toxin is easily digested with mammalian digestive juice. In the in vitro digestibility test, Cry toxin was rapidly degraded using simulated gastric fluids[4,20], and bioactivity of the toxin also decreased[20]. In addition, preheating of Cry toxin (Cry toxin was boiled before the protease treatment) dramatically increased the digestibility of the toxin by simulated intestinal fluid[38]. Considering these results, the potential of Cry toxin to be bioactive and/or a food allergen in the mammalian digestive tract should be extremely low. Furthermore, amino acid sequence homology comparison did not reveal any significant sequence similarity between Cry toxin and known protein allergens[20].

Fate of transgenic plant DNA and protein

There is growing interest in the fate of foreign genes and proteins in parallel with the wholesomeness of genetically modified plants because consumers and farmers are concerned about the transfer of recombinant genes and proteins into animal products. In response to this concern, many studies on the fate of transgenic plant DNA and proteins have been conducted. Chowdhury et al. found that Cry toxin and *cry* gene were not totally degraded and were detected in gastrointestinal contents, but not in peripheral blood and visceral organs by immunological tests and PCR when Bt corn was fed to calves and pigs[9–12]. Wiedemann et al. examined the time-dependent ruminal degradation of transgenic DNA and Cry toxin using an in situ technique in which nylon bags filled with test corn samples were positioned within the rumen of rumen-cannulated cows. They found that ruminal digestion decreased the presence of functional *cry* gene fragments and that the full-size, functional Cry toxin was only detectable up to 8 h after incubation in the rumen[60]. Duggan et al. reported that only a short *cry* gene (211–bp) was detected in rumen fluid when sheep were fed Bt corn[19]. Rossi et al. detected a *cry* gene (1800–bp) only in gizzard contents, and there were no significant differences in the detection frequency of the other corn genes between Bt and isogenic corn fed to broilers[40]. They concluded that DNA derived from transgenic feed undergoes the same fate as isogenic feed. No one has detected the transfer of *cry* gene and Cry toxin into blood, visceral organs, muscle, or eggs in samples from both laying hens and broilers fed Bt corn[1,17,29,55,62]. In addition, the transfer of *cry* gene was investigated in a long-term feeding study. Flachowsky et al. ascertained that a short *cry* gene (211–bp) was detected in the stomach and along the whole gastrointestinal tract, but not in muscle, liver, stomach, spleen, kidney, heart, or egg from quails of each generation when Bt corn was fed to quails for ten generations[21]. However, there is a report that verified the transfer of *cry*

Table 2. Research on in vitro safety evaluation

Authors	Type of study	Results	Reference No.
Nishiitsutsuzi-Uwo et al. (1980)	Toxicity test on mammalian cells	No morphological changes and no changes in the liberation of UV-absorbing substances.	36
Sacchi et al. (1986)	Assessment on rabbit brush border membrane vesicles	No changes in the absorption of amino acid.	41
Hofmann et al. (1988)	Search for receptor	No Cry toxin receptor was discovered on the intestinal epithelial cells of rat.	27
Okunuki et al. (2002)	In vitro digestibility assay	Cry toxin was rapidly digested by simulated gastric and intestinal fluid with preheating.	38
Shimada et al. (2003)	Toxicity test on mammalian cells	No morphological changes and no changes in the liberation of lactate dehydrogenase or in the secretion of albumin.	44
Tsuda et al. (2003)	Clarification for mode of action	An unsusceptible mammalian cell was made susceptible to Cry toxin by transferring the receptor gene.	56
Shimada et al. (2006)	Toxicity test on mammalian cells	No changes in the membrane potential of human intestinal epithelial cells.	45
Shimada et al. (2006)	Search for receptor	No Cry toxin receptor was discovered on the intestinal epithelial cells of cattle.	46

gene into tissue sample. Mazza et al. reported that a small fragment of the *cry* gene (519–bp) was detected in blood, liver, spleen, and kidney from piglets fed Bt corn, but intact *cry* gene or its minimal functional unit was never detected[34].

Some researchers detected a small fragment of *cry* gene in the contents of the gastrointestinal tract from various livestock, and Mazza et al. found a small fragment of the gene in blood, liver, spleen, and kidney from piglets. However, such a small fragment of *cry* gene is very unlikely to transmit genetic information. Therefore, the direct effect of the contamination should be negligible even if the short *cry* gene contaminates animal products. Cry toxin was also detected only in the gastrointestinal tract content as a degraded short fragment, and if any Cry toxin fragments contaminate animal products, the effect should be negligible as in the case of the short *cry* gene fragment.

Conclusion

Biotechnology accelerates improvements in the breeding of agricultural crops and the efficiency of crop production and is expected to be a key technology for resolving breadbasket issues and global environmental problems. The Bt plant, a genetically modified plant, is considered to be as safe for mammalians as conventional plants as demonstrated in this review. Furthermore, it has secondary merits of reducing mycotoxin in corn and decreasing pesticide costs and time spent spraying chemical pesticides, in addition to the intended purpose of providing resistance to harmful insects. However, there are still some concerns of the flow of transgenic genes into the environment and the perturbation of the expression of constitutive components in a recipient plant by incorporating transgenic genes that are not yet fully clarified with the current molecular biological techniques. There is also political resistance to the popularization of genetically modified plants, in addition to the above scientific problems. Although an inquisitive attitude is an inevasible right even in the production of food, the biotechnology for developing genetically modified plants is currently dominated by some sophisticated companies. These companies reap huge profits by the monopolistic sale of their genetically modified plants. If this situation worsens, it is possible that these companies will dominate the food industry. In fact, implanting the resistance gene for their herbicide apparently conflicts with the profit common to people all over the world.

As mentioned above, we should clarify the unexplained aspects of genetically modified plants by further studies, confirm their safety scientifically, and resolve the political problems. For persons involved in science, politics and government, whether or not the benefit originating from genetically modified plants can equally benefit all humanity should be a significant issue in the future.

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