

Genetically modified crop vs Hybrid crops and their impact on health and environment

ABSTRACT

Genetically modified crop (GMC) is a technology which includes transferring Deoxyribonucleic acid (DNA) in plant cells. On the other hand, Hybrid Crops are naturally occurring crops but it also involves manmade crosses to have at least 15-20% higher yield potential over high yielding inbred crop varieties using almost the same level of inputs and also can perform better even under unfavourable environments like drought and saline condition. These days, hybrid crops are one of the most commonly consumed foods for humans. In line with this GM crops have high yield potential and adaptive capability under wide range of environments even under fragile ecosystems. There are different aspects of both these types of crops. Human consumption of these crops has been a highly debatable topic in recent times. In this study, a brief discussion on GM crops and hybrid crops will be presented. Additionally, a comparison between them, in terms of health and productivity, will also be discussed.

Keywords: Carbon Sequestration, Crops, Environment, Food, Human health.

1. Introduction

A hybrid crop is a result of two different varieties of the plant which is cross-pollinated to create an off-spring or hybrid that contains the best traits of each of the parents [1]. In hybridization, pollination is carefully controlled to ensure that the right plants are crossed to get the desired combination of characteristics, such as bigger size or better disease tolerance hybrids having some combination of these favorable traits: dependability, less required care, early maturity, higher yield, better flavor, target plant size, and/or better disease resistance. It is one of the main contributors to the dramatic rise in agricultural output during the last half of the 20th century. The Green Revolution of the 1960s and 1970s was spurred by traditional breeding and adoption of high-yielding crop varieties in developing countries [2]. The more recent development of modern biotechnology, especially genetic engineering (GM crops), extends these processes of biological innovations.

Usually Genetically modified crops developed through DNA transformation using genetic engineering methods. The main objective is to introduce one or more new better traits to the plant which does not naturally occur in the existing plants. For Instance, in food crops, it is

done to attain tolerance to specific pests, diseases, environmental stresses, or against chemical treatments. Aside from food crops, this technology is applicable in pharmaceutical agents, biofuels, bioremediation and other industrial goods. The aim of some traits, such as virus and insect tolerance or drought tolerance, is to reduce the impact of agricultural practices on the environment. Genetically modified crops impart number of health benefits for human as it contains improved nutrient profile. The principle GM crops grown are soybean, maize, potato, cotton and canola. Farmers have widely adopted genetically modified technology. It is the fastest adopted crop technology in the world. Acreage increased from 1.7 to 185.1 million hectares within 1996 to 2016, 12% of global cropland. GM technology adoption had reduced chemical pesticide use by 37%, increased crop yields by 22%, and increased farmer profits by 68% [3]. This reduction in pesticide use has been ecologically beneficial. Yield and profit gains are higher in developing countries than in developed countries (ISAAA, 2015) However, opponents have objected to GM crops on several grounds, including environmental concerns and human health aspects, whether food produced from GM crops is safe, and needed to address the world's food demand, whether the foods are readily accessible to poor farmers in developing countries. Powerful scientific techniques have caused dramatic expansions of GMC leading to altered agricultural practices posing direct and indirect environmental effects [5]. The advent of GM crops has led not only to concerns over food safety but also to question about their potential impact on the environment. Despite the enhanced yield potential, risks and biosafety concerns associated with such GM crops are the fundamental issues to be addressed [6].

In plants, scientific identification of hybrids is thought to have begun in 1716, when Cotton Mather described corn (*Zea mays*) and squash (*Cucurbita* spp.) And the first genetically modified crop was produced in 1982, an antibiotic-resistant tobacco plant. The first field trial occurred in France and the USA in 1986, when tobacco plants were engineered for herbicide resistance [7]. In 1987, Plant Genetic System (Ghent, Belgium), founded by Marc Van Montagu and Jeff Schell, was the first company to genetically engineer insect-resistant (tobacco) plants by incorporating genes that produced insecticidal proteins from *Bacillus thuringiensis* [8]. The People's Republic of China was the first country to allow commercialized transgenic plants, introducing a virus-resistant tobacco in 1992, which was withdrawn in 1997 [9]. The first genetically modified crop approved for sale in the USA in 1994, was the Flavr Savr tomato [10]. It had a longer shelf life, because it took longer to soften after ripening. In 1995 canola with modified oil composition, Bt maize, bromoxynil-

resistant cotton, Bt cotton, glyphosate resistant soybeans, virus resistant squash, and additionally delayed ripening tomatoes were approved [9]. In 2000, Vitamin A-enriched golden rice was developed, though as of 2016 it was not yet in commercial production [11].

In this study information on both positive and negative effects of Hybrid crops and GM crops on human health and environment including its characteristics, history and current status have been depicted.

2. Hybrid plants and Genetically Modified Crops

A hybrid plant is a cross-breed plant resulting from cross pollinating two or more unrelated inbred plants [1]. Hybridization has made notable improvements in plant kingdom, like more vigorous plants, unregulated disease tolerance, earlier maturity, more uniform growth, and higher yield.

Genetically modified crops can be defined as crops in which the genetic material (DNA) has been modified in a way that does not occur naturally by mating and/or natural recombination. This technology is also termed as modern biotechnology, gene technology, or genetic engineering. This mechanism permit genes to be transferred from one biomes into another, even between two non-related species [12]. With the development of science and technology hybrid crops are now modified genetically for better results and better characteristics.

2.1 Hybrid crops

Hybrid varieties are relatively more vigorous and higher productive due to heterosis or hybrid vigour is fully imbedded in these varieties. All the individuals or plants of a hybrid variety are genetically similar. Thus hybrid genotypes are heterozygous but produce homogeneous plant populations [13]. They have higher uniformity and more attractiveness resulting homogeneous in nature. Hybrids have wide range of adaptability to environmental hazards than inbreeds and pure line genotypes due to upregulated inherent buffering capacity and genetic from two divergent alit parents. Hybrids can be derived from both cross and self-pollinated species depending upon the magnitude of heterosis. Nevertheless, hybrids are more common phenomenon in cross pollinated plants than self-pollinated plants. Hybrids are generally more tolerant to biotic and abiotic stresses than inbred and pure-line varieties [14].

2.2 Genetically modified crops

Genetic engineering within food crops is done to create pest and disease resistance, improve crops, and improve product characteristics. It is usually made by certain changes in plants'

genomes by inserting the genes of *Bacillus thuringiensis* which enable them to create resistance against diseases and pests naturally [15]. For instance BT (*Bacillus thuringiensis*) corn and BT cotton. Likewise, cold water fish genes have been introgressed in the tobacco and potato plants to save their seedling from chilling injury [16]. Scientists have developed such types of plants having tolerance to herbicides. For instance, soybeans have been genetically modified in a way that they do not get affected by the herbicides and grow in a usual environment.

Aside from food shortage, many countries across the globe are suffering from starvation and malnutrition. They only depend on single food like rice which cannot provide all the essential nutrients. It is possible that if rice has been genetically modified and essential nutrients are incorporated in it, it can fulfill the needs of all necessary nutrients. As blindness is a common problem in children specially in underdeveloped countries. It was a long awaited cherished dream of scientists to develop vitamin-A enriched rice through a transgenic approach, finally this dream came true after the development of golden rice (GM) which can provide essential nutrients along with beta carotene [17]. The overall beneficial characteristics of GM crops compiled in Figure-1.

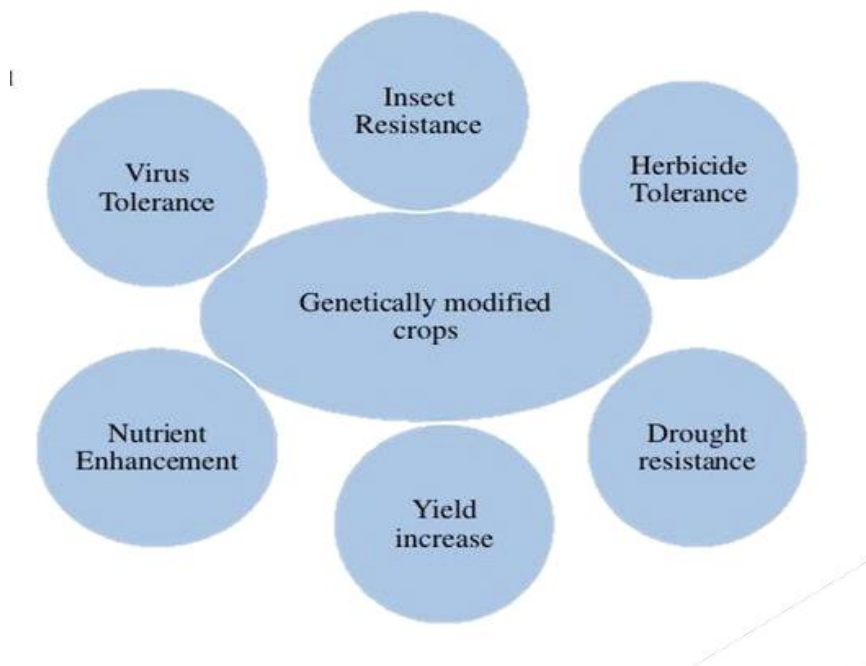


Fig. 1. Beneficial Characteristics of GM crops (Brook, 2016)

2.2.1 Current Status of GM Crops

In 2013, the average global adoption rates for biotech-improved seed were 79 % for soybean, 32 % for maize, and 70 % for cotton [18]. In 2014, seeds improved through biotechnology were grown by 16.5 million small farmers in 20 developing countries 230 million acres. These smallholders enjoyed increased income amounting to \$16.7 and \$16.2 billion, while benefiting from 50% reduction in pesticide applications on their crops.

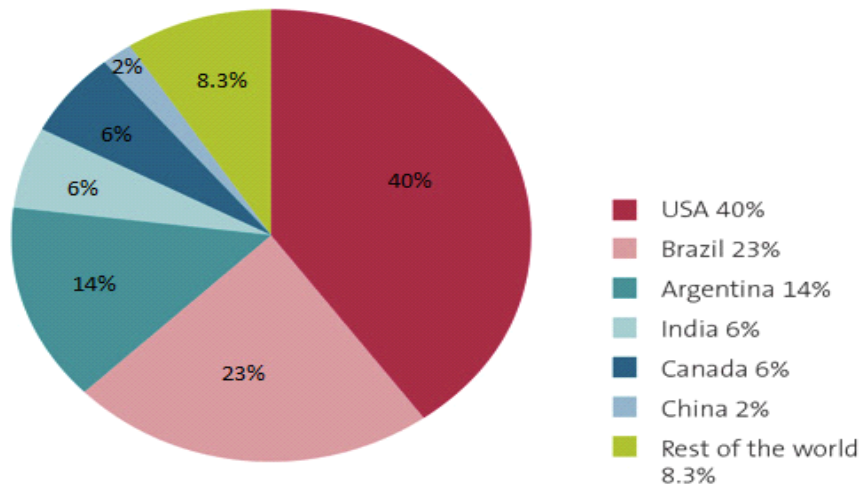


Fig. 2 GM crop producing major countries (by percentage) around the world [4]

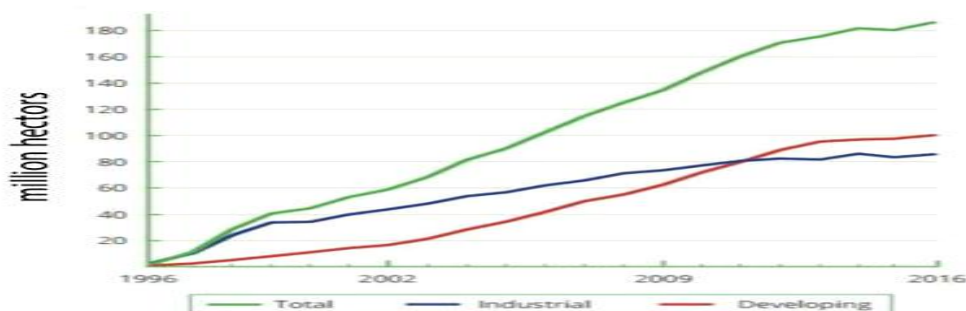


Figure 3. Areas of individual and developing countries under GM crops and global area in 1996-2016 [4]

2.2.2 GM Crops in Bangladesh

Biosafety approved cultivation of four indigenous varieties of brinjal incorporating a gene from the *Bacillus thuringiensis* to make it resistant to attacks by the fruit and in 2013, Bangladesh became the first nation to commercialise insect resistant Bt brinjal . At present, there are about 6,000 farmers growing four varieties Bt brinjal [19]. Adoption has resulted in an 80% - 90% reduction in insecticide use by the farmers who plant the crop. Bangladesh has become the first South Asian country to approve commercial cultivation of a GM food crop—brinjal. Bangladesh National Committee on Shoot Borer (FSB) opined that Bt brinjal would significantly reduce the use of pesticides. In Bangladesh more than three crops are under field trial, which are developed through agro-biotechnological approach. These are: late blight tolerant potato, Bt cotton and vitamin-A enriched Golden Rice. Taking into accounts the significance of the large cotton/textile industry in Bangladesh, Bt cotton is being evaluated in field trials as well as Golden Rice, could address the existing Vitamin-A deficiency in the country specially in children [20].

Rice does not contain any beta carotene. As South Asian people are mostly dependent on rice for their primary source of food, resulting Vitamin-A deficiency mostly found in children and pregnant women. Intake of only 150 gram of Golden Rice per day is expected to supply half of the recommended daily intake (RDA) of vitamin A for an adult. In accordance with World Health Organisation global database on vitamin A deficiency, one in every five pre-school children in Bangladesh is vitamin-A deficient. Among pregnant women, 23.7% suffer from the vitamin-A deficiency [21].

On the other hand, cotton is a non-food cash crop [22]. The BT cotton seeds are infused with genetic traits taken from a soil-dwelling bacterium *Bacillus thuringiensis* (Bt.) that effectively fights bollworm, a harmful caterpillar responsible for damaging cotton yields. Every year Bangladesh able to grows a paltry 0.15 million bales of cotton and spends around Tk. 20,000 corer for importing over 5 million bales more to meet the demand. Typical synthetic pesticides have become increasingly ineffective in fighting cotton bollworm, thereby causing up to 20 percent crop losses [23]. BT cotton is tolerant to important insect pests, especially cotton bollworms. It is reported that BT cotton adoption down-regulates the use of chemical pesticide and increases yields in farmers' fields, moreover Bt cotton had relatively higher yield (18%) than the non-Bt cotton across the season [24].

3. Positive Effects of GM Crops on Human Health

Human health is being benefited by GM crops as it is designed to fight against specific nutrient deficiency. Food security through the adoption of GM crops also affects human health indirectly.

3.1 Improvement of Nutrient Contents

One of the main claims of the biotechnology industry since genetically modified crops were first commercialised in the USA in 1996 has been that a "second generation" of GM will bring real consumer benefits, for example by improving nutritional value of foods use [25]. The biotech industry now hopes to boost their market with second generation nutritionally enhanced GM crops, which will help to alleviate malnutrition and improve health. However, claims about nutritionally enhanced foods fall into several categories: Enhanced vitamins (higher levels of beta carotene), enhanced minerals (more iron), enhanced healthy fatty acids content (omega-3 unsaturated fatty acids), enhanced amino acid (tryptophan), enhanced protein (in potatoes), enhanced levels of antioxidants to help fight cancer and reduced risk of allergic reactions (by silencing or removing genes such as wheat and peanuts) [26]

3.2 Recovery of Vitamin-A Deficiency

Vitamin-A deficiency (VAD) is a major health problem in Southeast Asia and Africa. Vitamin-A deficiency causes around 250-500 thousand children blind every year. "Golden Rice" has been using amid solution to VAD since 2000. As Golden Rice was genetically modified to produce beta carotene using a gene from the daffodil in the first instance, and later on a gene from maize. The latter modification using maize genes increased the amount of beta carotene produced by the rice after the daffodil version was heavily criticised because of the large amounts of rice required to be consumed to achieve the recommended intake of beta carotene [27]

3.3 Omega-3 Enhancement

Some nutritionists have highlighted the health-enhancing properties of a diet with a higher intake of omega-3 poly-unsaturated fatty acids, particularly in the prevention of cardiovascular disease [28]. The only direct sources of omega-3s are oily fish (such as mackerel) and other sea life, which takes them up from marine algae. This has led the Food Standards Agency to recommend minimum weekly intake of one portion of oily fish per

week. Farming marine algae has been considered, but so far this has not taken off commercially on a large scale. Some animal feed is enhanced with fish oil, and the resulting animal products are marketed as high in omega-3 [29]. The genetic modification of common foods to increase levels of antioxidants (which are believed to reduce the risks of cancer) has been given a good deal of publicity. Very recently "purple tomatoes, of the John Innes Centre (JIC), are told to be high in anthocyanins [30].

3.4 Food Security

Food security means when all people have physical and economic access to sufficient, safe, and nutritious food [31]. Regrettably, food security does not prevail for a significant proportion of the world population. There are three probable ways how GMC could impact food security. Firstly, GM crops could contribute to food production increases and thus improve the availability of food at global and local levels. Secondly, GM crops could affect food safety and quality. Thirdly, GM crops could influence the economic and social status of farmers, thus improving or diminishing their financial access to food. In 2012, 170 million hectares (~12% of the global arable land) were planted with GM crops, such as soybean, corn, cotton, and canola, but most of these crops were not grown primarily for direct food use [25]. GM crop technology has increased average yield which leads farmers' economic development. Economic development makes it possible for farmers to lead a standard living with better health.

4. Negative Effects of GM Crops on Human Health

Genetically modified foods currently sold internationally have passed risk assessments and are not likely to present risks for human health [32]. However, food safety experts have identified several possible human health hazards associated with GMOs. The hazards include the possibility of introducing a new allergen or new toxins to a food, a decrease in nutritional quality, and antibiotic resistance (Mellon and Rissler, 2003). As International Union for Conservation of Nature (IUCN) is representing GMOs negatively worldwide, reflected in the IUCN-GMO resolutions as well as surveys results from Europe and Japan in particular, where consumers worry about potential human and environmental effects [33].

4.1 Allergenicity

Worldwide there is controversy about allergenicity of GM crops and suspected to adverse health effects. They discovered that soybean plants engineered with a gene from Brazil nuts

produced beans that caused an allergic reaction in some people. Similar allergenic effects of GM crops were not published until 2005 when scientists from CSIRO, the national research arm of the Australian Government, reported that genetically modified pest-resistant peas induced allergic lung damage in mice. The researchers had transferred into the pea a gene for the protein from the common bean that is capable of killing pea weevil pests. The innocuous protein does not make an allergic reaction when extracted from the bean, but when expressed in the pea it is structurally different to the original bean. This substantial change may lead to the unexpected immune system seen in mice, thus interpreting the unpredictable impacts of gene transfer and the importance of using animal models to test the allergenic potential of GM foods [34]. In contrast, it is reported that GM foods do not appear to be more allergenic than their traditional product, and no incidence exists that consumption of GM proteins accelerates allergy to develop in that particular food into individuals who are not allergic initially [35].

4.2 Toxicity

Another risk of GMOs is the potential harmful effect of toxicity to humans and animals. One of the most recent GMC to be suspected of having toxicity is the GM maize line known as MON 863 (Yield Guard Rootworm Corn), which received approval in the US in 2003 and specifically targets the corn rootworm. MON 863 contains relatively less Bt toxin than most of the Bt maize varieties, producing the toxin primarily in the roots, which is the site of entry for the western corn rootworm. In the late 1980s, a food supplement produced using GM bacteria was toxic, initially killing 37 Americans and making more than 5,000 others seriously ill [36]. Several experimental GM food products (not commercialised) were found to be harmful, allergic to Brazil nuts had allergic reactions to soya beans modified with a Brazil nut gene [37].

4.3 Antibiotic Resistance

In order to expedite the success rate of genetic modification, scientists have used a technique evolving antibiotic resistance genes in addition to the desired gene to identify which plants have successfully absorbed the introduced gene. The antibiotic kanamycin is a frequently-used marker for plant modification yet is still used for treating many human infections [38]. As the genes usually come from bacteria, human pathogens could increase their antibiotic resistance. Although there is no definite evidence that these drug-resistant strains are necessarily more dangerous for humans, public health officials still view them with concern because they are more difficult to cure in people who need treatment [39]. The British

Medical Association, for example, opposes the use of antibiotic resistance markers in food. The risk is considered serious enough to encourage scientists to adopt techniques to remove the marker genes before a crop plant is developed for commercial use [40]. Scientists have also recently developed an alternative marker derived from tobacco rather than bacteria [41].

5. Positive Effects of GM Crops on Environment

Initially GM crops after its application in the field have drawn the attraction of a number of scientists in this research area with a number of advantages.

5.1 Reduction in Pesticide Use

Herbicide tolerant (HT) soybean, with 26 million ha grown globally is currently the dominant transgenic crop [42]. When comparing 1997 to 1998 the overall rate of herbicide uses in GM soybeans declined by nearly 10 percent. It is also reported that 2.5 million kg of glyphosate replaced 3.3 million kg of formulated products of other synthetic herbicides such as imazethapyr, pendimethalin and trifluralin [43]. The Dutch Centre for Agriculture and Environment has probably conducted the most comprehensive review on the effect of HT soybeans on herbicide use. The report concluded that in the USA the overall difference in pesticide use between GM and conventional soybeans ranged from +7 to -40% (1995 to 1998) with an average reduction of 10% [44].

Data from 431 farms in 20 locations in the USA to model the effects of introducing HT soybeans on herbicide use and their preliminary results indicate that HT soybean will reduce herbicide use by up to 10% [45]. In addition, the number of spray applications per ha was reduced by 15 million which is around 22% reduction of pesticide (Table 1).

Table 1. Reduction in Pesticide and Environmental Impact Quotient during 1996-2015

	1996-2014	1996-2015	2014 alone	2015 alone
Reduction in pesticides (million kgs actives ingredients, a.i.)	583.5	619	40.4%	37.4%
Pesticides saving	8.2%	8.1%	6.4%	6.1%
Reduction in (EIQ)*	18.5%	19%	17.6%	18.5%

*Environmental Impact Quotient (EIQ) = a composite measure based on the various factors contributing to the environmental impact of an individual active ingredient.

Source:[46].

5.2 Carbon Sequestration

The contribution of GM crop adoption to reducing the level of greenhouse gas (GHG) emissions has been recognized from the experiments of several scientists [47]. The three main Green House Gases are carbon dioxide (CO₂), nitrous oxide (N₂O) and methane (CH₄). The scope for GM crops contributing to lowering of GHG comes from three main sources. Overall, the reduction of GHGs can be measured in terms of the amount of carbon dioxide removed from the atmosphere from reduced consumption of fuel and additional storing of carbon in the soil with no/reduced tillage practices [48].

The surplus amount of soil carbon sequestered since 1996 has been equivalent to 203,560 million tonnes of CO₂ that has not been released into the global atmosphere. Accumulating the carbon sequestration benefits from reduced fuel use and additional soil carbon storage, the total carbon dioxide savings in 2013 are equal to about 28,005 million kg, equivalent to taking 12.4 million cars off the road per year. This is roughly equivalent to 43% of registered cars in the UK [49]. Table 2 presents the potential addition of carbon sequestration savings with the adoption of various GM crops in different countries.

Table 2: Relationship between carbon sequestration and adoption of GM crops.

Crop / Trait/Country	Additional Carbon Stored in Soil (mkg C)	Potential Additional Soil Carbon Sequestration Savings (mkg CO ₂)
US: GM HT Soybean	291	1,066
Argentina: GM HT Soybean	3,111	11,418
Brazil: GM HR Soybean	1,889	6,931
Bolivia, Paraguay, Uruguay: GM HT Soybean	700	2,569
US: GM HT Maize	815	2993
Canada: GM HT Canola	254	932
Total	7060	25,909

Source: [46, 50]

6. Negative Effects of GM Crops on Environment

GM crops also have considerable negative impacts on the environment

6.1 Conversion of Biodiversity

The potential impact of GM crops on biodiversity has been come into a hot topic both in general and specifically in the context of the Convention on Biological Diversity. The most direct negative impact of GM crops on biodiversity is due to the conversion of natural ecosystems into agricultural land. In that context, the potential impacts of GM crops are most

appropriately considered in relation to prevailing modern agricultural practices [51]. Another criticism of conventional agricultural practices is the extensive cultivation of uniform, high yielding crop varieties that has led to the replacement and loss of traditional crop varieties from agroecosystems; currently, at least 1,350 varieties face extinction, with an average of two breeds being lost each week [52]. Just as relying on monocultures may increase pest problems in conventional agricultural practices, experts warn that increasing reliance on a single gene in growing a variety of crops could also be dangerous [53].

A three-year German study found that herbicide-resistant genes in the canola transferred across to the bacteria and yeast inside the intestines of young bees. These findings imply horizontal gene transfer between species that are not normally compatible and at least points to uncertainties which require further investigation [54]. However, research in China found that insect-resistant cotton had no direct adverse impact on honeybees [55], illustrating that although GM may increase the probability of horizontal gene transfer, this is not the case for every GM application. It is reported from laboratory and field studies that no indication of direct effects of Bt plants on natural enemies of target species [56].

Aside from this Invasive alien species (IAS) have been cited as a leading cause of species endangerment and extinction and second only to habitat loss as a major cause of damage to the planet's biodiversity. For this reason, any potential for GMOs to become invasive must be taken seriously. The potential invasiveness of GM crops is through the Invasive Species and Pest Management risk criteria [57] are: firstly, changes in adaptive characteristics (that may increase the potential for establishment and spread). Secondly, adverse effects of gene transfer/flow that may result in the establishment and spread of pests or the emergence of new pests. Thirdly, adverse effects on non-target organisms, genotypic or phenotypic instability resulting the establishment and spread of organisms with new pest characteristics for instance loss of sterility genes designed to prevent out crossing. Aside from these, other risks, e.g. enhanced capacity for virus combination. In order to be categorised as a pest, a GMO has to be injurious or potentially injurious to plants or plant products under conditions in the pest risk analysis area.

6.2 Risks of Overused Glyphosate

Globally more than 80% genetically modified (GM) crops are engineered to tolerate glyphosate herbicides. The herbicide kills all plant life in the field other than the crop. These crops are known as glyphosate-tolerant crops. The idea behind such crops was to simplify

weed control at farmers level. The farmer could douse the entire field with glyphosate herbicide to subside all weeds without killing the crop. An industry report showed that, the area of US cropland infested with glyphosate-resistant weeds expanded to 61.2 million acres in 2012. GM glyphosate-tolerant crops have led to a 239 mkg (527 million pound) increase in herbicide use in the US between 1996 and 2011, relative to the amount that would have been used if the same acres had been planted to non-GM crops. Most of this increment is due to the spread of glyphosate-resistant super weeds [57].

6.3 Insecticidal Toxins from *B. thuringiensis* (Bt)

During sporulation, *B. thuringiensis* produces crystalline inclusions which are protoxins called d-endotoxins. These structures called cry proteins, when ingested by the insect, are diluted in the gut and cleft by digestive proteases activating the toxin. The toxin then binds to specific glycoprotein receptors on the surface of cells aligned the gut, causing an imbalance in ion concentration, destroying the cells, causing the death of the insect [58]. In addition, some strains of *B. thuringiensis* produce "vegetative insecticidal proteins" (VIPs) before sporulation [59]. Nonetheless, instability and degradation of cry proteins when exposed to ultraviolet radiation and short persistence on the plant (easily washable by rain and irrigation), have limitation large adoption of Bt pesticides by farmers. *B. thuringiensis* produces a wide spectrum cry proteins with a range of around 100 holotype toxins distributed in 40 groups (cry1, cry2, etc.) each one with several subgroups and a narrow range of host [60]. This variability is being used to develop transgenic plants tolerant to pest and diseases.

7. Future outlook and Conclusion

Every technology has merits and demerits; nonetheless, we can't condemn a beneficial technology because of the possible misuse. The simple solution is to use the technology with some precaution. In order to prevent potential hazards from entering the food supply, an extensive pre-market approval assessment is recommended. Currently, there are no standard protocols for testing GMOs before they are released into the environment. Government regulations can vary from a company notifying authorities they are selling a biotech crop to strict government regulations around the testing, traceability and labelling of GMOs. GM crops with specific traits, insect-resistant, drought-tolerant, and virus-resistant crops all have direct and indirect effects on the environment. These effects can be either positive or negative but in most cases they will have both positive and negative elements. GM crops are a topic of much deliberation and tension; very prevalent in some parts of the world and banned in some

other countries. The worldwide commercial cultivation of GM crops has raised concerns about potential ill effects on the environment resulting from the use of these crops. Consequently, the risks of GM crops for the environment, and especially for biodiversity, have been extensively assessed before and during their commercial cultivation. Substantial scientific data on the environmental effects of the currently commercialized GM crops are available today. The scope of environmental risk assessments and strict regulations ensure that the only GM crops brought into the market are those that do not have a greater negative impact on the environment than their non-GM counterparts.

Acknowledgements

Authors are grateful to the University of Dhaka and Bangabandhu Sheikh Mujibur Rahman Agricultural University, Gazipur-1706, Bangladesh providing the facilities.

Declarations

Competing interests The authors declare that they have no competing interests.

Consent for publication Not applicable.

Ethics approval and consent to participate Not applicable.

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