An Assessment of Relative Risks to Human/Ecological Health Biotech Crops versus Other Human Activities

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Abstract

The regulation of GM crops has been a subject of intense debate during the last two decades. These crops are being grown globally and the area occupied by these crops has been steadily increasing from a mere 1.7 million hectares in 1996 to a record level of >180 million hectares in the year 2014 covering 28 countries (for the first time the area decreased to 179.7mha in 2015). During the 20 years period of cultivation, no harmful effects of these crops have been reported anywhere. Despite this, there is a vehement opposition against cultivation of these crops, and unfortunately, this opposition is not based on science; those opposing the cultivation of these GM crops include civil society groups (CSGs), NGOs and a group of scientists. These groups constitute an anti-GM lobby, which doesn’t seem to be concerned about other human activities, which are more alarming and causing a major harm to human and environment health. Therefore in this communication, the current status of GM crops, along with the impact of their cultivation is being presented first and then the effects of other human activities on human health and environment health described. While presenting this information, the question is being addressed to these groups (constituting an anti-GM lobby) that if they are really concerned about human and environment health and the future of mankind, why are they not addressing the problem of adverse effects of other human activities on human health and environment health, which are much more alarming.

Introduction

In the age of biotechnology and genomics, often we are confronted with the question whether or not we are taking due precautions in conducting research involving recombinant DNA and in commercializing its products. Questions are also being asked whether or not our regulatory system is adequately addressing issues related to risks to human health and environmental pollution/degradation including biodiversity losses, while evaluating the products of genetic engineering. However, we often forget to examine and address the risks due to human activities other than those involving biotechnology and genomics, which may be more alarming. In this article, the perceived risks in using biotech crops for cultivation have been compared with those due to other human activities. While doing this, the civil society groups (CSGs), NGOs and a group of scientists, who really constitute an anti-GM lobby, are being asked to examine all human activities and then try to find out, which activities are causing relatively higher proven risks to human and environment health relative to the perceived (but not proven) risks that are believed to be associated with biotech crops and are only based on ‘Precautionary Principle’, which has been adopted in contrast to the “Principle of Substantial Equivalence”, which has been considered to be more appropriate by some. If they do so, they could perhaps also examine, if proven benefits accrued due to biotech crops far outweigh the perceived risks, particularly relative to those due to other human activities, so that one may allow commercialization of these biotech crops, while minimizing the risks, which may be involved. While doing this, the CSGs, NGOs and the politicians may perhaps also like to divert their energy and effort to control other human activities, which are causing the greatest harm to human and environment health.

I was prompted to address the above issue, by several reports that I came across in recent years. In June 2012, the issue of dual use research of concern (DURC) involving genetic engineering of influenza virus strain H5N1 to make it transmissible among mammals figured in several issues of Science and Nature; this debated issue was resolved by publication of the two highly debated studies, which fall under the category of DURC [1,2]. In contrast to this, in India the report of Parliamentary Standing Committee on GM Crops and also the Interim/Final Report of the Technical
Expert Committee (TEC) constituted by the Supreme Court of India recommended (with a divided opinion) that all open field trials involving GM food crops be banned (at least for a certain specified period) to avoid any perceived and unproven risks; this is in sharp contrast to a report submitted by the Science Advisory Committee (SAC) to the Prime Minister of India, which recommended that GM crops be adopted for commercial cultivation, since we have now reached a stage, when we know enough about the relative benefits and risks about these crops. Another recent controversy about biotech crops relates to the reported adverse health effects in rats fed with NK603 maize (corn), developed by Monsanto and approved for animal and human consumption in the European Union, United States and other countries [3,4]. A number of similar studies were also conducted earlier [5] Monarch Butterfly study on corn; Arpad Pusztai’s rat study on potato; [6] soybean study in Russia; [7] corn biodiversity study conducted in California, USA; see later for details). All such studies were questioned for the material and methodology used and for the inferences drawn [8]. In some cases, experiments were also conducted to prove that the findings of these studies were not based on good science and were not reproducible. Literature on studies involving animal feeding and those based on omics-techniques also suggested that GM crops are comparable to non-GM feed stocks [9,10].

Sometime back, I also came across an article entitled “Life in a Contaminated World” published in 28th September, 2012 Issue of Science, where the risks to human and ecological health associated with the use of pesticide and other chemicals were highlighted[11]. Hundreds of articles were also published during 2006-2016, where effects of exposure to pesticides (particularly neonicotinoids) on the individual-level, and colony-level traits of honey bees and other bees, which provide useful services as pollinators, were examined and discussed[12-15]. Harmful effects of pesticides were also examined using three human cell lines [16]. In an editorial published in Current Science also, the issue of particulate air pollution has been addressed, suggesting that immediate action is needed to reduce the local particulate air pollution [17].

According to a recent WHO estimate, globally, more than 3 million people die prematurely each year from prolonged exposure to air pollution; this figure is estimated to reach 6.6 million by 2050. WHO also reports that chronic exposure to air pollution particles contributes to the risk of developing cardiovascular and respiratory diseases as well as lung cancer? All this air pollution is due to human activities other than growing GM crops, and need immediate attention. The above literature prompted me to ask the question whether the risks involved in growing biotech crops are higher than those due to the use of excessive chemical fertilizers, harmful pesticides and environment unfriendly herbicides, and also those due to increasing use of fossil fuels, urbanization, industrialization, deforestation, etc., which are adding to the environmental degradation and pollution at an alarming rate. In this article, the present status of biotech crops is described first, followed by an analysis of the impact, which these biotech crops presumably had, and the concerns and risks expressed on the basis of experiments conducted, and finally the human activities, which are more alarming than the biotech crops in terms of risks to human and environment health.

Biotech Crops Present Status

As an annual feature [18], Clive James of ISAAA (International Service for the Acquisition of Agri-biotech Applications) recently gave a detailed account of the present status of biotech crops for the year 2015. The account presented in this section is largely based on this document.

Area occupied by biotech crops

The year 2015 was the 20th year of commercialization of biotech crops (1996-2015). From 1.7 million hectares occupied by these crops in the year 1996, the area steadily increased to 179.7 million hectares in 2015 (3% annual growth) covering 28 countries involving 18 million farmers, ~90% of these farmers being resource poor farmers from developing countries (for the first time, there was a decline in area from 181.5mha in 2014 to 179.7mha in 2015). This amounts to almost hundred-fold increase in cultivated area, thus making biotech crops the fastest adopted crop technology in the history of modern agriculture. In their eleven annual reports on global impact of biotech crops [19] (2006-2016), Brookes and Bar foot from UK also reported substantial, and sustainable, global socio-economic and environmental benefits due to the use of biotech crops for commercial cultivation. Three recent studies conducted during 2012-14 also confirmed that biotech crops are safe as animal feed.

Traits improved in biotech crops

Most of the biotech crops grown during the last 20 years carried either herbicide resistance or insect resistance or both of these traits stacked together. In 2015, herbicide tolerance accounted for 56% of GM crops, insect resistance (BT crops) accounted for 11%, while the remaining 33% GM crops had both these traits [20]. The major crops involved in commercialization of biotech crops globally included soybean (83%), cotton (75%), maize (29%) and canola (24%). In India, the only commercialized biotech crop (BT-cotton) occupied 11.6 million hectares (>90%) of the 11.76 million hectares of cotton area in 2015 (as against all time high of 12.8 million hectares in 2014). This represented >200% increase in BT-cotton area, ~50% reduction in pesticide application, and US $9.4 billion (global value $18.7 billion) increase in farm income during 2012 [21].

Cost of developing and bringing a biotech crop to the market

A number of cost estimates are available for discovery, development and authorization of a new plant biotechnology trait in a crop [22]. In an estimate, the cost of developing the first biotech
variety in a crop will approach 6.8 million Euros, which is equivalent to Rs 50 crores [23]. According to another recent survey, a biotech crop with an improved trait introduced between 2008 and 2012 has been estimated to cost US $136 million (Indian Rs. 680 Crores); the time taken from the initial discovery to commercial launch is 13.1 years on an average for all relevant crops. It has also been estimated that the time associated with registration and regulatory affairs is increasing from a mean of 3.7 years for an event introduced before 2002, to the estimated 5.5 years in 2011 [24].

Global value of commercial seeds and products of biotech crops

The global market value of commercialized seeds of biotech crops in 2015 was US $15.3 billion, which is slightly down from US $15.7 in 2014; of this US $10.9 billion (72%) was in the industrialized countries and the remaining $4.4 billion (28%) was in the developing countries. This might pick up in future. In 2011, this represented 22% of the US $59.6 billion global crop protection market, and 35% of the ~US $34 billion global commercial seed market. The market value of the global biotech crop market is based on the sale price of biotech seeds plus any technology fees that may apply.

Labeling of biotech crops (positive and negative labeling)

Another issue that has been widely discussed is the need for labeling of biotech food to provide an option to the consumer. Currently, 64 countries around the world require labeling of genetically modified foods [25] (this is described as positive labeling, as against negative labeling, where non-GM products have to be certified as GM-free). The above 64 countries include most developed countries including 28 nations in the European Union (EU), Japan, Australia, Brazil, Russia and developing countries like India and China. For instance, in EU, all food (including processed food) or feed, which contains greater than 0.9% of approved GMOs, must be labeled. Due to this law, several consignments from USA exported to EU were refused entry. There are also laws in some European countries (e.g. Germany and France), where negative labeling is required (all foods to be labeled as GM-free). But many countries in North America (including USA), Africa and Asia have no laws requiring labeling.

In USA, in October 20, 2012, the American Association for the Advancement of Science (AAAS) approved a statement that labeling of GM food could “mislead and falsely alarm consumers” and that “consuming foods containing ingredients from GM crops is no riskier than consuming the same foods containing ingredients from crop plants modified by conventional plant improvement techniques.” Despite this, the issue of labeling GM food was debated in several states in USA; some of these states also started formulating their own laws for mandatory labeling of GM foods. For instance, on July 1, 2016, the law for mandatory labeling of GM food became effective in Vermont (a small state) [26]. Following this, later in July 2016, the US Senate passed a bill that would create a mandatory national standard for labeling food made with GMOs [27]. This is being described as a win for food companies, farm groups, and biotech firms, which have been pushing the federal government to set a single national standard and ban state labeling laws like the one in Vermont.

The new federal legislation would block states from issuing mandatory labeling laws, and would require food manufacturers to use one of the three different options to inform consumers of the presence of GMOs in products (either a label that includes a USDA symbol indicating the presence of GMOs, or print a label using plain language, or add a scanner- or smart phone-readable QR code that links to ingredient information; small businesses also have the option to place a telephone number or internet website on packages that would direct customers to additional information). USDA would have two years to decide which products require labeling. In USA, GMO supporters and opponents, both are partly displeased with the above bill. For opponents, the bill falls short of what consumers rightly expect: “a simple at-a-glance disclosure on the package”. Keeping this in view, the GMO critics say that the bill fails to adequately protect consumers, who want to know if a product contains GM ingredients. GMO supporters, who are against labeling, meanwhile, argue that the whole issue of labeling is ridiculous, since ample evidence is available suggesting that GM foods are just as safe to eat as regular foods.

Need of marker-free biotech crops

It is widely known that a marker gene imparting resistance against an antibiotic or herbicides is found in each transgenic crop. The rare possibility of transfer of these genes to weeds and wild crop relatives throughout crossing and to soil and intestinal microorganisms through horizontal transfer cannot be ruled out. This may lead to development of pathogens against which antibiotics currently being used are rendered ineffective. Although many scientists do not consider it a risk, this has not received public acceptance, because it is difficult to prove through experiments that herbicide/antibiotic markers presently in use pose no risks to biodiversity loss or human or animal health. There are several ways to either avoid or get rid of selectable marker genes [28]. Marker genes that have no harmful biological activities have also been suggested. Gene for green florescent protein (GFP) is one such example. Development of techniques for genome editing and gene targeting (ZFN, TALEN, CRISPR-Cas) have also been suggested, so that use of marker genes may be avoided.

Biotech crops in the pipeline (2015 and onwards)

Several novel GM crops that were developed during 2015 include the following: (a) an improved multi-trait potato (innate 17TM) grown on 160 hectares in 2015; an improved version of this event, Innate 2™ (stacked with resistance to potato late blight) was also approved in 2015. (b) Two varieties of Arctic® apples,
with less bruising and less browning (when sliced) approved for planting in USA and Canada (6 hectares planted in the USA alone in 2015). The company ‘Okanagan Specialty Fruits’ from Canada, which developed Arctic® apple, also applied the same technology to other perishable fruits including peaches, pears and cherries; (c) In 2016, Harv XtraTM, a low lignin alfalfa (stacked with Round Up Ready), with less acid detergent lignin (ADL) and higher neutral detergent fiber digestibility (NDFD) and 15-20% higher yield, made available for sale and planting in USA.

In a recent report, the status of GM crops in the pipeline (as in 2014-2020), was presented [29]. It was shown that in 2014, 49 GM events were in commercial cultivation and 53 events were at the pre-commercial stage, making a total of 102 GM events authorized in at least one country. In addition, 43 events were at the regulatory stage and at least 77 GM events at the advanced R&D stage. It was also estimated that in 2020, a total of 219 GM crop events might be authorized (of which 96 events would be in commercial cultivation and the rest at the pre-commercial stage). As mentioned above, in 2015 four GM crops, which dominated the market included soybeans, cotton, maize and oilseed rape. Among the new crops, BT brinjal reached the Bangladesh market in 2013-14, potatoes and alfalfa reached the US market in 2015-16, while GM rice is expected to reach the market by 2020. Other crops that were at the pre-commercial stage in 2014 included a Chinese insect-resistant poplar, Brazilian virus-resistant bean, Indonesian drought-tolerant sugarcane and Canadian herbicide-tolerant flax [30].

Among the traits, although herbicide tolerance and insect resistance were still the prevailing input traits in 2016, following other agronomic traits were used for development of GM crops: virus resistance, drought tolerance and increased yield. Drought-tolerant GM maize was already in the market and drought tolerant sugarcane may soon reach the market. GM crops tolerant to new herbicides (other than glyphosate) were also produced; these included crops tolerant to sulfonylurea, 2,4-d (2,4-dichlorophenoxyacetic acid), dicamba (3,6-dichloro-2-methoxybenzoic acid), isoxa- flutole and oxynil. Also new Bt genes are being deployed for insect resistance. Among quality traits, ‘biofortified’ crops with a modified nutritional content for food and feed and crops with improved industrial characteristics were produced. Other quality traits included modified oil composition for increased content of omega-3 fatty acids or vitamins and amino acids. GM quality traits for industrial purposes included better sources of biomass for liquid fuels and industrial products. GM maize suitable for bioethanol production and soybean/oilseed rape varieties for biodiesel or other oleochemicals are also in the pipeline.

GM crops with stacked traits are also becoming common, so that several crops that are both insect resistant and herbicide tolerant have been developed. Future GM crops with stacked traits will include insect/herbicide resistance combined with quality traits. These GM crops include GM soybean with modified fatty acids content and GM maize/cotton with multiple genes for insect resistance. Up to eight GM transformation events have already been combined in single commercial GM maize (SmartStaxTM), which carries multiple genes for herbicide resistance and insect resistance, providing resistance against a range of herbicides and insects; consequently, SmartStax also has reduced refugia requirement of 5% against 20% that is normally used in BT crops [31]. Similarly, cotton triple-stack combines two BT genes with the glyphosate resistance gene. It is estimated that in future 2,000 triple-stacks and over 12,000 quadruple-stacks may enter the pipeline [32]. Future stacks are likely to involve not only multiple pest/herbicide resistance, but also combination of these traits with engineered metabolic pathways, and simultaneous introductions of multiple pathways through metabolic engineering (for example, pathways for beta carotene, ascorbate, folate and vitamin E synthesis [33].

**Impact of Growing Biotech Crops**

**Effect of pesticide and herbicide use**

During 1996-2014, the pesticides use on the GM crop area has been estimated to be reduced by 581.4 million kg of active ingredient (8.2% reduction) [34]. Similarly, the volume of herbicides used in GM maize crops also decreased by 213.7 million kg (1996-2014), an 8.4% reduction; the overall environmental impact associated with herbicide use on these crops decreased by 12.6%. The environmental impact associated with herbicide and insecticide use on these crops, as measured by the EIQ indicator, fell by 18.5% (for EIQ, see later). In a recent study, it was also shown that during 1996-2011, although the use of insecticides decreased, but that of herbicides increased, so that there has been a net increase in the use of pesticide [35]. It was shown that although in the first six years of commercial use (1996-2001) of HT and Bt crops, the use of pesticide decreased by 31 million pounds (~2%), compared to what it would have been in the absence of GE crops, but later due to increase in the use of environment-friendly herbicides and in some cases also that of insecticides, the overall pesticide use increased by 404 million pounds from 1996 through 2011 (527 million pound increase in herbicides, minus the 123 million pound decrease in insecticides). In 2011 alone, the overall pesticide use was about 20% higher on each acre planted to a biotech crop, compared to the pesticide use on acres not planted to GE crops. But this increase in the use of pesticide was largely due to increase in the use of environment friendly herbicides, so that its impact on environment degradation should be minimal. It has been argued in the past that the cultivation of glyphosate-based HT crops and BT corn and BT cotton led to reductions in the risks related to use of pesticide. However, as mentioned above, it seems that the volumes of both Bt toxins and glyphosate brought into the environment has markedly increased, and new research will be needed to find out the impact of this higher exposures to glyphosate and Bt toxins on the health.
of human and animal health and also on the environmental. We assume that a reduction in the use of insecticide will certainly reduce the risks, as compared to the risk due to increased use of benign herbicides like glyphosate.

**Impact on Greenhouse Gas (GHG) Emissions**

The use of GM crops has also contributed to a reduction in GHG emissions, since use of environment friendly herbicide and fewer sprays of insecticide allowed a switch to reduced and no-till farming systems and consequent reduction in use of fuel that was earlier required for tilling. This in turn resulted in a annual reduction of CO2 emissions by 2,396 million kg, the cumulative reduction during 1996-2014 being 21,689 million kg arising from reduction in fuel use by 8,124 million liters. In addition to reduction in CO2 emission due to reduced fuel use, more carbon remains in the soil and this leads to lower GHG emissions (due to no till/reduced tillage farming systems in North and South America, the reduction in CO2 emission has been estimated to be of the order of extra 19,998 million kg of CO2 that has not been released into atmosphere). In the year 2014 alone, the above estimated total reduction in GHG attributed to GM crop-related CO2 emission (due to reduced fuel use and additional soil carbon sequestration) was equivalent to the removal from the roads of 9.95 million cars, equivalent to 34% of all registered cars in the UK. It has also been estimated that reduced or no tillage agriculture (due to HT GM crops) during 1996-2016 must have reduced CO2 emission that is equivalent to taking 83 million cars off the road. This estimate is the maximum; actual level of reduction in CO2 may be lower.

**Socio-economic and environmental impact**

For the last 11 years, Brookes and Barfoot of PG Economics Ltd, UK has been publishing regular annual reports on global socio-economic and environmental impact of growing GM crops. The last report brought out in 2016 described the impact for the year 2014 [36] (for methodology followed for this analysis, refer to original reports). The following account is largely based on these annual reports. Socio-economic impact. It is estimated that global farm income due to GM crops during 1996-2014, increased by $150.3 billion (for 2014, it was $17.7 billion). This is equivalent to having added 7.2% to the value of global production of the four main GM crops (soybeans, maize, canola and cotton). Almost ~50% of this benefit was derived by the farmers in developing world. The average yield increase since 1996 has been +11.7% for maize and +17% for cotton [36].

A study was also conducted to investigate the effect of BT cotton on farmers’ family income and food security during 2002-2008; this study involved 1,431 farm households in India [37]. According to the findings, the adoption of BT cotton has significantly improved calorie consumption and dietary quality, mainly due to increase in family income. It was also estimated that the GM technology reduced food insecurity by 15-20% among cotton-producing households. A meta-analysis using all published reports on socio-economic impacts of GM, crops was also conducted [38]. In this analysis, it was shown that due to use of GM crops for cultivation, the use of chemical pesticides was reduced by an average of 37%, the crop yields increased by 22%, and farmer profits increased by 68%. Yield gains and pesticide reductions were found to be larger for insect-resistant crops than for herbicide-tolerant crops. Yield and profit gains were found to be higher in developing countries than in developed countries.

**Environmental impact**

Impact of growing GM crops on the environment has been widely discussed and the civil society groups and NGOs have been advocating about the possible negative impact of GM crops on the environment. Some of the perceived ecological risks of growing biotech crops, which were initially listed by Rissler and Mellon [39] and later widely discussed include the following: (a) the biotech crops could become weeds with undesirable effects; (b) the biotech crops might transfer new genes (through pollen) to wild plants, which could then become weeds; (c) biotech crops could facilitate the creation of new, more virulent or more widely spread viruses; (d) insect/herbicide resistant biotech crops produce substances that are toxic to other non-target organisms; (e) biotech crops may disturb an ecosystem in ways that are difficult to predict; and (f) biotech crops might threaten centers of crop diversity. For none of these presumed risks, solid experimental evidence published in peer-reviewed journals is available. However, it is argued that absence of evidence does not mean that the risks do not exist. One would like to know, whether or not a technology with demonstrated benefits could be dropped, just because there are unproven risks, which may or may not occur in distant future.

In contrast to the above unproven risks, the positive impact of biotech crops on the environment is enormous and has been documented with experimental evidence and through surveys that have been conducted. These include the following: (a) reduction in the use of pesticide and herbicide, thus reducing the cases of pesticide poisoning among humans; (b) reduction in greenhouse gas (GHG) emissions (as discussed above), which are causing greenhouse gas effect (climate change). Brookes and Barfoot of PG Economics Ltd., UK utilized the indicator known as the Environmental Impact Quotient (EIQ) to assess the broader impact of GM crops not only on the environment, but also on animal and human health [28]. The EIQ takes into consideration the various environmental and health impacts of individual pesticides in different production systems (both GM and conventional) and converts it into a single ‘field value per hectare’. Therefore, it provides a better measure of the impact of various pesticides on the environment and human health than estimation of the impact of an active ingredient alone. However, EIQ is an indicator only and does not take into account all environmental issues and impacts. Using the above approach involving estimation of EIQ, it was shown...
that the use of insect/herbicide resistant biotech crops contributed to a significant reduction in the adverse environment impact of these chemicals (discussed elsewhere in this article). For instance, the environmental impact associated with the use of both a benign herbicide and BT insecticide, as measured by the EIQ indicator fell by 17.1%. This favorable environmental impact is associated with cultivation of Bt-cotton, HT-soybean and Bt/HT-maize. These favorable environmental benefits (1996-2009), when partitioned, accounted for 54% benefits in the developed (54%) and developing countries (46%). Over three-quarters of the environmental gains in developing countries have been from the use of insect resistant Bt-cotton.

Impact on biodiversity: can biotech crops really lead to biodiversity loss?

It is often argued that commercialization of biotech crops may lead to loss of biodiversity. However, while examining the causes of loss of biodiversity during last few decades, the loss of biodiversity has been attributed to a number of factors [40], but biotech crops is not one of them, although we have been growing these crops for 20 years now? Seven following most important documented causes of biodiversity loss include the following, which largely include human activities other than cultivation of GM crops [41] (a) escalating human population; (b) habitat destruction (deforestation) and fragmentation; (c) overuse of natural resources; (d) impact of non-native/exotic species; (e) climate change; (f) natural calamities; (g) energy resources. We know that rapid environmental changes involving biodiversity loss are taking place due to several human activities, causing habitat loss and species extinctions. To understand this problem, in May 2000, Nature brought out a special issue in the form of ‘Nature Insight’ [42] that focused on the science of biodiversity, with the financial support of the Center for Applied Biodiversity Science (CABS), a division of Conservation International. This Insight covered underlying concepts, pure and applied research, and biodiversity loss.

We know that Earth’s biodiversity is being destroyed at an unprecedented rate, with far-reaching and irreversible consequences for life on our planet. The 1992 Convention on Biological Diversity, signed by 175 countries, reflects a global consensus of the importance of biodiversity in maintaining the planet’s life-sustaining systems. Yet, traditional reactive approaches will not suffice if we are to confront successfully the complex conservation challenges. The Center for Applied Biodiversity Science (CABS), a division of Conservation International, is working to change this equation by anticipating harmful scenarios before such situations are beyond repair: By providing early warning systems for threats to biodiversity and its many components, CABS is trying to make conservation possible. An estimate for annual extinction rate of 27,000 species has been obtained using species-area relationships [43], which means loss of one species every twenty minutes. This and similar estimates have attracted criticism, but recent work has shown that levels of species loss are really rising [44]. The Nature Conservancy, for example, has documented that one-third of the plant and animal species in the United States are now at risk of extinction due to human activities other than growing GM crops; in contrast, there are reports suggesting that GM crops may actually reduce biodiversity losses, due to reduced tillage, reduced use of insecticide, use of more environmentally benign herbicides and increase in yields to alleviate pressure for converting additional land to be used for food production [45,46].

Impact on IPM: biotech crops as an important component

Integrated Pest Management (IPM) involves careful consideration and integration of all available and appropriate measures to reduce development of pest populations, while minimizing the risks to human and animal health and the environment. This will thus allow one to grow a healthy crop with the least possible disruption of agro-ecosystems. In the past, biopesticides and bio agents have been utilized for IPM, but their use has been extremely low owing to a number of factors. However, current BT crops are playing a major role in IPM systems of cotton and maize with benefits to farmers and the environment. It is known that insect pest populations develop resistance against insect resistant GM crops during the course of cultivation of BT crops. As of 2016, seven cases of resistance in five major insect pest species have been confirmed worldwide [47]. Therefore, insect resistance management (IRM) as a component of integrated pest management (IPM) has been and will be used successfully to prevent/delay pest resistance to insecticides like glyphosate; however, the threat remains [48,49]. It is thus obvious that GM crops have contributed to the development of an effective IPM system, which in turn provided means to protect GM crops from resistant pest populations, which otherwise would develop rapidly, and make insect resistant GM crops susceptible to the target insect populations.

Impact on seed industry: are multinationals a real threat?

GM events that are used for development of GM crops are generally patented, so that a GM event that is commercialized by a multinational company (MNC) cannot be multiplied by farmers for growing the following crop and cannot be marketed by any local seed company. This led to the argument that if GM crops are allowed, few MNCs will control the entire commercialization of GM seeds, and will thus have monopoly in the seed market; some of these MNCs in GM seed market include Monsanto, Bayer, Syngenta, DuPont and Dow. The multinational companies that patent and produce GMO seeds also produce environment friendly herbicides, and will thus also control the market for herbicides to be used with herbicide resistant GM crops (e.g. ‘Roundup Ready’ crops). Many felt that GM crops were a means for these MNCs to impose a monopoly on crops and maximise their profits. This perception has been criticized by those, who are engaged in research and production of GM crops. We know that although many of the initial GM crops were commercialized by MNCs, but this provided an opportunity.
to local seed companies and public institutions to expand their activities in the field of transgenic research and breeding of GM crop, and thus compete and develop their own GM crops. Significant progress in this direction has already been made. For instance GM mustard developed at University of Delhi South Campus (UDSC) is currently awaiting approval by the regulatory system [50]. The fear of monopoly of MNCs is also misplaced in a system, when foreign investment is being encouraged and a policy of “make in India” is being followed by the present Government of India.

Experiments Suggesting Concerns/Risks Associated with Biotech Crops: Are the Experiments Flawed?

After the release of the first transgenic crop for commercial cultivation in 1996, and starting in late 1990s, results of several studies have been reported, where harmful effects of transgenic crops were apparently observed. However, in almost all such cases, the experiments were shown to be flawed, and in some cases, the results of such studies were found to be not reproducible, as discussed in this section.

Monarch butterfly and GM corn

In 1999, experimental evidence was presented in a publication, suggesting that pollen from Bt maize dusted onto milkweed leaves could harm monarch butterfly, which is a non-target insect in corn-fields [51]. Several groups later studied the phenomenon in the field and in the laboratory, and concluded that any risk posed by the corn to butterfly populations under real-world conditions was negligible [52]. A 2002 review of the scientific literature also concluded that “the commercial large-scale cultivation of current Bt–maize hybrids did not pose a significant risk to the monarch population” [53].

Arpad Pusztai’s study on rats

Experiments involving feeding of rats on transgenic potato carrying a gene for lectin (a toxic protein), were conducted in UK. The results were publicly announced in 1998 and were later published and discussed in the journal ‘The Lancet’ [54]. It was shown that rats fed with raw or cooked potato had thickening of the stomach mucosa, stunted growth and repressed immune system, when compared with controls. This caused frenzy both in media and the scientific community leading to suspension of Arpad Pusztai, who was also directed not to speak publicly about this work. His work was later also criticized on the grounds that any rats fed only on potatoes will suffer from a protein deficiency.

Gene flow and Mexican maize diversity study in California

In a report published in Nature in 2001, evidence was presented for cross-breeding of BT maize with unmodified maize in Mexico, thus suggesting that there is a risk of transfer of the transgenic to local varieties and wild germplasm [55]. The data in this paper was later described as originating from an artifact, so that the journal Nature later stated, “the evidence available is not sufficient to justify the publication of the original paper” [56,57]. In several future studies, it was unequivocally shown that although pollen transfer from biotech crops to other cultivated or wild species is a reality, but generally the fertilization will fail, and even if it occurs the progeny may not survive or may not be fertile, so that the consequences cannot be alarming.

Star Link corn in US food stores

Star Link carrying Cry9C (not earlier used for any other BT crop) was developed by Piant Genetic System (PGS, a seed company in USA); this event was approved in 1998 to be used as animal feed only (not for human consumption). Star Link corn food was subsequently found in food stores in the US, Japan, and South Korea, so that the sales of Star Link seed had to be discontinued, and the registration for Star Link varieties was voluntarily withdrawn, although subsequent studies did not find any harmful effects associated with Star Link [58].

Ermakova and Surov’s soybean studies in Russia

A group of scientists from Russia (led by IV Ermakova and AV Surov) conducted experiments with GM soybean fed to rats to find out if GM soybean that is grown on 91% of US soybean fields, leads to problems in growth or reproduction. Ermakova at the Institute of Higher Nervous Activity and Neurophysiology of the Russian Academy of Sciences found that the mortality rate of the offspring of rats fed with genetically modified soybean flour was six times higher than that of rats raised with feed from conventional soybean, and had significantly lower body weight compared to control groups [59]. AV Surov later found that by the fourth generation, most GM soy-fed hamsters suffered with high level of mortality, slower growth and infertility (not able to produce any offspring). Some soy-fed hamsters also had hair growing inside their mouths [60]. These results of two Russian studies appear compelling, but could not be repeated elsewhere. Even if these results are considered reliable, one would like to understand the molecular mechanism that is responsible for these abnormal symptoms. Unfortunately, no suitable explanation is available for these abnormal results that were attributed to GM soybean.

Seralini’s study on GM corn fed rats in France

A group of scientists led by G-E Seralini in France published results of their experiments, which involved feeding of herbicide RoundUp resistant maize (event NK603) and the herbicide RoundUp to rats, over two-years. The results claimed that RoundUp resistant maize and the herbicide RoundUp are toxic; these results were widely questioned. A detailed analysis of the procedures and data obtained suggested that there were flaws and inaccuracies in this study, and thus caused irreparable damage to the credibility of science and researchers in the field [61]. It was argued that the sample size and the duration of the study were small and that there was high incidence of tumors in the species of rats that was used in the study. In view of this, the paper was retracted by the journal in November 2013, although this retraction was criticized by some [62], so that the paper was republished in another journal in June 2014, once again inviting sharp reaction by many scientists.

Use of CaMV 35s Promoter

According to some recent studies, the CaMV 35S promoter (derived from cauliflower mosaic virus) that is present in almost all transgenic crops approved for commercial cultivation may be highly unsafe, because this promoter sequence overlaps the coding sequence of cauliflower mosaic virus gene VI encoding the protein P6. Fifty-four transgenic events certified for release in USA contain up to 528bp of ORF VI [63]. As P6 is a multifunctional protein, whose full range of functions is unknown, there is some concern that expression of one or more of its domains may have unforeseen consequences in the transgenic organisms. Recent studies have attempted to determine what length of CaMV 35S promoter has the least chance of inadvertently producing P6 domains, while still retaining full promoter activity. As one might expect, using shorter promoter lengths decreases the number of P6 domains included and also decreases the likelihood of unwanted effects.

Negative Impact of Human Activities

The subject of negative impact of human activities on the environment, leading to its degradation (a health hazard) has been widely discussed. This information has been summarized under the sub-titles “List of 30 Top Environment Concerns” and “How do Humans Affect the Environment” [64]. It also lists the following five major public concerns of Americans, selected on the basis of a series of gall up-polls conducted during 1997-2008: (a) contamination of drinking water; (b) water pollution; (c) soil contamination; (d) wild life conservation; and (e) air pollution. Obviously, genetic engineering including GM crops is not a major concern, but only one of the top 30 environmental concerns that have also been listed. The water, soil and air pollution are largely caused due to human activities, which can be minimized. Some programs are also underway to address these issues, but not at the level at which GM crops are being opposed without substantial evidence for their harmful effects. We like to discuss some of the human activities, which cause these harmful effects, and did not receive the desired attention of the CSGs and NGOs, the way GM crops have been opposed, although during 20 years of cultivation and consumption of GM crops, no harmful effects have been reported.

Pesticide use and the risks to human/environment health

In order to protect food, pesticides (including insecticides, herbicides, fungicides and rodenticides) have been used for centuries. In the past (several decades ago), use of pesticides in agriculture was considered to be an effective technique to protect crops from damage due to insect pests without any major risk to human health (with the exception of some examples of harmful consequences). The use of pesticide was, therefore, welcome and was considered desirable. However, in 1962, a debate about the harmful effects of pesticides was initiated with the publication of the literary classic ‘Silent Springs’ written by Rachel Carson [65]. The book was widely read, although the merit of the book and the scholarship of its author as a scientist was questioned by some [66]. Thirty years after the publication of this book, a workshop was convened in Nairobi in September 1992 with the aim to update the public on the harmful effects of pesticides and to develop environmentally safe use of pesticide as a part of integrated pest management (IPM). The proceedings of this workshop were published in the form of a book ‘Beyond Silent Spring: Integrated Pest Management and Chemical Safety’. The book gives an overview of papers presented at the workshop. More recently in 2006, an overview of the circumstances that led to the publication of ‘Silent Springs’, and the criticism and appreciation that it received was also published, 44 years after its publication [67].

Effect on human health

In 2012, in an article published in Science, experimental evidence was presented, which shows that the exposure to pesticides and other chemicals can have long-term effects on human and ecological health. In this article, the authors cited several studies, where harmful effects of early exposure to pesticides involving endocrine disruption have actually been documented. This endocrine disruption has been shown to be responsible for altered gene expression profiles that were witnessed, causing a variety of abnormalities. Transmission of these effects to the next generations was also observed, meaning thereby that hereditary changes may also be caused due to exposure to pesticides. They also cite examples, where it was shown that exposure of human subjects early in embryonic development to chemicals like those used in pesticides alters gene expression patterns that can lead to altered health later in life [68]. In all such studies, although we can measure the effects of acute high dose of chemicals, but one cannot estimate the effect of chronic low-dose exposure, to which everybody living on this earth is exposed every day. The question therefore is being asked, whether or not the non-GM food grain produced using pesticides and chemical fertilizers safe to eat?

Effect on honey bees, bumble bees and other bees: the pollinators. A number of useful non-target insects (e.g. honey bees, bumble bees, etc.) are important pollinators for a large number of flowering plants, and are chronically exposed to cocktails of agrochemicals. Sufficient evidence is available that bees, which contribute to 80% of insect pollination, have been disappearing at an alarming rate since 2006, and also that this is partly due to sub-lethal effects of insecticides, particularly, neonicotinoids [69]. Pesticide exposure can also impair both detoxification mechanisms and immune responses, rendering bees more susceptible to parasites. Keeping the above in view, a restriction was imposed in European Union on the use of three neonicotinoids (clothianidin, imidacloprid and thiamethoxam) from 1 December 2013. This decision of EU is being reviewed and the review is expected to be available in 2017. Meanwhile, even in one state of USA (Maryland), use of neonicotinoids has been banned, when it was
noticed that in recent years, bee population there was dropped by 61% (presumably due to the use of pesticides). The subject has attracted so much of attention of environmentalists and zoologists that during the last more than a decade, >200 studies have been conducted to understand the reasons for the decline in honey bee population. In these studies, it has been documented that use of insecticides/pesticides is one of the major causes of this decline in bee population, although diseases caused by pathogens is another major reason; susceptibility to pathogen is also often attributed to exposure to pesticides [70]. However, the debate continues on the issue, whether or not insecticides like neonicotinoids are the major cause of observed significant drop in bee population.

Food quality and safety; a threat to human health

It is also widely known that foodstuff of animal and plant origin may present intrinsic hazards, due to microbiological contamination and adulterations caused due to careless handling of food and also for monetary benefits. Although methods are available for assessing the safety and quality of foods, these tests is not mandatory in many countries including India, and even if these are mandatory, the implementation has not been effective. Also, microbiological testing of finished food products alone is inefficient to guarantee the safety of a foodstuff tested. The safety of the foodstuffs must principally be ensured by a more preventative approach, such as product and process design and the application of Good Hygiene and Manufacturing Practices (GHP, GMP) and the Hazard Analysis Critical Control Point (HACCP) principles.

It is also known that some diseases, such as brucellosis, salmonellosis and listeriosis, can be transmitted to humans through contaminated food. Although there is legislation in some countries in Europe and USA to prevent diseases caused due to contaminated food, implementation of this legislation in a country like India needs to be examined. Several unsuccessful attempts were made to standardize food quality and safety internationally. International conferences are also held every year to address the issue of food safety, with no major success. These attempts did, however, eventually led to the establishment of the Codex Alimentarius Commission (CAC) in 1962 by the Food and Agriculture Organization of the United Nations (FAO) and the World Health Organization (WHO) to implement the joint FAO/WHO Food Standards Program. In brief, the purpose of the Program is to protect the health of consumers, ensure fair practices in the food trade and coordinate international food standardization work. Governments in different countries have the responsibility for the establishment and operations of national food safety programs and quality control systems that must ensure safe and wholesome food that meet the nutritional needs of consumers and do not endanger the consumer’s health through chemical, biological or other contaminants. They must also ensure that food sold is presented in an honest and non-deceptive or non-fraudulent manner. Consumer protection and the prevention of food-borne diseases are two essential elements of a food safety program and they are the shared responsibilities of governments, the food industry and the consumer.

Keeping the above in view, India has made significant strides over the past several decades in food production and in the export and health sectors. There are several key issues that require attention [71]. In India, the Ministry of Health and Family Welfare (MOH&FW) in the Central Government is the nodal Ministry for ensuring the quality and safety of food marketed in the country. A comprehensive legislation called the Prevention of Food Adulteration Act (PFA Act) was enacted in 1954, which came into effect from June 1, 1955, with the objective of assuring the quality and safety of food as well as to encourage fair trade practices. It is also known that farmers are using hormone shots to expedite the growth of vegetables overnight to double the size. For instance oxytocin, a drug, which is banned for use on animals, is injected in pumpkins, watermelons, brinjals, gourds and cucumber for quick increase in fruit size and for perfect look. In this manner, green vegetables, which are considered to provide health benefits, may instead cause nervous breakdowns, sterility and neurotic complications, because of malpractices used for growth promotions. It is also used (implanted or injected) in livestock for increased milk production. Such hormones will cause irreparable damage to human health, if used for extended period of time. Oxytocin injections are also being used by midwives for early child birth without the knowledge of the pregnant ladies, and for accelerating puberty in young girls dragged into flesh trade. There are examples, when actions have been taken to stop these malpractices, but apparently there seems to be no effect of these actions, which can be compared with the effects of activities of anti-GM lobby in stopping the commercialization of GM foods, for which, there is no evidence of any harmful effects.

Excess use of fossil fuels and increasing number of autos, ACs and refrigerators: a threat to the environment

It has also been shown that with improvement in the living standard of people in the developing world, there are more cars on the road and more air conditioners and refrigerators at residences causing substantial emission of CO2 and other harmful gases like chloro-fluoro carbon (CFC). In contrast, there is evidence that growing GM crops can lead to reduction in CO2 emission due to reduced tillage and other agronomic practices (discussed earlier in this article). Similarly, it is estimated that in mid-term (5-10 years), quantity of nitrogen (N) used as fertilizer may be reduced to half through the use of GM crops with improved nitrogen use efficiency (currently 100 million tons of N fertilizer is used on crops at an annual cost of US $50 billion; up to half of the N applied is not taken up by the crops and causes pollution, particularly in waterways).

Population explosion and the environment

Rapid increase in human population has been witnessed over the past three centuries, more so during the last 50 years. Therefore, there has been concern, whether the planet Earth
will be able to sustain with this increase in population with its limited and depleting resources. Other problems associated with overpopulation include the increased demand for resources such as fresh water, food and other natural resources (such as fossil fuels) faster than the rate of regeneration. Urbanization has also contributed to the fast depletion of resources. Therefore, one may ask the question, why we are not raising a voice for population control in geographical areas, which are responsible for population explosion at the global level.

**Fracking and ecological effects**

Hydraulic fracturing, or “fracking”, is the process of drilling and injecting fluid into the ground at a high pressure in order to fracture shale rocks to release natural gas inside. There are more than 500,000 active natural gas wells in the US alone. Proponents of fracking point to the economic benefits from vast amounts of formerly inaccessible hydrocarbons, which the process can extract. However, the opponents point to potential environmental impacts, including contamination of ground water and air, the migration of gases and hydraulic fracturing chemicals to the surface, surface contamination from spills and flow-back and the effects it has on human health. For these reasons hydraulic fracturing has come under scrutiny internationally, with some countries suspending or even banning it [72].

**Summary and Conclusion**

The biotech crops are being grown globally for the last 20 years without any reliable and authentic report of any harmful effect on human/environment health, and the area occupied by these crops has been steadily increasing (179.7 hectares in 2015). In contrast, other human activities due to urbanization, industrialization, economic growth, population explosion, and rising standard of living in developing countries like India have caused serious problems to human and environment health. These problems include water shortage, climate change, and environment degradation (including soil, water and air pollution). Many new diseases are being discovered, some of them resulting due to environment degradation. Therefore, one would like to compare the perceived risks due to commercialization of biotech crops with well known and estimated risks due to other human activities. If this is done the CSGs, NGO’s and other groups constituting an anti-GM lobby will serve better by diverting their energy and effort to control these other human activities, which are causing the greatest harm to human and environment health. Some efforts are being made in this direction, but major efforts are needed, if we want to ensure that future generation may live in a clean environment without any major risk to human and environmental health.

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