

A Review on Impacts of Genetically Modified Food on Human Health

Charu Verma¹, Surabhi Nanda², R.K. Singh³, R.B. Singh⁴ and Sanjay Mishra^{1,2,*}

¹Department of Biotechnology & Microbiology, Institute of Foreign Trade & Management, Lodhipur Rajput, Delhi Road, Moradabad 244001, U.P., India

²Department of Biotechnology, College of Engineering & Technology, IFTM Campus, Lodhipur Rajput, Delhi Road, Moradabad 244001, U.P., India

³Kumaon Engineering College, Dwarhut, Uttarakhand Technical University, Dehradun, Uttarakhand, India

⁴Halberg Hospital & Research Center, Civil Lines, Moradabad 244 001, U.P., India

Abstract: Biotechnology offers a variety of potential benefits and risks. It has enhanced food production by making plants less vulnerable to drought, frost, insects, and viruses and by enabling plants to compete more effectively against weeds for soil nutrients. In a few cases, it has also improved the quality and nutrition of foods by altering their composition. However, the use of biotechnology has also raised concerns about its potential risks to the environment and people. For example, some people fear that common plant pests could develop resistance to the introduced pesticides in GM crops that were supposed to combat them. Genetic engineering provides a means to introduce genes into plants via mechanisms that are different in some respects from classical breeding. A number of commercialized, genetically engineered (GE) varieties, most notably canola, cotton, maize and soybean, were created using this technology, and at present the traits introduced are herbicide and/or pest tolerance. Gene technology enables the increase of production in plants, as well as the rise of resistance to pests, viruses, frost, etc. Gene transfer is used to modify the physical and chemical composition and nutritional value of food. Gene transfer in animals will play a part in boundless possibilities of improving qualitative and quantitative traits. The yield, carcass composition and meat characteristics the use of nutritive substances ? not sure what is being said here?, and resistance to diseases can be improved. On the other hand, negative effects of gene technology on animals, human, and environment should be considered. The present review article is the compilation of various studies that present both positive and negative impacts of genetically modified food on human health.

Keywords: *Bacillus thuringiensis*, genetically modified food, Gene Technology, Human Health, Pharmaceutical Drugs, transgenic plants.

INTRODUCTION

Genetically modified organisms (GMOs) are defined as organisms (except for human beings) in which the genetic material has been altered in a way that does not occur naturally by mating and/or natural recombination. GMOs have widespread applications as they are used in biological and medical research, production of pharmaceutical drugs, experimental medicine, and agriculture. The use of gene technology in food production has become interesting due to increased needs of food as well as its improved quality. With the application of gene technology to plants and animals, goals can be achieved more quickly than by traditional selection. Consequently, ethical dilemmas are opened concerning the eventual negative effects of production of genetically modified food. It seems that supplementation of nutraceuticals and wild foods as well as wild lifestyle may be protective, whereas western diet and lifestyle may enhance the expression of genes related to chronic diseases. Our

genes or pathways are most likely regulated by microRNA [1-4]. The prevalence and mortality due to multifactorial polygenic diseases; hypertension, coronary artery disease (CAD), diabetes and cancer vary depending upon genetic susceptibility and environmental precursors because they have identifiable Mendelian subsets. Rapid changes in diet and lifestyle may influence heritability of the variant phenotypes that are dependent on the nutraceutical or functional food supplementation for their expression. It is possible to recognize the interaction of specific nutraceuticals, with the genetic code possessed by all nucleated cells. There is evidence that South Asians have an increased susceptibility to CAD, diabetes mellitus, central obesity and insulin resistance at younger age, which may be due to interaction of gene and nutraceutical environment [5]. The negative consequences can affect the health, environment, etiology, society and ethics [6].

TECHNOLOGY TO PRODUCE GENETICALLY MODIFIED ORGANISMS

Several methods of production of genetically modified organisms (GMO) are known. The foreign gene that has been inserted into the cell of a microorganism, a plant or an

*Address correspondence to this author at the Department of Biotechnology, College of Engineering & Technology IFTM Campus, Delhi Road, Moradabad 244001, U.P., India; Tel: +91-591-2360817; Fax: +91-591-2360818; E-mail: sanjaymishra66@gmail.com

animal is called a transgene. It is integrated into the genome of the recipients which are called transgenic. The transgenes are genes with known traits or mutated variants of known genes. In most cases also marker genes are used because of identification of transgenic organism. The integration of transgene into the cell is carried out by different methods: (a) Transduction with the use of bacteriophages (b) Transgene injection using pronuclear microinjection [7]; (c) Transfer using modified viruses and plasmids (d) Electroporation method by which higher permeability of cell membrane is achieved.

For transfer of foreign gene also artificial chromosomes or fragments of chromosomes can be used. Transgenes can be transferred into the egg-cell by spermatozoa containing fragments of chromosomes [6]. Developed world, having material and intellectual capacities, leads the studies on transgenic technology for production increase and improved food quality. In fact, there is not only enough but even too much food in the developed world. However, developing countries that need this technology to exceed the food shortage cannot afford it [8]. Hence, gene technology is not a remedy to prevent the world from starvation. Transgenic seeds that developed countries can provide to developing countries to diminish the rate of malnutrition seems to be the best idea of genetic engineering. Transgenic plants that are resistant to pests will cause higher resistance in pests; consequently stronger herbicides and insecticides should be used in the future. Finally, it has been proposed that transgenic food can cause certain allergies.

GM FOODS ARE PROMOTED WHY?

The term GM foods or GMOs (genetically-modified organisms) is most commonly used to refer to crop plants created for human or animal consumption using the latest molecular biology techniques. These plants have been modified in the laboratory to enhance desired traits such as increased resistance to herbicides or improved nutritional content. Genetic engineering can create plants with the exact desired trait very rapidly and with great accuracy. For example, plant geneticists can isolate a gene responsible for drought tolerance and insert that gene into a different plant. The new genetically-modified plant will gain drought tolerance as well. Not only can genes be transferred from one plant to another, but genes from non-plant organisms also can be used. The best known example of this is the use of B.t. genes in corn and other crops. B.t., or *Bacillus thuringiensis*, is a naturally occurring bacterium that produces crystal proteins that are lethal to insect larvae. B.t. Crystal protein genes have been transferred into corn, enabling the corn to produce its own pesticides against insects.

ADVANTAGES OF GM FOODS

- **Pest resistance:** Farmers typically use many tons of chemical pesticides annually. Consumers do not wish to eat food that has been treated with pesticides because of potential health hazards, and run-off of agricultural wastes from excessive use of pesticides and fertilizers can poison the water supply and cause harm to the environment. Growing GM foods such as B.t. corn can help to eliminate the application of chemical pesticides and reduce the cost of bringing a crop to market [9, 10].

- **Herbicide tolerance:** Crop plants genetically-engineered to be resistant to one very powerful herbicide could help to prevent environmental damage by reducing the amount of herbicides needed. For example, Monsanto has created a strain of soybeans genetically modified to be not affected by their herbicide product Roundup. A 2010 study has found that long-term exposition to environmental relevant concentrations of a Roundup formulation causes metabolic disruption in *Leporinus obtusidens* [11]. A farmer grows these soybeans which then only require one application of weed-killer instead of multiple applications, reducing production cost and limiting the dangers of agricultural waste run-off [12].

- **Disease resistance:** There are many viruses, fungi and bacteria that cause plant diseases. Plant biologists are working to create plants with genetically-engineered resistance to these diseases [13,14].

- **Cold tolerance:** An antifreeze gene from cold water fish has been introduced into plants such as tobacco and potato. With this antifreeze gene, these plants are able to tolerate cold temperatures that normally would kill unmodified seedlings [15].

- **Drought tolerance/salinity tolerance:** As the world population grows and more land is utilized for housing instead of food production, farmers will need to grow crops in locations previously unsuited for plant cultivation. Creating plants that can withstand long periods of drought or high salt content in soil and groundwater will help people to grow crops in formerly inhospitable places [16,17].

- **Nutrition:** Malnutrition is common in third world countries where impoverished peoples rely on a single crop such as rice for the main staple of their diet. However, rice does not contain adequate amounts of all necessary nutrients to prevent malnutrition. If rice could be genetically engineered to contain additional vitamins and minerals, nutrient deficiencies could be alleviated. For example, blindness due to vitamin A deficiency is a common problem in third world countries. Researchers at the Swiss Federal Institute of Technology Institute for Plant Sciences have created a strain of "golden" rice containing an unusually high content of beta-carotene (vitamin A) [18]. Plans were underway to develop golden rice that also has increased iron content.

- **Pharmaceuticals** Medicines and vaccines often are costly to produce and sometimes require special storage conditions. Researchers are working to develop edible vaccines in tomatoes and potatoes [19, 20]. These vaccines will be much easier to ship, store and administer than traditional injectable vaccines.

- **Phytoremediation:** Plants such as poplar trees have been genetically engineered to clean up heavy metal pollution from contaminated soil [21].

SOME CRITICISMS AGAINST GM FOODS

GM foods fall into three categories: environmental hazards, human health risks, and economic concerns.

Environmental Hazards

- **Unintended harm to other organisms:** pollen from B.t. corn caused high mortality rates in monarch butterfly

caterpillars. Monarch caterpillars consume milkweed plants, not corn, but the fear is that if pollen from B.t. corn is blown by the wind onto milkweed plants in neighboring fields, the caterpillars could eat the pollen and perish. B.t. toxins kill many species of insect larvae.

- Reduced effectiveness of pesticides just as some populations of mosquitoes developed resistance to the now-banned pesticide DDT; many people are concerned that insects will become resistant to B.t. or other crops that have been genetically modified to produce their own pesticides.
- Gene transfer to non-target species is another concern that crop plants engineered for herbicide tolerance and weeds will cross-breed, resulting in the transfer of the herbicide resistance genes from the crops into the weeds. These "superweeds" would then be herbicide tolerant as well.

Human Health Risks

- Allergenicity Many children in the US and Europe have developed life-threatening allergies to peanuts and other foods. There is a possibility that introducing a gene into a plant may create a new allergen or cause an allergic reaction in susceptible individuals. A proposal to incorporate a gene from Brazil nuts into soybeans was abandoned because of the fear of causing unexpected allergic reactions [22].
- Unknown effects on human health: A recent article published in Lancet examined the effects of GM potatoes on the digestive tract in rats [23, 24]. Moreover, the gene introduced into the potatoes was a snowdrop flower lectin, a substance known to be toxic to mammals.

Economic Concerns

Bringing a GM food to market is a lengthy and costly process. Yet consumer advocates are worried that patenting these new plant varieties will raise the price of seeds so high that small farmers and third world countries will not be able to afford seeds for GM crops, Patent enforcement may also be difficult, as the contention of the farmers that they involuntarily grew Monsanto-engineered strains. One way to combat possible patent infringement is to introduce a "suicide gene" into GM plants. These plants would be viable for only one growing season and would produce sterile seeds that do not germinate. Farmers would need to buy a fresh supply of seeds each year. However, this would be financially disastrous for farmers [25].

APPLICATION OF TRANSGENIC PLANTS IN HUMAN NUTRITION

Genetically modified foods are classified into three categories according to their usage and legal regulations [26].

1. Food is genetically modified (potato, tomato, soya, maize, sunflowers, rice, pumpkins, melons, rape, etc.)
2. Food contains components of genetically modified plants (starch, oil, sugar, aminoacids, vitamins, etc.)
3. Food contains genetically modified organisms (yoghurt contains transgenic microorganisms).

Gene technology enables higher yields in plants, resistance to pests and frost, as well as mechanical properties of fruits, etc. We can also modify physical and chemical composition in order to improve nutritional and physiological value of foods. Transgenic plants also enable production of more healthy food (more unsaturated fatty acids, transfer of proteins from legumes into wheat, increased content of essential amino acids, transfer of proteins from sunflowers into maize, etc.). Thus, dangers of heart diseases, allergies are diminished and malignancy prevented [27].

GENETICALLY MODIFIED CROPS

BT COTTON

Cotton is an important fibre crop of India being cultivated over an area of about 9.5 million hectares (mha) representing approximately one quarter of the global area of 35 million hectares under this crop. After China, India is the largest producer and consumer of cotton. Much of this success owes itself to the introduction of Bt cotton in 2002 prior to which cotton production suffered huge losses due to its susceptibility to insect pests. Among the insects, cotton bollworms are the most serious pests of cotton in India causing annual losses of at least US\$300 million. Insecticides valued at US\$660 million are used annually on all crops in India, of which about half are used on cotton alone [28, 29]. Bt or *Bacillus thuringiensis* is a ubiquitous soil bacterium first discovered in 1901 by Ishiwata, a Japanese microbiologist [30]. Later it was found that some Bt strains (Cry+) were highly toxic to larvae of certain insect species which are also plant pests. Bt was first sold as a spray formulation in 1938 in France for the management of European corn borer. Subsequent research has revealed that Bt carries proteinaceous crystals that cause mortality in those insects which carry receptor proteins in gut membranes that bind to Bt proteins. Other organisms that do not contain receptors to Bt proteins are not affected by the toxin.

The advent of genetic transformation technology made it possible to incorporate cry genes and thus the ability to produce Bt proteins in plant cells so that target insect larvae infesting the crop plants are effectively killed. The first Bt crops viz., Bt cotton, Bt corn and Bt potato were commercialized in USA in 1996. Bt crops are currently cultivated in 23 countries over an area of 46 mha [31]. The advent of genetic transformation technology made it possible to incorporate cry genes and thus the ability to produce Bt proteins in plant cells so that target insect larvae infesting the crop plants are effectively killed. The first Bt crops viz., Bt cotton, Bt corn and Bt potato were commercialized in USA in 1996. Bt crops are currently cultivated in 23 countries over an area of 46 mha [31]. It is also recognized that GM technology may entail rare unintended risks and hazards to environment, and human and animal health. These risks include toxicity and allergenicity, emergence of new viruses, development of antibiotic resistance in microorganisms, adverse effects on non-target organisms, erosion of crop diversity, and development of new weeds [32]. Bt cotton is in many ways an ideal candidate for introduction as a transgenic commercial crop. It is basically grown as a fibre crop, while cotton seed oil used for consumption is free of proteins, including Bt protein. The safety of Bt toxins in terms of toxicity and allergenicity towards mammals and

other non-target organisms is well documented [33, 34]. Lack of receptors that bind to Bt toxins and their instant degradation in human digestive system makes them innocuous to human beings. Community exposure to Bt spray formulations over a period of last six decades has not resulted in any adverse effects. Lack of homology to any allergenic protein/ epitope sequences makes Bt toxins non-allergenic. The safety of Bt crop-derived foods has also been well established [35, 36]. In recent years, the effects of Bt crop cultivation on non-target organisms including insect predators, parasitoids and pathogens have been investigated quite extensively [25, 37-42].

GOLDEN RICE

The bright orange color of carrots comes from beta-carotene, which forms vitamin A in our bodies. Yet 250 million people suffer from vitamin A deficiency. Each year a half million children become blind from lack of vitamin A and over half of these die within months. Ideally, everyone would have a varied diet with lots of produce that supplied ample vitamin A and other nutrients. Better nutrition could prevent up to two million deaths in children under the age of four each year. But that requires more prosperity for much of the world – something that's a long way off. Nearly half the world's population survives on a daily bowl of white rice, which contains no vitamin A. Making rice more nutritious, could improve people's lives tremendously [43].

A team of researchers decided to try creating rice that contains beta-carotene (the compound we convert to vitamin A). They were inspired by the bright yellow daffodil. How did it produce beta-carotene? They found that several daffodil enzymes manufacture beta-carotene from other molecules. Rice has those other molecules, but it doesn't produce the enzymes to rearrange them into beta-carotene in its kernel. Could they give rice the genes for those enzymes and get them to work together? Previous researchers had inserted several genes that worked individually to make separate products. No one had successfully inserted a group of genes that had to work in sync to make one product. They tried putting the genes in a gene gun and shooting them into rice cells. That didn't work, so they put two genes in one *Agrobacterium* and another gene in another *Agrobacterium*. Both bacteria "infected" the rice cells, inserted the new genes, and soon the lab grew rice plants carrying all three genes. It was easy to see that the genes worked because of the kernels' golden glow. A bowl of this "golden rice" provides enough vitamin A to keep a person healthy. Meanwhile, researchers are working on a related nutritional problem. White rice also contains very little useable iron, and without iron, children don't grow or learn well. Iron deficiency causes 40 million mothers to have premature and low weight babies. Many of these mothers and babies die of anemia. The solution also involves several genes from several sources: a fungus, another kind of rice, and a green bean. These genes produce proteins in the rice kernel that help the human body absorb and store iron. Again, they are using *Agrobacterium* to get the genes into rice. Someday, researchers may crossbreed the rice plant that makes beta-carotene with one that makes iron to produce a hybrid that makes both essential nutrients. The research team worked ten years on golden rice. They are working out legal issues so

they can donate this rice to farmers in developing countries [43, 44].

POTATOES

Many poor countries can't afford vaccines or can't get them to remote villages. Clinics often can't refrigerate the vaccines or sterilize needles. These problems make safeguarding millions of children extremely difficult. In addition, most vaccines are made from the infectious organism that causes the disease. Every once in a while such vaccine can cause harmful side effects, even the disease they are supposed to prevent. In 1991 the World Health Organization challenged scientists to create a simpler, safer, cheaper way to vaccinate children. Some scientists began to brainstorm about plants. Since plants naturally make a number of different compounds, they could be reprogrammed to make edible vaccines [43].

Researchers tried making a cholera vaccine using plants. Cholera is a bacterial disease that causes deadly diarrhea. It spreads rapidly where people don't have clean water and it kills two to three million children each year. Researchers pinpointed part of the cholera bacterium that the human immune system can recognize, so it could be used as a vaccine. Scientists found the genes that make that bacterial part. After some trial and error, they put those genes into potatoes to turn potatoes into a handy vaccine. Potatoes grow in many areas of great health need, and they can withstand long shipping and storage. But there is a snag. People don't eat raw potatoes. So scientists cooked them and found that some of the vaccine still survives. When people ate these cooked potatoes, their bodies made some of the antibodies that can protect them from cholera [44]. Imagine getting your vaccines and boosters from potatoes or some other food instead of painful shots! But that's still a ways off. With the cholera vaccine, researchers need to adjust the dose in each bite and find ways to package them. Of course, people will get their vaccine bits from nurses and clinics, not from the supermarket. Ideally, edible vaccines wouldn't spoil, which would cut the cost and difficulty of delivering them in the developing world. They'd be more pleasant, too.

In industrialized countries, most people don't suffer from too little food. They suffer from too much. Obesity is a major health problem even for children. We all know that we should avoid greasy French fries and sugary sodas, but it's hard! If we can't take the junk food away from people, maybe we can take the "junk" out of food – but keep the taste in. Again, scientists are looking at the potato. When it's fried, oil replaces the water in the potato. But the starchier the potato, the less oil it soaks up. Restaurants pay a premium price for high starch potatoes because they make crisper, less greasy fries. Scientists are trying to develop potatoes with even more starch so they will soak up even less oil. Another way to make a healthier fry is to make healthier oil. Scientists have already modified plants like soybean and canola to produce a less saturated, healthier fat. Future plants may make even healthier oils that actually strip away fatty deposits from your arteries. What about that soda with your fries? Scientists are working on that, too. They are modifying the sugar beet to produce an enzyme that changes sugar (sucrose) to fructan. Fructan tastes like sugar, but we don't digest fructan so it adds no calories. They have also

cloned the gene for a protein in an African plant that tastes a thousand times sweeter than sugar! We could get the same sweetness with a thousand times less sweetener [43, 44].

BT BRINJAL

The Genetic Engineering Approval Committee's approval of Bt brinjal, the first genetically modified crop for human consumption in India, has sparked off protests across the country. On October 15, 2009, the Genetic Engineering Approval Committee (GEAC) of the ministry of environment, the regulatory body for approving genetically modified crops (GM crops) in India, approved Bt brinjal, the first GM crop for human consumption in India, for commercial use [45, 46]. The approval came following the review of reports submitted by the Maharashtra Hybrid Seeds Company Limited (Mahyco), the Indian subsidiary of the US-based company Monsanto, that uses biotechnology to produce high yielding, pest resistant crops. Bt Brinjal is a genetically modified plant in which a gene from the soil bacterium bacillus thuringiensis is inserted into the genome of the brinjal, which can then produce a protein, Cry1Ac. This protein behaves as a toxin against the shoot and fruit borer (SFB), a pest that commonly affects brinjal. The gene modification also includes the addition of two antibiotic resistance marker genes.

GENETICALLY MODIFIED ANIMALS AND HUMAN NUTRITION

Important advancement in production and processing of transgenic plants has encouraged studies in animals [47]. Like in plants, microinjection and similar techniques are used to inject foreign gene (DNA) into the nucleus of fertilized egg-cell in animals. When egg is developed to blastula it is transferred to the uterus of an animal where transgenic organism develops. Genetic linkage maps for cattle, pigs and sheep elucidating chromosomal regions for economically important traits will considerably contribute to better quality and amounts of meat [48]. Gene technology is prosperous in farm animal production and in improvement of quality and quantity traits [26, 49, 50]. Gene technology stimulates the yields, higher nutrient consumption, and animal welfare. These traits can be improved directly by gene transfer or using growth hormones, vaccines, antibodies, immunity stimulants and anti-allergy DNA produced by genetic engineering. Gene transfer is expected to improve those production traits in animals that are poorly inherited (low heritability rate, h^2), for example number of weaned piglets per sow [51] reported that transgenic plants that produced vaccines, which animals consumed with forage, were produced. The gene for resistance enables breeding of animals resistant to diseases. Vaccine for immune castration of animals, which is painless in male animals and diminishes aggressiveness while female animals are free of negative effects of oestrus, positively affects the economically important trait carcass composition [52]. The possibilities of biotechnological interventions are numerous but the application depends on economic, social and cultural conditions. Transgenic technique can improve the carcass traits and meat quality. The percentage of meat in carcass increases; taste and water binding improve, diminish the percentage of fat and improve the fatty acid composition of meat (more non-saturated fatty acids [53]. Milk has been modified with

transgenes and in most cases without any harm to transgenic animals. Proteins that are used in pharmaceutical industry were obtained from milk of transgenic animals, like human antitrypsin in sheep, plasminogene activator in goat and human protein C in pig.

Transgenic milk can be used as: (a) Food for wide use; (b) raw materials for milk products; (c) food for infants; (d) source of biologically active substances for pharmaceutical industry [50, 51].

Even non-protein compounds of human milk, like oligosaccharides, are highly appreciated in milk of transgenic animals. Mammary gland produces milk proteins and lactose under the influence of hormones during late pregnancy and lactation period. Caseins and lactoglobulins are synthesized only during lactation period. Genes from mentioned compounds are used for transgenic milk production that is used for cheese production and for substitute to human milk for infant nutrition [50] reported on wide use of bovine growth hormone (somatotropin) in cattle to increase production of milk and meat [53]. The bovine growth hormone gene had implied as the prediction of the possibilities of production of ideal pork with ultra low fat content and favorable fatty acids composition with transgenic pigs took place.

HEALTH RISK OF GENETICALLY MODIFIED ORGANISMS

"Several animal studies indicate serious health risks associated with GM food," including infertility, immune problems, accelerated aging, insulin regulation, and changes in major organs and the gastrointestinal system.

GMOS ARE INHERENTLY UNSAFE

There are several reasons why GM plants present unique dangers. The first is that the process of genetic engineering itself creates unpredicted alterations, irrespective of which gene is transferred. This creates mutations in and around the insertion site and elsewhere [54]. The biotech industry confidently asserted that gene transfer from GM foods was not possible; the only human feeding study on GM foods later proved that it does take place. The genetic material in soybeans that make them herbicide tolerant transferred into the DNA of human gut bacteria and continued to function [55]. That means that long after we stop eating a GM crop, its foreign GM proteins may be produced inside our intestines.

GM DIET SHOWS TOXIC REACTIONS IN THE DIGESTIVE TRACT

The very first crop submitted to the FDA's (Food & Drug Administration) voluntary consultation process, the FlavrSavr tomato, showed evidence of toxins. Out of 20 female rats fed the GM tomato, 7 developed stomach lesions [56]. The type of stomach lesions linked to tomatoes could lead to life-endangering hemorrhage, particularly in the elderly who use aspirin to prevent blood clots [57]. Dr. Pusztai believes that the digestive tract, which is the first and largest point of contact with foods, can reveal various reactions to toxins and should be the first target of GM food risk assessment. Mice fed potatoes engineered to produce the Bt-toxin developed abnormal and damaged cells, as well as

proliferative cell growth in the lower part of their small intestine (ileum) [58]. Rats fed potatoes engineered to produce a different type of insecticide (GNA lectin from the snowdrop plant) also showed proliferative cell growth in both stomach and intestinal walls.

GM DIETS CAUSE LIVER DAMAGE

Rats fed the GNA lectin potatoes had smaller and partially atrophied livers [59]. Rats fed Monsanto's Mon 863 corn, engineered to produce Bt-toxin, had liver lesions and other indications of toxicity [60]. Rabbits fed GM soy showed altered enzyme production in their livers as well as higher metabolic activity [61]. Rats fed Roundup Ready soybeans also showed structural changes in their liver [44].

GM FEED ANIMALS HAD HIGHER DEATH RATES AND ORGAN DAMAGE

The cells in the pancreas of mice fed Roundup Ready soy had profound changes and produced significantly less digestive enzymes [62]; in rats fed a GM potato, the pancreas was enlarged [60]. In various analysis of kidneys, GM fed animals showed lesions, toxicity, altered enzymes production or inflammation [61-63]. Enzyme production in the hearts of mice was altered by GM soy, [61] and GM potatoes caused slower growth in the brain of rats [60].

REPRODUCTIVE FAILURE AND INFANT MORTALITY

The testicles of both mice and rats fed roundup ready soybeans showed dramatic changes. In rats, the organs were dark blue instead of pink. In mice, young sperm cells were altered [64]. Embryos of GM soy-fed mice also showed temporary changes in their DNA function, compared to those whose parents were fed non-GM soy [65].

GM CROPS TRIGGER IMMUNE REACTIONS AND MAY CAUSE ALLERGIES

Allergic reactions occur when the immune system interprets something as foreign, different and offensive and reacts accordingly. All GM foods, by definition have something foreign and different. And several studies show that they provoke reactions. GM potatoes caused the immune system of rats to responded more slowly [60]. And GM peas provoked an inflammatory response in mice, suggesting that it might cause deadly allergic reactions in people [66]. In addition to the herbicide tolerant protein, GM soybeans contain a unique, unexpected protein, which likely came about from the changes incurred during the genetic engineering process. Scientists found that this new protein was able to bind with IgE antibodies, suggesting that it may provoke dangerous allergic reactions. Organic farmers and others have sprayed crops with solutions containing natural Bt bacteria as a method of insect control. The toxin creates holes in their stomach and kills them. Genetic engineers take the gene that produces the toxin in bacteria and insert it into the DNA of crops so that the plant does the work, not the farmer. The fact that we consume that toxic pesticide in every bite of Bt corn hardly appetizing. Studies verify, however that natural Bt-toxin is not fully destroyed during digestion and does react with mammals. The Bt—toxin produced in GM crops is vastly different from the bacterial (Bt-toxins) used in organic and traditional farming and

forestry. The plant produced version is designed to be more toxic than natural varieties [67]. Just like the GM soy protein, the Bt protein in GM corn varieties has a section of its amino acid sequence identical to a known allergen (egg yolk), the protein is too resistant to break down during digestion and heat. If Bt—toxin causes allergies, then gene transfer carries serious ramifications. If Bt genes relocate to human gut bacteria, our intestinal flora may be converted into living pesticide factories, possibly producing Bt-toxin inside of us year after year.

SAFETY ASPECTS OF GMO FOOD

It has been well discussed whether the consumption of DNA in approved novel foods and novel foods ingredients can be regarded as safe as consumption of DNA in existing form [68]. All DNA, including DNA from GMOs are composed of the same 4 nucleotides. Genetic modification results in the re-assortment of sequences of nucleotides leaving their chemical structures unchanged. Therefore, DNA from GMOs is chemically equivalent to any other DNA. The only uniqueness is restricted to differences in the DNA sequence, which occurs also in natural variations. The present use of recombinant techniques in the food chain does not introduce changes in the chemical characteristics of the DNA. There is no difference in the susceptibility of recombinant DNA and other DNA to degradation by chemical or enzymatic hydrolysis. There are no indications that ingested DNA has allergenic or other immunogenic properties that would be of relevance for consumption of food derived from GMOs. Uptake integration and expression of any residual extracellular DNA fragments from foods by microorganisms of the gastrointestinal tract can not be excluded. Each of these circumstances is a rare event and would have happen sequentially. *In vivo* uptake of DNA fragments by mammalian cells after oral administration has been observed. There are effective mechanisms to avoid genomic insertion of foreign DNA. There is no evidence that DNA from dietary sources has ever been incorporated into the mammalian genome [69] studied the animal nutrition with GMOs. Their conclusions are similar as they from [68].

They didn't find differences in physiological and nutritive values in food of animal's products when the animals are feed with GM plants. Adverse health effects need to be screened for, because health effects are dependent upon the modifications made [68]. Most feeding trials have observed no toxic effects and saw that GM foods were equivalent in nutrition to unmodified foods, although a few reports attribute physiological changes to GM food. However, some scientists [69] and advocacy groups such as Greenpeace and World Wildlife Fund consider that the available data do not prove that GM food does not pose risks to health, and call for additional and more rigorous testing before marketing genetically engineered food [69]. A 2008 review published by the Royal Society of Medicine noted that GM foods have been eaten by millions of people worldwide for over 15 years, with no reports of ill effects [70]. However, a 2009 review in *Nutrition Reviews* found that although most studies concluded that GM foods do not differ in nutrition or cause any detectable toxic effects in animals, some studies did report adverse changes at a cellular level caused by some GM foods, concluding that "More scientific effort and investigation is needed to ensure

that consumption of GM foods is not likely to provoke any form of health problem" [71]. A study published in 2009 found clear negative impact on liver and kidney function in rats consuming GM maize varieties for 90 days [72]. However, if the product has no natural equivalent, or shows significant differences from the unmodified food, then further safety testing is carried out [43]. Worldwide, reports of allergies to all kinds of foods, particularly nuts, fish and shellfish, seem to be increasing, but it is not known if this reflects a genuine change in the risk of allergy, or an increased awareness of food allergies by the public [73]. A 2005 review in the journal *Allergy* of the results from allergen testing of current GM foods stated that "no biotech proteins in foods have been documented to cause allergic reactions" [74].

LEGISLATION AND LABELLING OF TRANSGENIC FOOD

Foods from GMO have already appeared at European market. Hence some methods of identification of these foods have been developed [43,73,74]. Beer, soya oil, tomatoes and its products, potato, maize, and some spices are on the market. Gene transfer has started many contradictory and emotional discussions especially on the German spoken market. Some sound requirements on adequate labeling of the genetically transformed food in EU have been passed so that consumers can choose according to their beliefs (religious, ethic, medical). Therefore EU introduced new system of NOVEL-FOOD classification on May 17, 1997 [73-75]. NOVEL-FOOD has been classified into two groups: (a) Foods that are genetically modified organisms or that contain genetically modified organisms (tomato, yoghurt); (b) Foods that are produced from genetically modified organisms (oil produced from herbicide resistant soya, enzymes, and vitamins) [73-75].

NOVEL-FOOD classification does not enquire any special requirements, it is just a wide assortment of various foods and supplements. The products should be consistently labeled; they should not misguide the consumers and should enable the verification of data. Also other foods that enter the EU market should be properly labeled, for example gene transfer free. The consumer should be informed about the food. New products appear every day, so the legislation is not final. The level of 0.9% of GMO contamination has been set as a threshold for labeling of genetically modified food. All current and future products should be irreproachable to health, environment, ethics and society. In the latest EU legislation EU No. 1829/2003 and 1830/2003 genetically modified food is taken from the Novel-Food Classification. It is classified, together with the feedstuffs made from the genetically modified organisms, as genetically modified products, which have to be declared [73-76].

CONCLUSIONS

The latest development of biotechnology, particularly molecular biology, genetic engineering and transgenic technology has a very large number of potential applications in food production, including micro-organisms, plants and animals. Transgenesis is much more difficult to apply to farm animals than to plants or micro-organisms. Genetic modification has increased production in some crops. But the technology has too few challenges in few crops. Genetic

modification is not a good in itself but it is a tool where public & private science can balance each other. Genetically modified foods have various advantages like high yield, salinity tolerant, insect resistance etc. GM foods have a lot of health effects on living beings. GM foods have both positive and negative effects. These may be either direct effects, on organisms that feed on or interact with the crops, or wider effects on food chains produced by increases or decreases in the numbers of other organisms. As an example of benefits, insect-resistant Bt-expressing crops will reduce the number of pest insects feeding on these plants, but as there are fewer pests, farmers do not have to apply as much insecticide, which in turn tends to increase the number of non-pest insects in these fields. Other possible effects might come from the spread of genes from modified plants to unmodified relatives, which might produce species of weeds resistant to herbicides. Conclusively, the present article is the compilation of various selective studies presenting both positive and negative impacts of GM foods on human health.

ACKNOWLEDGEMENTS

The authors are grateful to Prof. R. M. Dubey (Managing Director) and Prof. A. Srivastav (Director), CET, IFTM Campus, Moradabad, U.P, India) for providing the necessary facilities and encouragement. The author, CV, is a Ph.D. scholar and registered at Uttarakhand Technical University, Dehradun, Uttarakhand, India.

REFERENCES

- [1] Singh RB, Niaz MA. Genetic variation and nutrition, in relation to coronary artery disease. *J Assoc Physicians India* 1999; 47: 1185-90.
- [2] Rodenhiser D, Mann M. Epigenetics and human disease: translating basic biology into clinical applications. *Can Med Assoc J* 2006; 174: 341-8.
- [3] Jones PA, Baylin SB. The epigenomics of cancer. *Cell* 2007; 128: 683-92.
- [4] Trojer P, Reinberg D. Histone, lysine, demethylases and their impact on epigenetics. *Cell* 2006; 125: 213-7.
- [5] Mishra S, Singh RB, Dwivedi SP, *et al.* Effect of Nutraceuticals on Genetic Expressions. *Open Nutra J* 2009; 2: 70-80.
- [6] Ruttloff H, Proll J, Leuchtenberger A. *Lebensmittel Biotechnologie und Ernährung*. Berlin, Springer-Verlag 1997; 121-30.
- [7] Wong RWC, Sham M-H, Lau Y-L, Chan S-Y. An efficient method of generating transgenic mice. *Mol Biotechnol* 2000; 15: 155-9.
- [8] Smolin LA, Grosvenor MB. *Nutrition, Science and Applications*. Fort Worth, Harcourt College Publishers 2000.
- [9] Moellenbeck DJ, Peters ML, Bing JW, *et al.* Insecticidal proteins from *Bacillus thuringiensis* protect corn from corn rootworms. *Nat Biotechnol* 2001; 19(7): 668-72.
- [10] Baum JA, Gilmer AJ, Mettus A-L, Inventors; Monsanto Technology LLC (St. Louis, MO), assignee. Lepidopteran-resistant transgenic plants. United States Patent US 6313378. Nov 2001.
- [11] Salbego J, Pretto A, Gioda, C, *et al.* Herbicide formulation with glyphosate affects growth, acetylcholinesterase activity, and metabolic and hematological parameters in piava (*Leporinus obtusidens*). *Arch Environ Contamin Toxicol* 2010; 58(3): 740-5.
- [12] Ohkawa H, Tsujii H, Ohkawa Y. The use of cytochrome P450 genes to introduce herbicide tolerance in crops: a review. *Pestic Sci* 1999; 55(9): 867-74.
- [13] Dahleen LS, Okubara PA, Blechl AE. Transgenic approaches to combat fusarium head blight in wheat and barley. *Crop Sci* 2001; 41(3): 628-37.
- [14] Scorza R, Callahan A, Levy L, Damsteegt V, Webb K, Ravelonandro M. Post-transcriptional gene silencing in plum pox virus resistant transgenic European plum containing the plum pox potyvirus coat protein gene. *Transgenic Res* 2001; 10(3): 201-09.
- [15] Kenward KD, Brandle J, Mc Pherson J, Davies PL. Type II fish antifreeze protein accumulation in transgenic tobacco does not confer frost resistance. *Transgenic Res* 1999; 8(2): 105-17.

- [16] Zhang HX, Blumwald E. Transgenic salt-tolerant tomato plants accumulate salt in foliage but not in fruit. *Nat Biotechnol* 2001; 19(8): 765-8.
- [17] Tang W. Peroxidase activity of desiccation-tolerant loblolly pine somatic embryos. *In Vitro Cell Dev Biol Plant* 2000; 36(6): 488-91.
- [18] Paine JA, Shipton CA, Chaggar S, *et al.* Improving the nutritional value of Golden Rice through increased pro-vitamin A content. *Nat Biotechnol* 2005; 23: 482-7.
- [19] Daniell H, Streatfield SJ, Wycoff K. Medical molecular farming: production of antibodies, biopharmaceuticals and edible vaccines in plants. *Trends Plant Sci* 2001; 6(5): 219-26.
- [20] Perr HA. Oral immunization with hepatitis B surface antigen expressed in transgenic plants. *Proc Natl Acad Sci USA* 2001; 98(20): 11539-44.
- [21] Ahmed M, Focht DD. Phytodetoxification of hazardous organo-mercurials by genetically engineered plants. *Nat Biotechnol* 2000; 18(2): 213-17.
- [22] Nordlee JA, Taylor SL, Townsend JA, *et al.* Identification of a Brazil-nut allergen in transgenic soybeans. *N Engl J Med* 1996; 334(11): 688-92.
- [23] Hartmann B, Subramanian B, Zerner C. Effect of diets containing genetically modified potatoes expressing *Galanthus nivalis* lectin on rat small intestine. *Lancet* 1999; 354(9187): 1353-4.
- [24] Mitchell P. Safety of genetically modified food questioned: Interview with gene scientist, Dr Arpad Pusztai (<http://www.wsws.org/articles/1999/jun1999/gmo-j03.shtml>)
- [25] Naranjo S. Impacts of Bt crops on non-target invertebrates and insecticide use patterns. *CAB Reviews: Perspectives in Agriculture, Veterinary Science, Nutr Nat Resour* 2009; 4: 1-11.
- [26] Cephin S, Cephin N, Salobeir KV. Possibilities and dilemmas of using transgenic food in human nutrition. *Acta Agric Sloven* 2004; 1: 105-11.
- [27] Prieto PA, Kopchick JJ, Kelder B. Transgenic animals and nutrition research. *J Nutr Biochem* 1999; 10: 682-95.
- [28] Manjunath TM. Bt cotton in India: The technology wins as the controversy wanes 2004. <http://www.monsanto.co.uk/news/ukshowlib.html?wid=8478>.
- [29] Rai M, Acharya SS, Virmani SM, Aggrawal PK. State of Indian Agriculture. National Academy of Agricultural Sciences, New Delhi 2009.
- [30] Kumar PA, Sharma RP, Malik VS. Insecticidal proteins of *Bacillus thuringiensis*. *Adv Appl Microbiol* 1996; 42: 1-43.
- [31] James C. Global Status of Commercialized Biotech/GM Crops. ISAAA Briefs No. 39. International Service for the Acquisition of Agri-Biotech Applications. Ithaca, NY 2008.
- [32] Gupta K, Karihaloo JL, Khetarpal RK. Biosafety Regulations in Asia-Pacific Countries. Asia-Pacific Association of Agricultural Research Institutions, Bangkok; Asia-Pacific Consortium on Agricultural Biotechnology, New Delhi and Food and Agricultural Organization of the United Nations, Rome 2008.
- [33] Glare TR, O'Callaghan M. *Bacillus thuringiensis*: Biology, Ecology and Safety. Wiley, New York 2000.
- [34] Betz FS, Hammond BG, Fuchs RL. Safety and advantages of *Bacillus thuringiensis* protected plants to control insect pests. *Regul Toxicol Pharm* 2000; 32: 156-73.
- [35] OECD. Organization for Economic Co-operation and Development. Consensus document on safety information on transgenic plants expressing *Bacillus thuringiensis* derived insect control proteins; Paris 2007.
- [36] Lemaux PG. Genetically engineered plants and foods: A scientist's analysis of the issues. *Annu Rev Plant Biol* 2008; 59: 771-812.
- [37] Clark BW, Phillippe TA, Coates JR. Environmental fate and effects of *Bacillus thuringiensis* (Bt) protein from transgenic crops: a review. *J Agric Food Chem* 2005; 53: 4643-53.
- [38] Romeis J, Meissle M, Bigler F. Transgenic crops expressing *Bacillus thuringiensis* toxins and biological control. *Nat Biotechnol* 2006; 24: 63-71.
- [39] Marvier M, McCreedy C, Regetz J, Kareiva P. A meta-analysis of effects of Bt cotton and maize on non-target invertebrates. *Science* 2007; 316: 1475-7.
- [40] Babendreier D, Reichhart B, Romeis J, Bigler F. Impact of insecticidal proteins expressed in transgenic plants on bumblebee microcolonies. *Entomol Exp Appl* 2008; 126: 148-57.
- [41] Chen M, Zhao JZ, Collins HL, *et al.* A Critical Assessment of the Effects of Bt Transgenic Plants on Parasitoids. *PLoS One* 2008; 3(5): e2284.
- [42] Lawo NC, Wackers FL, Romeis J. Indian Bt cotton varieties do not affect the performance of cotton aphids. *PLoS One* 2009; 4(3): e4804.
- [43] Magaña-Gómez JA, de la Barca AM. Risk assessment of genetically modified crops for nutrition and health. *Nutr Rev* 2009; 67(1): 1-16.
- [44] Irina Ermakova. Experimental Evidence of GMO hazards. Presentation at Scientists for a GM Free Europe, EU Parliament, Brussels, June 12, 2007.
- [45] Conservation and survey division, genetic engineering approval committee. Decision taken in the 97th meeting of the GEAC held on 14th October, 2009 [Internet]. Ministry of Environments and Forest 2009 Oct 14 [cited 2009 Nov 27]. Available from: <http://www.envfor.nic.in/divisions/csurv/geac/information.html>
- [46] Menon S. Experts' panel approves Bt brinjal, final okay now with Jairam. *Business Standard* [Internet]. 2009 Oct 15 [cited 2009 Nov 27]. Available from: <http://www.business-standard.com/india/news/experts/-panelapproves- bt-brinjal-final-okay-nowjairam/373318>
- [47] Berkowitz DB. The food safety of transgenic animals: Implications from traditional breeding. *J Anim Sci* 1993; 71: 43-6.
- [48] Kappes SM. Utilization gene mapping information in livestock animals. *Theriogenology* 1999; 51: 135-47.
- [49] Bonneau M, Laarveld B. Biotechnology in animal nutrition, physiology and health. *Livest Prod Sci* 1999; 59: 223-41.
- [50] Prieto PA, Kopchick JJ, Kelder B. Transgenic animals and nutrition research. *J Nutr Biochem* 1999; 10: 682-95.
- [51] Mason HS, Ball IM, Shi JJ, Jiang X, Estes MK, Arntzen CJ. Expression of Norwalk virus capsid protein in transgenic tobacco and potato and its oral immunogenicity in mice. *Proc Natl Acad Sci USA* 1996; 93: 5335-40.
- [52] Remy JJ, Counture L, Rabesona H, Haertle T, Salesse R. Immunization against exon 1 decapeptides from the lutropin/choriogonadotropin receptor or the follitropin receptor as potential male contraceptive. *J Reprod Immunol* 1996; 32: 37-54.
- [53] Solomon MB, Pursel VG, Paroczay EW, Bolt DJ. Lipid composition of carcass tissue from transgenic pigs expressing a bovine growth hormone gene. *J Anim Sci* 1994; 72: 1242-6.
- [54] Wilson A, Latham JR, Steinbrecher RA. Transformation - induced mutations in transgenic plants: Analysis and biosafety implications. *Biotechnol Genet Eng* 2006; 23: 105-9.
- [55] Netherwood T, Martín-Orúe SM, O'Donnell AG, *et al.* Assessing the survival of transgenic plant DNA in the human gastrointestinal tract. *Nat Biotechnol* 2004; 22: 204-9.
- [56] Department of Veterinary Medicine, FDA, correspondence June 16, 1993. As quoted in Fred A. Hines, Memo to Dr. Linda Kahl. "Flavr Savr Tomato..... Pathology Branch's Evaluation of Rats with Stomach Lesions From Three Four - Week Oral (Gavage) Toxicity Studies... and an Expert panel's Report." Alliance for Bio- Integrity (June 16, 1993) <http://www.BioIntegrity.org/FDAdoes/17/view1.html>
- [57] Pusztai A. Genetically Modified Foods: Are They a Risk to Human/Animal Health? Action Bioscience 2001. www.Actionbioscience.org/biotech/pusztai.html.
- [58] Fares NH, El-Sayed AK. Fine structural changes in the ileum of mice fed on endotoxin treated potatoes and transgenic potatoes. *Nat Toxins* 1998; 6: 219-33.
- [59] Pusztai A. Can science give us the tools for recognizing possible health risk of GM? *Nutr Health* 2002; 16: 73-84.
- [60] Tudisco R, Lombardi P, Bovera F, *et al.* Genetically Modified Soya Bean in Rabbit Feeding: Detection of DNA fragments and evaluation of metabolic effects by enzymatic analysis. *J Anim Sci* 2006; 82: 193-99.
- [61] John MB. 13-week Dietary Subchronic Comparison study with Mon 863 Corn in rats Preceded by a 1-week Baseline Food Consumption Determination with PMI Certified Rodent Diet#5002, December 17, 2002.
- [62] Malatesta M, Biggiogera M, Manuali E, *et al.* Fine structural analyses of pancreatic acinar cells nuclei from mice fed on GM soybean. *Eur J Histochem* 2003; 47: 385-88.
- [63] Vecchio L, Cisterna B, Malatesta M, Martin TE, Biggiogera M. Ultrastructural analysis of tests from mice fed on genetically modified soybean. *Eur J Histochem* 2004; 48: 449-54.
- [64] Oliveri *et al.* Temporary Dpression of Transcription in mouse Pre-implantation Embryos from mice fed on Genetically Modified

- Soybean, 48th Symposium of the Society for histochemistry, Lake Maggiore (Italy), September 7-10, 2006.
- [65] Prescott VE, Campbell PM, Moore A, *et al.* Transgenic Expression of Bean α -Amylase Inhibitor in Peas Results in Altered Structure and Immunogenicity. *J Agric Food Chem* 2005; 53: 176-88.
- [66] Dutton A, Klein H, Romeis J, Bigler F. Uptake of Bt-toxin by herbivores feeding on transgenic maize and consequences for the predator *Chrysoperla carnea*. *Ecol Entomol* 2002; 27: 441-7.
- [67] Romeis J, Dutton, Bigler F. *Bacillus thuringiensis* toxin (Cry 1 Ab) has no direct on larvae of the green lacewing *Chrysoperla carnea* (stephens) (Neuroptera: Chrysopidae). *J Insect Physiol* 2004; 50: 175-83.
- [68] Jonas DA, Elmadfa I, Engel KH, *et al.* Safety considerations of DNA in food. *Ann Nutr Metab* 2001; 45: 235-54.
- [69] Flachowsky A, Aulrich K. Lebensmittel tierischer Herkunft nach Einsatz von Futtermitteln aus gentechnisch veränderten Pflanzen (GVP). *Ernährungs-Umschau* 2002; 49: 84-93.
- [70] Seralini GE, Cellier D, Spiroux de Vendomois J. New analysis of a rat feeding study with a genetically modified maize reveals signs of hepatorenal toxicity. *Arch Contamin Environ Toxicol* 2007; 52: 596-602.
- [71] Le Curieux-Belfond O, Vandelaer L, Caron J, Seralini G E. Factors to consider before production and commercialization of aquatic genetically modified organisms: the case of transgenic salmon. *Environ Sci Policy* 2009; 12: 170-89.
- [72] Key S, Ma JK, Drake PM. Genetically modified plants and human health. *J R Soc Med* 2008; 101(6): 290-8.
- [73] de Vendômois, Joël Spiroux, Roullier F, Cellier D, Seralini GE. A Comparison of the effects of three GM corn varieties on mammalian health. *Int J Biol Sci* 2009; 5: 706-26.
- [74] Safety Evaluation of Foods Derived by Modern Biotechnology: Concepts and Principles. Organisation for Economic Co-operation and Development. http://www.agbios.com/docroot/articles/oeed_fsafety_1993.pdf. Retrieved 21 June 2009.
- [75] Kuehn BM. Food allergies becoming more common. *JAMA* 2008; 20: 2358.
- [76] Lehrer SB, Bannon GA. Risks of allergic reactions to biotech proteins in foods: perception and reality. *Allergy* 2005; 60(5): 559-64.

Received: September 16, 2010

Revised: November 26, 2010

Accepted: November 27, 2010

© Verma *et al.*; Licensee *Bentham Open*.

This is an open access article licensed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/3.0/>) which permits unrestricted, non-commercial use, distribution and reproduction in any medium, provided the work is properly cited.