GM crops: Rationally irresistible

Syamal Krishna Ghosh

Genetically modified (GM) crops have a great role to play in Indian agriculture, when we need more from lesser resources. The transgenics have the potentiality to resist biotic and abiotic stresses and result in increased productivity in addition to better nutritional quality. The hue and cry on the impact of GM crops on biodiversity has created hype regarding economic, social and ethical concerns. Though several workers have contradicted the fears expressed regarding the risks and hazards of GM crops, concerns on the safety of GM foods are still creating controversies. India must avoid taking extreme decisions and has to develop a symbiotic relationship between the public and private sectors, to use new technological inputs to complement the traditional methods for making an ‘Evergreen Revolution’.

Since a long time, the plant breeders have been developing new crop varieties by using the existing genetic variability through crossing diverse genotypes. In conventional breeding, incompatibility and species difference is the main barrier for gene transfer. Genetic modification technology has made possible the insertion of desired foreign gene(s) and helped in overcoming incompatibility and species barriers. This genetic modification technique is known as genetic engineering (GE) and the outcome is a transgenic/genetically modified (GM) product.

If Indian economy has to grow at 7% per annum and also if the export base has to be expanded, the value of agricultural output must increase at an annual rate of 4.5% between 1997 and 2002, which was about 2.77% during the period 1980 to 1994 (ref. 1). The productivity level in India is below the global average for most of the crops. According to Norman E. Borlaug, 93% of the increased food production has to come from increased productivity per unit land in increasingly complex circumstances. The topic of food ‘security’ and ‘sufficiency’ is much discussed. To meet the growing demands of the population, a steady yield improvement is essential for all food crops. Food security is not only associated with the higher production, but also its availability and access to the lower-income group without deprivation.

In order to increase yield or to keep the present rates of genetic gains achieved, new breeding strategies have to be developed to widen the genetic base. The biotechnological advances in agriculture, such as transgenic crops, are expected to be major players in food production in the future. Major concerns are huge investments and economic and social concerns. A report from the International Rice Research Institute (IRRI)2 has stated that the cost of molecular breeding is only $2 per plant, while that of traditional breeding is $30. According to J. Crouch2 of International Crop Research Institute for Semi-Arid Tropics (ICRISAT), Hyderabad the figure for molecular breeding is close to $4. The governments of both developing and developed countries have identified biotechnology as a promising and key research area, with widespread applications in diverse fields of agriculture3,5, industrial products,7 healthcare,8 and environmental management5,10.

Global GM crop area has increased within a very short span from 1.7 m ha (1996) to 44.2 m ha (2000) (see Table 1)11. The area under GM crops in 1999 has increased by 44% compared to total GM crop area of 1998. In 2000, the global GM crop area increased by 11% compared to that in 1999. Global market for GM products has grown rapidly from $75 million in 1995 to $2.1–2.3 billion in 1999 and is projected to reach approximately $3 billion in 2000 and $8 billion by 2005 (ref. 12). Globally, 3647 field trials of GM crops were conducted, out of which 796 were in Western Europe13 and the rest in USA, Canada, Latin America and Asia14.

As expansion of transgenic crops continues, a shift will occur from the current generation of ‘input’ agronomic traits to the next generation of ‘output’ quality traits to satisfy high value-added market. In India, the GE technology should not be followed with the same goals as in the West, but it should be applied to our problems where conventional breeding has not succeeded. We must find ways of realizing the promise, while avoiding pitfalls like issues concerning IPR, ethics and safety.

Issues and concerns

Despite the promises of the genetically modified organisms (GMO), it is thought that it may be harmful to
public health and environment. The concerns raised on these aspects are as follows:

- GM crops are a threat to environment and biosafety.
- GM crops themselves may become weeds and wild population leading to ‘superweeds’.
- They may lead to adverse allergic reactions to human beings.
- Antibiotic resistance gene in GMO may lead to development of resistance to the antibiotics used to treat human and animal diseases.
- It may disturb the ecosystem by eliminating the natural populations/biotic communities, by altering nutrient cycles due to introduction of certain microbes and plants.
- It may aggravate the genetic uniformity, vulnerability to diseases and narrow down the genetic diversity.
- Dependence of farmers on multinational companies.

**Effect on biodiversity**

Biotechnology has the potential to help society to solve serious problems of malnutrition through golden rice, nutritionally-improved potatoes, etc. but the new technology has to be assessed properly regarding its effects on the flora and the fauna. The impact of GM crops in developing countries has not been studied extensively in relation to the risks involved. Concerns regarding the possible effect of transgenics on biodiversity are probably raised because of lack of understanding of modern commercialized agriculture. GM crops may affect the stability and diversity of an eco-system, but it is the trait or acquired property which interacts with the environment that determines the potential impact, but not the transgenic plant per se.

Several authors have examined environmental aspects and biosafety of transgenic plants. The concerns that GM crops themselves become weeds and may lead to wild weed population and ‘superweeds’ is contradicted by Crawley and coworkers, who concluded from their experiments that GM crops are less persistent than their conventional counterparts and are less invasive. Hence, the fear of loss of entire biodiversity needs further critical examination. Experiments with transgenic rapeseed for gene flow indicated that such events are probably infrequent and appear to be strongly influenced by the genotype of the plants. Mcpartlan and Dale reported that the extent of gene flow from transgenic to non-transgenic potato depends on the distance between them. In the past, several exotic species like *Triticale* (a cross between durum wheat and rye) and *Trifolium* (a cross between wheat and oat) released for cultivation, where these risks prevailed, did not result in such controversies. The main component of gene flow is the out-crossing rate. But it is reported that even in highly self-pollinated crops, interspecies out-crossing takes place to some extent. Langen on reported reported 1–52% hybrid seed set, in weedy red rice growing sympathetically with the cultivated rice in Louisiana. Therefore, the chance of gene flow cannot be ruled out, both for conventional and GE breeding methods.

Weediness could be a matter of concern when the herbicide resistance genes flow and get introduced into wild relatives of the crop. The escape of transgene providing pest resistance to wild relatives may not have serious environmental problems, as genes for resistance are often found in wild relatives. As the gene flow from herbicide-resistant GM crops has serious implications in wild populations, there is a need to search for ways to reduce its escape from GM to wild weedy species. Interspecies gene flow is extremely low and depends on the presence of a large population of related species in the centre of diversity. Gene flow from a GM crop would depend on the mode of reproduction, rate of out-crossing, sexual compatibility, proximity with wild relatives and relative fitness of crop–weed hybrid. In case of self-pollinated crops the extent is less than 5%, whereas in cross-pollinated crops, it is up to 50% and in case of wild and weedy relatives, the gene flow is extremely less (<1%). Assessment of realistic risk for gene transfer through pollen is available for many regions and agriculturally sound procedures need to be developed for different regions.

**Health hazards**

Presence of *Bt* gene in GM crops has not lead to adverse effects in higher animals, including mammals. There were no major changes in the chemical composition of GM tomato fruits and they did not pose any risk to human and animal health. No statistically significant differences in survival or body-weight have been observed in broilers reared on meshed diets prepared with transgenic and control maize. Food safety studies of *Bt*-cotton for seeds, oil and cake have shown that *Bt*-cotton is safe for ruminants, birds, mammals, fish or to beneficial insects. Seeds from the *Bt*-cotton line are compo-
sitionally equivalent to and are as nutritious as the seeds from the other commercial cotton varieties\textsuperscript{31}. Antibiotic resistance gene, the basic requirement for selection of transgenics in laboratory as selectable markers, also raised concerns regarding its biosafety on human and animal health. Experiments conducted on this aspect have provided evidence that the presence of marker genes and gene products does not impose any risk to human health or environment\textsuperscript{32,33}. Nowadays, methods\textsuperscript{34} are available to inactivate the marker and for transformation without selectable markers.

Monarch butterflies, the delicate orange-black-winged ‘flying jewellery’ were reported to be killed by the pollen of GM corn hybrid. Studies conducted on these butterflies, by feeding them exclusively on the pollen of GM corn pollen grains, showed that the situation is different. In USA, through GM corn occupies a majority of the corn areas, a bumper crop of monarch butterflies was observed, which defies the earlier information\textsuperscript{35}. The effect of a diet containing GM potatoes (for insect resistance) expressing snowdrop lectin on rats\textsuperscript{36}, resulted in media publicity causing worldwide public concern. Lectins are a group of proteins which bind to specific sugar moieties on body tissues. Lectins as such, are found\textsuperscript{37} in most of the food stuffs and tubers like cereals, beans, potatoes, etc. Boiling of the food stuffs causes loss of lectin activity\textsuperscript{37}. GM crops are expected to be resistant to insects like aphids, leaf and plant hoppers. Lectins being highly resistant to digestion also suppress immune system and are reported to cause allergic reactions. To test the toxicity of GM crops to mammal systems, a trial was conducted by the team headed by Pusztai. The experiment showed that rat intestine was affected if fed with GM potatoes continuously for 110 days. On the other hand, experiments by Gatehouse (who developed the GM potato) did not show that GM potatoes stunted the growth and damaged the immune system of rats. Investigations made on the issue found that Pusztai went public about his views before complete and consistent data were available from his experiment\textsuperscript{37}. This episode clearly represents misinformation of scientific facts to the public and the consequences are the concerns on the safety of GM foods.

John Heritage and his associates (UK)\textsuperscript{38} reported that GM maize with \textit{bla} gene confers resistance to European corn borer by producing toxin. So far they have not been able to get any bacteria to pick up and activate \textit{bla}, which confers resistance to ampicillin. EuropaBio\textsuperscript{39}, the European Association for Bioindustries, has reported that insect-resistant crops are beneficial for both agriculture and the environment.

Effect on non-target organisms

One of the major concerns of GM crops is their effect on non-target organisms. \textit{Bt} proteins affect the stomach of vertebrates; however there is a chance of affecting beneficial insects, although such effects are less severe\textsuperscript{38} compared to those of broad-spectrum insecticides. Field experiments showed that \textit{Bt}-cotton\textsuperscript{40} and GM tobacco\textsuperscript{41} did not affect the natural enemies and predator insects. The incidence and dynamics of natural enemies in \textit{Bt} and non-\textit{Bt} fields have been observed to be almost the same\textsuperscript{42}. Even the GM crops with trypsin inhibitor and wheat germ agglutinin did not show acute toxicity to honey bee\textsuperscript{43}. Proteinase inhibitor gene in GM soybean\textsuperscript{44} does not produce any harmful effects in honey bees. But trypsin endopeptidase inhibitors and soybean trypsin inhibitors are found to be toxic\textsuperscript{45} to adult honey bees. GM rapeseed does not appear to have any harmful effect on the lifespan and behaviour of honeybees\textsuperscript{46}, but further tests may be necessary to come to a conclusion.

GM vs non-GM crops

To protect the non-GM crops from dreaded insect pests and diseases requires more spraying compared to that for GM crops. The major problems arise because of continued and over usage of chemicals and persistence of pesticide residues in foodstuffs\textsuperscript{47,48}, pollution of underground water\textsuperscript{49}, alteration in the beneficial organisms\textsuperscript{50}, development of resistance among pests\textsuperscript{51} and harm to non-target organisms\textsuperscript{52}. The toxic residues due to pesticides and herbicides in foodstuffs, affect the central nervous, respiratory and the gastro-intestinal systems of human beings\textsuperscript{53} causing depression, insomnia, oral automatism and hyper-reflexia leading to health hazards. Reports are also available on the presence of toxic residues due to chemicals on birds\textsuperscript{54} and aquatic organisms\textsuperscript{55}. From Table 2 it is clear that Indians take about 40 times more pesticides through food items than the average American’s intake. Generally, the tolerance limit for DDT is 12.5 mg/day/person, though it varies according to pesticides\textsuperscript{57}.

<table>
<thead>
<tr>
<th>Country</th>
<th>Average dietary intake (mg/day/person)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>DDT complex</td>
</tr>
<tr>
<td>Australia</td>
<td>20.0</td>
</tr>
<tr>
<td>Canada</td>
<td>10.8</td>
</tr>
<tr>
<td>Germany</td>
<td>149.0</td>
</tr>
<tr>
<td>UK</td>
<td>12.0</td>
</tr>
<tr>
<td>USA</td>
<td>6.5</td>
</tr>
<tr>
<td>Yugoslavia</td>
<td>98.0</td>
</tr>
<tr>
<td>India: Vegetarians</td>
<td>238.1</td>
</tr>
<tr>
<td>Non-vegetarians</td>
<td>224.1</td>
</tr>
</tbody>
</table>

Source: Awasthi\textsuperscript{42}.
GENERAL ARTICLES

Worldwide, pesticides account for about 3 million cases of acute poisoning with 220,000 deaths/year (ref. 56). Apart from inducing cancer, a large number of pesticides have been reported to reduce the immune system’s ability to deal with infectious agents. This is important, especially in developing countries where infectious diseases account for the majority of deaths and at least 2 billion people living and working in farming areas are exposed to pesticides. Moreover, cases of blindness, cancer, deformities, diseases of liver and nervous system from pesticide poisoning have been identified in the cotton-growing districts of Andhra Pradesh and Maharashtra. Continuous use of pesticides also results in developing resistance in the pests, which thereby become difficult to be controlled by other means. Currently, more than 500 species of insects show resistance to one or more chemicals and few serious pests resist nearly all the poisonous pesticide chemicals.

In case of GM crops also, the evolution of new insect biotypes is another area of concern. However, there is no direct relationship between the deployment of insect-resistant cultivars and the evolution of new insect biotypes. Tabashnik reported that 10 species of moth, 2 species of beetle and 4 species of flies have evolved resistance against Bt toxin under laboratory conditions, but it was confirmed that there has been no sign of any bollworm species showing resistance to GM crops. Plant breeders incorporate new resistance genes, while insects and pathogens for their survival, as mechanisms to overcome the resistance. So in this case also the chance cannot be avoided and it does not mean that resistant varieties will not be bred, accepted and cultivated.

Transgenic plants are engineered for the promise of pest resistance and the major breakthrough has been the inclusion of Bt toxin gene, cowpea trypsin inhibitor or secondary metabolites. Field experiments showed that the performance of transgenic Bt-cotton varieties was the same as other cotton varieties, except for high resistance to bollworm and bud worm and an average of 70% less chemical insecticide use than for conventional cotton varieties. Herbicide-tolerant soybean in USA resulted in reduced herbicide requirements by 20% (ref. 62), better control of weeds, no carryover of herbicide residues and much more flexibility in agronomic management of the crop. A study in USA showed that agribio-tech can bring down insecticide spraying by 80%, herbicide use by 20%, and can increase biodiversity in the soil.

Organic food – Is it safe?

The hue and cry that GM food is not safe for consumption is creating a public furore. On the other hand, there is a campaign for organic foods. How far is organic food safe for consumption? The myth about organic food is that it is devoid of carcinogenic compounds, but the plants have natural toxins to protect themselves and these natural toxins are highly carcinogenic at high doses. Toxicologists have reported that higher levels of natural toxins are present when the crops are raised by organic farming. Even crops grown using organic manure are highly dangerous, as the manure is a natural habitat for bacteria like E. coli, Salmonella, etc. which can infect the plant tissue. A study among the Americans consuming organic or natural food products showed eight times greater risk of contracting the deadly E. coli. Several self-defensive substances made by plants are highly toxic to mammals and in such cases the source of the transgene is of no relevance in assessing the toxicological aspects of foods from GM plants. According to Prakash, gene revolution is far more environment-friendly compared to its predecessor the ‘Green Revolution’.

Can GM crops benefit the farmers?

This technology will encourage the private sector for research on the so-called ‘forgotten crops’ and traditional open-pollinated varieties and pure lines. It will also stimulate a diverse and competitive marketplace for improved varieties of seeds for farmers to choose from. According to one estimate, growing of Bt-cotton in India in about 25% area with 20% increased yield will provide a competitive edge to the Indian cotton-farmer. From the field experiments conducted in India for Bt-cotton, it was found that there was an increase in the productivity ranging from 26 to 60% in 1998 and 29 to 88% in 1999 (ref. 30). Extensive field trial data in USA have shown that yield with Bt-maize hybrids is 10 to 15% higher than that of corresponding conventional maize hybrids.

A study in USA showed that Bt resulted in insecticide savings by as much as US $140 to 280/ha in 1996 and 70% of the Bt-cotton area required no insecticide spraying. In 1997, the total benefit was $190.1 million on planting Bt-cotton, out of which the US farmer’s share was 42%, Monsanto received 35% and the rest of the world, 23% of the total economic benefit. An annual loss of US $1 billion was estimated using European corn borer, but by using borer-resistant Bt-maize, the benefits were estimated at US $19 million in 1996 and US $190 million in 1997. James reported that insect-resistant Bt-potatoes in USA resulted in effective control of Colorado beetle during 1996.

Bioremediation – An answer to agricultural pollution

The process of cleaning toxic pollutants and heavy metals contamination from the soil and groundwater by
using plants is called phytoremediation and use of microorganisms for removing hazardous toxic pollutants from the soil and groundwater is known as bioremediation. This technology is also called ‘green’ technology. In the process of phytoremediation, plants exclude toxicants, extract and store them in their body or convert them into volatile form that can be released into the air. The use of plants for their own support system offers a cheap, renewable and promising method for sustainable development. Thlaspi caerulescens is a hyperaccumulator plant for cadmium. Bacteria, fungi, algae, lichens and higher plants also play an important role in improving the quality of the environment. Agriculturally-important plants like Brassica juncea, also do a good job in cleaning the contaminated soil and water by detoxifying them. Pesticide bioremediation of soil and water is also possible by rhizobacteria and plants, which act on the dissipation and biotransformation of pesticide contamination from the soil and water.

Advances in GE also opened ways to enhance the biodegradable and reclamation abilities of naturally-occurring microorganisms, higher plants and incorporation of these useful genes in agricultural field crops. Poplar tree engineered genetically with bacterial mercuric reductase (mer) gene A and mer B, can detoxify mercury from contaminated sites. In Indian mustard, Young and coworkers introduced the E. coli gene, gsh II. The transgenic mustard is reported to have very fast biomass accumulation leading to accumulation of 40–90% higher cadmium concentration in the transformed shoots. This ‘green’ technology will not only help farmers to grow crop on acidic soils, but could also be used by environmentalists and industries to clean-up the toxic metal-contaminated sites.

Indian context

Now Europe’s demand for organic food and boycott of GM food is more worrying for developing countries, as it affects the acceptance of GM crops. It is not that organic farming should be discouraged, but at the same time new technologies should also be incorporated for agricultural development, as developing countries can barely feed their populations. However, it would be less destructive in Europe, where over-production is common. Therefore, the consumers should be well-informed regarding the risks associated with both the organic and GM food products. Consumer research conducted during 1996–97 reported that approximately 65–70% of European consumers support biotechnology and are willing to accept food enhanced by GE. In the European Union, objection was raised by the Green Peace and according to the President of RFF, the opposition is to possible domination of the food chain by American companies.

Modern biotechnology is rather new to India and its application would increase as the products show the potential to provide better solutions to health problems, improve the quality of life, increase agricultural productivity and produce cheap industrial bio-products.

Conclusion

In the new millennium, biotechnology may play the pivotal role for developing countries with respect to food and nutritional security. It may have negative effects like substitution of indigenous technologies, industrialization of agriculture and privatization of knowledge and technology. In fact, genetic manipulation has been going on for hundreds of years and genetically altered antibiotics, vaccines and vitamins have improved our health and oil-eating bacteria have helped to protect the environment. Now biotechnology is the only alternative available to cope up with the burgeoning population. The tools of biotechnology offer both challenges and opportunities for growth and development of mankind. These technologies should be used to complement the traditional methods for enhancing productivity and quality, rather than to replace the conventional methods.

To adopt these technologies, GM crops and their products, awareness has to be created among the farming and consumer communities regarding their benefits and effects on human life, by the scientific communities and national leaders. It is neither wise to denigrate a technology itself nor to consider it as an universally-accepted one, but assessment should be made on a case-by-case basis.

Note: The views expressed in this article are personal and not related to the organization.

Alpha-terthienyl: A plant-derived new generation insecticide

Manish Nivsarkar*, Bapu Cherian and Harish Padh

Department of Pharmacology and Toxicology, B. V. Patel Pharmaceutical Education and Research Development Centre, Thaltej Gandhinagar Highway, Thaltej, Ahmedabad 380 054, India

Alpha-terthienyl, a naturally occurring secondary plant metabolite is found in abundance in the roots of Tagetes species (family Asteraceae). It is activated by ultraviolet light and is toxic to a number of insect species. It generates oxygen radical species and has capacity to inhibit several enzymes like both in vivo and in vitro. Alpha-terthienyl possesses all the desirable properties of a good insecticide/pesticide. It is fast acting, non-toxic, economic and a property of degradation makes it more user friendly and safe. Secondary plant metabolites will play an important role in future insecticide development programme.

Man has suffered from the activities of mosquito since time immemorial. It is believed that mosquitoes rank as man’s most important insect pest. They influenced and still influence his selection of living and working sites. They scourge him with their vicious biting attacks and continuous singing, but more serious are the diseases that they transmit to man and his pets (Table 1).

Synthetic insecticides such as organochlorines, organophosphorous, carbamates, synthetic pyrethroids, etc. are commonly used to control these pests. Consumption of these insecticides/pesticides is very high, specially in India (Figure 1).

The greatest harm from chemical insecticides is that, once introduced into the system, they may remain there forever or for a very long duration. Thus they pose a threat to life and help insects to develop resistance against them. This is the reason there has always been a need for such an insecticide which is more powerful, with lesser side effects and degrading after sometime, reducing the chance to develop resistance against it. Scientists are now accepting the fact that such resistance is inevitable and that it is just matter of time before all pesticides are neutralized by some adaptive mechanism of the pests. The exact impact of these residues is not known, but tests conducted on the affected animals show frightening evidence of genetic defects and cancer.

Plant-derived insecticides

Plants have always been a rich source of chemicals and drugs for man. During the 20th Century, a few of these natural compounds like nicotine, rotenone and pyrethrins have been used commercially as insecticides. However, plants produce thousands of other compounds that are insecticidal and have diverse modes of action like hormonal, neurological, nutritional or enzymatic. Phototoxins are unique among these plant compounds in that their toxicity is greatly increased when irradiated with light.

A number of plant families are known to produce alkaloids, phenolics and oils which have been used for insect control since a long time. They were called as insect killers and were used by Romans and Chinese. Another group of plant products discovered in the last two decades are known as secondary plant metabolites. These were considered as waste products from plants for a long time, because they were of no nutritional significance to insects. These secondary plant metabolites having insecticidal/pesticidal properties are of several types, viz. repellents, antifeedants, phagostimulants and toxins.

Secondary plant metabolites

The plant family which is important in producing such secondary plant metabolites is Asteraceae, which has been considerably exploited to extract phototoxic com-

<table>
<thead>
<tr>
<th>Disease</th>
<th>Vector</th>
<th>Host</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malaria (several kinds)</td>
<td>Anopheles species</td>
<td>Humans, monkeys, birds</td>
</tr>
<tr>
<td>Yellow fever</td>
<td>Aedes aegypti and other sp.</td>
<td>Humans, monkeys</td>
</tr>
<tr>
<td>Filariasis</td>
<td>Anopheles and Aedes</td>
<td>Humans, dogs, wild carnivores</td>
</tr>
<tr>
<td>Dengue fever</td>
<td>Aedes and Culex</td>
<td>Humans</td>
</tr>
<tr>
<td>Encephalitis</td>
<td>Aedes and Culex</td>
<td>Humans</td>
</tr>
<tr>
<td>Equine encephalitis</td>
<td>Aedes</td>
<td>Horses</td>
</tr>
</tbody>
</table>

*For correspondence. (e-mail: manishnivsarkar@yahoo.com)