Genetically Modified Foods: Are They a Risk to Human/Animal Health?

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articlehighlights

Genetically modified (GM) crops and food are being grown and consumed by the public, even though:

- *there is little scientific study about their health risks*
- *safety test technology is inadequate to assess potential harm*
- *they can carry unpredictable toxins*
- *they may increase the risk of allergenic reactions*

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Scarcity of safety tests

How can the public make informed decisions about genetically modified (GM) foods when there is so little information about its safety? The lack of data is due to a number of reasons, including:

Information is scarce about health hazards, such as toxicity in genetically modified (GM) crops.

Soybeans were genetically engineered to make them herbicide resistant. Photo: Scott Bauer.

- It's more difficult to evaluate the safety of crop-derived foods than individual chemical, drug, or food additives. Crop foods are more complex and their composition varies according to differences in growth and agronomic conditions.
- Publications on GM food toxicity are scarce. An article in *Science* magazine said it all: "Health Risks of Genetically Modified Foods: Many Opinions but Few Data".[1] In fact, no peer-reviewed publications of clinical studies on the human health effects of GM food exist. Even animal studies are few and far between.
- The preferred approach of the industry has been to use compositional comparisons between GM and non-GM crops. When they are not significantly different the two are regarded as "substantially equivalent", and therefore the GM food crop is regarded as safe as its conventional counterpart. This ensures that GM crops can be patented without animal testing. However, substantial equivalence is an unscientific concept that has never been properly defined and there are no legally binding rules on how to establish it.[2]

GM foods may cause bacteria to become resistant to antibiotics.

When food-crops are genetically modified, ("genetically modified" food is a misnomer!) one or more genes are incorporated into the crop's genome using a vector containing several other genes, including as a minimum, viral promoters, transcription terminators, antibiotic resistance marker genes and reporter genes. Data on the safety of these are scarce even though they can affect the safety of the GM crop. For example:

They can also

- DNA does not always fully break down in the alimentary tract.[3,4] Gut

produce allergies.

bacteria can take up genes and GM plasmids5 and this opens up the possibility of the spread of antibiotic resistance.
- Insertion of genes into the genome can also result in unintended effects, which need to be reduced/eliminated by selection, since some of the ways the inserted genes express themselves in the host or the way they affect the functioning of the crop's own genes are unpredictable. This may lead to the development of unknown toxic/allergenic components, which we cannot analyze for and seriously limiting the selection criteria.

Current testing methods need radical improvements.

Currently, toxicity in food is tested by chemical analysis of macro/micro nutrients and known toxins. To rely solely on this method is at best inadequate and, at worst, dangerous. Better diagnostic methods are needed, such as mRNA fingerprinting, proteomics and secondary metabolite profiling.[6] However, consuming even minor constituents with high biological activity may have major effects on the gut and body's metabolism, which can only be revealed from animal studies. Thus novel toxicological/nutritional methods are urgently needed to screen for harmful consequences on human/animal health and to pinpoint these before allowing a GM crop into the food chain.[7]

Safety tests on commercial GM crops

GM tomatoes: The first and only safety evaluation of a GM crop, the FLAVR SAVR™ tomato, was commissioned by Calgene, as required by the FDA. This GM tomato was produced by inserting kanr genes into a tomato by an 'antisense' GM method. The test has not been peer-reviewed or published but is on the internet.[8] The results claim there were no significant alterations in total protein, vitamins and mineral contents and in toxic glycoalkaloids.[9] Therefore, the GM and parent tomatoes were deemed to be "substantially equivalent."

In acute toxicity studies with male/female rats, which were tube-fed homogenized GM tomatoes, toxic effects were claimed to be absent. In addition, it was concluded that mean body and organ weights, weight gains, food consumption and clinical chemistry or blood parameters were not significantly different between GM-fed and control groups. However:

Some rats died within a few weeks after eating GM tomatoes.

- The unacceptably wide range of rat starting weights (±18% to ±23%) invalidated these findings.
- No histology on the intestines was done even though stomach sections showed mild/moderate erosive/necrotic lesions in up to seven out of twenty female rats but none in the controls. However, these were considered to be of no importance, although in humans they could lead to life-endangering hemorrhage, particularly in the elderly who use aspirin to prevent thrombosis.
- Seven out of forty rats on GM tomatoes died within two weeks for unstated reasons.
- These studies were poorly designed and therefore the conclusion that FLAVR SAVR™ tomatoes were safe does not rest on good science, questioning the validity of the FDA's decision that no toxicological testing of other GM foods will in future be required.

GM maize: Two lines of Chardon LL herbicide-resistant GM maize expressing the gene of Phosphinothricin Acetyltransferase Enzyme (PAT-PROTEIN) before and after ensiling showed significant differences in fat and carbohydrate contents compared with non-GM maize and were therefore substantially different. Toxicity tests were only performed with the PAT-PROTEIN even though with this the unpredictable effects of the gene transfer or the vector or gene insertion could not be demonstrated or excluded. The design of these experiments was also flawed because:

Rats' ability to digest was decreased after eating GM corn.

- The starting weight of the rats varied by more than ±20% and individual feed intakes were not monitored.
- Feed conversion efficiency on PAT-PROTEIN was significantly reduced.
- Urine output increased and several clinical parameters were also different.

The weight and histology of the digestive tract (and pancreas) was not measured.

Thus, GM maize expressing PAT-PROTEIN may present unacceptable health risks.

Compositional studies

Allergen content increased when soybeans were genetically modified.

GM soybeans: To make soybeans herbicide resistant, the gene of 5-enolpyruvylshikimate-3-phosphate synthase from *Agrobacterium* was used. Safety tests claim the GM variety to be "substantially equivalent" to conventional soybeans.[10] The same was claimed for GTS (glyphosate-resistant soybeans) sprayed with this herbicide.[11] However, several significant differences between the GM and control lines were recorded[10] and the statistical method used was flawed because:

- Instead of comparing the amounts of components in a large number of samples of each individual GTS with its appropriate parent line grown side-by-side and harvested at the same time, the authors compared samples from different locations and harvest times.
- There were also differences in the contents of natural isoflavones (genistein, etc.) with potential importance for health.[12]
- Additionally, the trypsin inhibitor (a major allergen) content was significantly increased in GTS.[10]

Because of this, and the large variability (± 10% or more), the lines could not be regarded as "substantially equivalent."

GM potatoes: There is only one peer-reviewed publication on GM potatoes that express the soybean glycinin gene.[13] However, the expression level was very low and no improvements in the protein content or amino acid profile were obtained.

GM rice: The kind that expresses soybean glycinin gene (40-50 mg glycinin/g protein) has been developed[14] and is claimed to contain 20% more protein. However, the increased protein content was probably due to a decrease in moisture rather than true increase in protein putting a question mark over the significance of this GM crop.

The toxin level of GM cotton is unpredictable.

GM cotton: Several lines of GM cotton plants have been developed using a gene from *Bacillus thuringiensis* subsp. *kurstaki* providing increased protection against major lepidopteran pests. The lines were claimed to be "substantially equivalent" to parent lines[15] in levels of macronutrients and gossypol, cyclopropenoid fatty acids and aflatoxin levels were less than those in conventional seeds. However, because of the use of inappropriate statistics it is questionable whether the GM and non-GM lines were truly equivalent, particularly as environmental stresses could have unpredictable effects on antinutrient/toxin levels.[16]

Nutritional/toxicological studies

Herbicide-resistant soybean: Studies have been conducted on the feeding value[17] and possible toxicity[18] for rats, broiler chickens, catfish and dairy cows of two GM lines of glyphosate-resistant soybean (GTS). The growth, feed conversion efficiency, catfish fillet composition, broiler breast muscle and fat pad weights and milk production, rumen fermentation and digestibilities in cows were claimed to be similar for GTS and non-GTS. However:

- These experiments were poorly designed since the high dietary protein concentration and the low inclusion level of GTS could have masked any GM effect.
- No individual feed intakes, body or organ weights were given and no histology was performed, except some qualitative microscopy on the pancreas.

- The feeding value of the two GTS lines was not substantially equivalent either because the rats grew significantly better on one of the GTS lines than on the other.
- The experiment with broiler chicken was a commercial and not a scientific study.
- The catfish experiment showed again that the feeding value of one of the GTS lines was superior to the other.
- Milk production and performance of lactating cows also showed significant differences between cows fed GM and non-GM feeds.
- Moreover, testing of the safety of 5-enolpyruvylshikimate-3-phosphate synthase which renders soybeans glyphosate-resistant[18] was irrelevant because in the gavage studies an *E. coli* recombinant and not the GTS product was used. Their effects could be different as the differences in post-translational modification could have impaired their stability to gut proteolysis.

Thus, the claim that the feeding value of GTS and non-GTS lines was substantially equivalent is at best premature.

Rats had meager weight gain when fed GM soybeans.

In a separate study[19] it was claimed that rats and mice which were fed 30% toasted GTS or non-GTS in their diet had no significant differences in nutritional performance, organ weights, histopathology and production of IgE and IgG antibodies. However, under the unphysiological — basically, starvation — conditions of these experiments when, instead of the normal daily growth of 5-8 g per day, the rats grew less than 0.3 g and mice not at all, no valid conclusions could be drawn.

GM corn: One broiler chicken feeding study with rations containing transgenic Event 176 derived Bt corn (Novartis) has been published.[20] However, the results of this trial are more relevant to commercial than academic scientific studies.

GM peas: The nutritional value of diets containing GM peas expressing bean alpha-amylase inhibitor when fed to rats for 10 days at two different (30% or 65%) dietary inclusions, was shown to be similar to that of parent-line peas.[21]

GM peas seem to have no harmful effects on animals but that doesn't mean they are safe for humans.

- Even at 65% level the difference was small mainly because the alpha-amylase inhibitor expressed in the peas was quickly digested in the rat gut and its antinutritive effect abolished. Unfortunately no gut histology was done or lymphocyte responsiveness measured.
- Although some organ weights, mainly the caecum and pancreas were different, those of others were remarkably similar suggesting that GM peas may be used in the diets of farm animals at low/moderate levels if their progress was carefully monitored.

However, to establish its safety for humans a more rigorous specific risk assessment will have to be carried out with several GM lines. This should include:

- An initial nutritional/toxicological testing on laboratory animals
- If no harmful effects are then detected, it should be followed by clinical, double-blind, placebo-type tests with human volunteers, keeping in mind that any possible harmful effects would be particularly serious with the young, old, and disabled.

A protocol for such testing was given at the OECD conference in Edinburgh, February 2000 and subsequently published.[22]

GM potatoes: In a short feeding study to establish the safety of GM potatoes expressing the soybean glycinin gene, rats were daily force-fed with 2 g of GM or control potatoes/kg body weight.[23] Although no differences in growth, feed

intake, blood cell count and composition and organ weights between the groups was found, the potato intake of the animals was too low and unclear, whether the potatoes were raw or boiled.

Toxins were found in mice after eating GM potatoes.

Feeding mice with potatoes transformed with a *Bacillus thuringiensis* var. *kurstaki* Cry1 toxin gene or the toxin itself was shown[24] to have caused villus epithelial cell hypertrophy and multinucleation, disrupted microvilli, mitochondrial degeneration, increased numbers of lysosomes and autophagic vacuoles and activation of crypt Paneth cells. The results showed that despite claims to the contrary, CryI toxin was stable in the mouse gut and therefore GM crops expressing it need to be subjected to "thorough tests…to avoid the risks before marketing.[24]

When the health risks of GM potatoes were revealed in some studies, a debate ensued.

In another study, young, growing rats were pair-fed on *iso*-proteinic and *iso*-caloric balanced diets containing raw or boiled non-GM potatoes and GM potatoes with the snowdrop (*Galanthus nivalis*) bulb lectin (GNA) gene.[25] The results showed that the mucosal thickness of the stomach and the crypt length of the intestines of rats fed GM potatoes was significantly increased. Most of these effects were due to the insertion of the construct and not to GNA which had been been pre-selected as a non-mitotic lectin unable to induce hyperplastic intestinal growth[26] and epithelial T lymphocyte infiltration. Although there is controversy about the tests, most of the adverse comments on this Lancet paper were personal, non-peer reviewed opinions and, as such, of limited scientific value. The findings, on the other hand, were published in a peer-reviewed publication[25] and the criticism replied to.[7] The work, however, has not been repeated nor results contradicted and it is therefore imperative that the effects on the gut structure and metabolism of all other GM crops developed using similar techniques and genetic vectors should be thoroughly investigated before their release into the food chain.

GM tomatoes: This study with a GM tomato expressing *B. thuringiensis* toxin CRYIA(b) gene was published in a book and not in a peer-reviewed journal. However, its importance was underlined by the immunocytochemical demonstration of *in vitro* binding of Bt toxin to the caecum/colon from humans and rhesus monkeys.[27] Although *in vivo* the Bt toxin was not bound by the rat gut, this was possibly due to the authors' use of recombinant Bt toxin.

Allergenicity studies

One of the major health concerns with GM food is its potential to increase allergies and anaphylaxis in humans eating unlabeled GM foodstuffs.

Allergies are a major concern with GM food, especially if ingredients are not labeled in packaged food.

- When the gene is from a crop of known allergenicity, it is easy to establish whether the GM food is allergenic using *in vitro* tests, such as RAST or immunoblotting, with sera from individuals sensitised to the original crop. This was demonstrated in GM soybeans expressing the brasil nut 2 S protein[28] or in GM potatoes expressing cod protein genes.[29]
- It is also relatively easy to assess whether genetic engineering affected the potency of endogenous allergens.[30] Some farm workers exposed to *B. thuringiensis* pesticide were shown to have developed skin sensitization and IgE antibodies to the Bt spore extract. With their sera it may now therefore be possible to test for the allergenic potential of GM crops expressing Bt toxin.[31] It is all the more important because Bt toxin Cry1Ac has recently been shown to be a potent oral/nasal antigen and adjuvant.[32]

There are no reliable ways to test GM foods for allergies.

Assessment of the allergenicity of a GM foodcrop, however, is difficult when the gene is transferred from a source not eaten before or with unknown allergenicity or on gene transfer/insertion a new allergen or adjuvant is developed or the expression of a minor allergen is increased. Unfortunately, while there are good animal models for nutritional/toxicological testing, no such models exist for allergenicity testing.

- Presently only indirect and rather scientifically unsound methods, such

as finding SHORT sequence homologies (at least 8 contiguous amino acids) to any of the about 200 known allergens, are used for the assessment of allergenicity.

- The decision-tree type of indirect approach based on factors (such as size and stability) of the transgenically expressed protein[33] is even more unsound, particularly as its stability to gut proteolysis is assessed by an in vitro (simulated) testing[34] instead of *in vivo* (human/animal) testing and this is fundamentally wrong. The concept that most allergens are abundant proteins is also misleading because for example Gad c 1, the major allergen in codfish, is not a predominant protein.[29]

- However, when the gene responsible for the allergenicity is known, such as the gene of the alpha-amylase/trypsin inhibitors/allergens in rice, cloning and sequencing opens the way for reducing their level by antisense RNA strategy.[35]

Thus, in the absence of reliable methods for allergenicity testing, it is at present impossible to definitely establish whether a new GM crop is allergenic or not before its release into the human/animal food/feed chain.

In conclusion

We need more and better testing methods before making GM foods available for human consumption.

One has to agree with the piece in *Science*[1] that there are many opinions but scarce data on the potential health risks of GM food crops, even though these should have been tested for and eliminated before their introduction. Our present data base is woefully inadequate. Moreover, the scientific quality of what has been published is, in most instances not up to expected standards. If, as claimed, our future is dependent on the success of the promise of genetic modification delivering wholesome, plentiful, more nutritious and safe GM foods, the inescapable conclusion of this review is that the present crude method of genetic modification has so far not delivered these benefits and the promise of a superior second generation is still in the future. Although it is argued by some that small differences between GM and non-GM crops have little biological meaning, it is clear that most GM and parental line crops fall short of the definition of "substantial equivalence." In any case, this crude, poorly defined and unscientific concept outlived its possible previous usefulness and we need novel methods and concepts to probe into the compositional, nutritional/toxicological and metabolic differences between GM and conventional crops and into the safety of the genetic techniques used in developing GM crops if we want to put this technology on a proper scientific foundation and allay the fears of the general public. We need ***more*** science, not less.[6,7]

Arpad Pusztai, Ph.D., received his degree in Chemistry in Budapest, Hungary and his B.Sc. in Physiology and Ph.D. in Biochemistry at the University of London in England. Over his nearly 50-year career, he worked at universities and research institutes in Budapest; London; Chicago, U.S.; and Aberdeen, Scotland (Rowett Research Institute). He has published close to 300 primary peer-reviewed papers and wrote or edited 12 scientific books. In the last 30 years he pioneered research into the effects of dietary lectins (carbohydrate-reactive proteins), including those transgenically expressed in GM crop plants, on the gastrointestinal tract. Since his contract was not renewed with Rowett as a result of disagreements, Dr. Pusztai has been lecturing on his GM potato research all over the world and acting as a consultant to groups starting up research into the health effects of GM food.
http://en.wikipedia.org/wiki/%C3%81rp%C3%A1d_Pusztai

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The Ecological Impacts of Agricultural Biotechnology
Dr. Miguel Altieri presents an analysis of the damaging effects of GM crops on our environment in an article on this site.
http://www.actionbioscience.org/biotech/altieri.html

GM food quiz
How much do you know about GM food? Take this online quiz created by the Environmental News Network.
http://www.hort.purdue.edu/hort/courses/HORT250/GM%20Food%20Quiz

Food for our future
This U.K. Food Future site explains GM crops and foods, examining both benefits and concerns. Also features a glossary of GM food terms.
http://www.foodfuture.org.uk/

Alliance for Bio-integrity
The executive director of this organization explains "Why concerns about health risks of genetically engineered food are scientifically justified."
http://www.biointegrity.org/health-risks/health-risks-ge-foods.htm

How are genes engineered?
Using a minimum of technical terms, this brief how-to explains how genes are manipulated in genetic engineering.
http://www.geneticengineering.org/dna7/default.htm

Transgenic (GM) crops on the market
Colorado State University provides a descriptive list of transgenic crops in the U.S. and other parts of the world. The second link takes you to their home page where you will find other menu options and resources.
http://cls.casa.colostate.edu/TransgenicCrops/current.html
http://cls.casa.colostate.edu/TransgenicCrops/index.html

Myths about GE food
New Zealand's Consumers for Education about Genetic Engineering has prepared this helpful guide to debunk misconceptions about genetic engineering.
http://www.prorev.com/genetic.htm

More on Dr. Pusztai's work
A web page run by Dr. Pusztai's colleague, Dr. Thorkild of the University of Copenhagen, is devoted to an examination of Dr. Pusztai's research and other GMO information.
http://www.plab.ku.dk/tcbh/Pusztaitcbh.htm

Biotechnology resources
Biotechnology-related news, books and web resources.
http://www.bioworld.com/

getinvolved links

Campaign to label genetically modified food
If you believe that food products should contain GM information on labels, join this campaign which provides an opportunity for you to send letters to US congress, government agencies, grocery stores and food manufacturers as well as to send emails to the media about your views on the issue.
http://www.thecampaign.org/

Center for Food Safety campaigns
If you oppose the FDA's regulations on genetically modified food, take action through this site.
http://www.foodsafetynow.org/page4.cfm

True Food Network
This network is a free service from Greenpeace to connect consumers who want to take action to end the use of genetically engineered (GE) ingredients in our foods.
http://www.truefoodnow.org/

Campaign to ban genetically modified food
The Natural Law Party of the UK invites you to join their campaign against GMOs.
http://www.btinternet.com/~nlpwessex/Documents/gmocarto.htm

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author glossary

Copy gene - genetic material that contains the genetic code for a desirable trait which has been copied from the DNA of the donor to transfer to the host organism. (Currently, it is not technically possible to take a gene from a donor organism and insert it directly into the host organism).
DNA - Deoxyribonucleic acid, the fundamental genetic material of all cells, that acts as the carrier of genetic information.
Gene - the biological unit of inheritance, which transmits hereditary information of a physical, behavioral, or biochemical trait.
Genetic modification - a technique for copying and transferring individual genes to another living organism to alter its genetic make up, thereby incorporating or deleting specific characteristics into or from the organism.
Toxin - a poison, usually originating in a plant or microorganism.

educatorresources

ActionBioscience.org original lesson

This lesson has been written by a science educator to specifically accompany the above article. It includes article content and extension questions, as well as activity handouts for different grade levels.

Lesson Title: ***GM Foods: Are They Safe?***
Levels: high school - undergraduate
Summary: This lesson examines potential benefits and risks of genetically modified foods. Students can interview a biotech company, design enhanced GM food products or packaging labels, form a GM food lobby group… and more!
Download/view lesson.
(To open the lesson's PDF file, you need *Adobe Acrobat Reader* free software.)

Useful links for educators

» Environmental Inquiry Cornell University offers background information and classroom activities, including lab work using bioassays, to examine toxicology.
http://ei.cornell.edu/toxicology/

Useful links for student research

In addition to the links in the "learn more" section above:

» Genetic Engineering Glossary The International Forum for Genetic Engineering provides an online glossary of terms for genetics and genetic engineering.
http://www.ifgene.org/glossary.htm

» Genetically-Modified Crops Glossary The European Commission provides a brief glossary of terms related to GM crops that may be useful to student research.
http://www.europa.eu.int/comm/agriculture/publi/gmo/glossary.htm

» FDA (Food and Drug Administration) USA Main U.S. government agency responsible for safety of GM foods to consumers. Has many links to pages and articles, press releases, links on a variety of aspects of food safety.
http://www.fda.gov/

» American Society of Plant Biologists (ASPB) Includes a book collection of "Editor's Choice" articles devoted to biotechnology and genetically modified crops. The articles are online or the book can be ordered.
http://www.aspb.org

» The National Center for Biotechnology This organization in the U.K. has extensive information about GMOs and biotechnology.
http://www.ncbe.reading.ac.uk/NCBE/GMFOOD/menu.html

Since animals fed genetically modified foods experienced such a wide variety of issues, susceptible people might react to genetically modified foods with multiple symptoms. In the first nine years after the large scale introduction of genetically modified crops, the incidence of people who experience three or more chronic diseases nearly doubled.Â d) Genetically Modified Foods: Are They a Risk to Human/Animal Health www.actionbioscience.org/biotechnology/pusztai.html. Similar Documents. UN World Food Safety Day - 7th June Annually - United Nations Global World Food Safety Awareness Day yearly on 7th June aims to strengthen efforts to ensure food we eat is safe.