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Don't Look, Don't Find: Health Hazards of Genetically Modified Food

Claire Robinson, MPhil

Genetically modified (GM) foods are derived from crops or animals that have had their DNA changed by the insertion of DNA from foreign and unrelated organisms in a way that would not happen naturally.[1] Genetic engineering is different from conventional breeding, which can only take place between closely related organisms, such as wheat with wheat. Genetic engineering allows DNA to be transferred across species barriers, conferring new properties on the organism.

GM foods were first released onto world markets in the mid-1990s. The European Union and other countries require GM foods to be labelled, but the United States, where the bulk of GM foods are grown and consumed, does not. Canada also does not require labelling. Genetic modification is mostly confined to a few commodity crops: soy, maize, canola, sugar beet, and cotton. Almost all commercially available GM crops are engineered to tolerate being sprayed with herbicide or to express a pesticide, or both.[2]

The most detailed scientific study ever performed on the health effects of a GM food was published last year. The findings of the research study, led by Prof Gilles-Eric Séralini at the University of Caen, France, were shocking. Rats fed over a two-year period with GM maize and the Roundup herbicide with which it is grown had increased rates of severe organ damage, tumours, and premature death.[3]

The study should have been a wake-up call to the world, but most members of the public and healthcare practitioners are in danger of learning nothing from it. The reason? Within hours of the study's release, a concerted media campaign swung into action to discredit it. Quotes from scientists criticizing the paper were circulated by the UK-based Science Media Centre,[4] an organization that takes funding from GM companies.[5]

One of the critics pointed to the unexpected nature of Séralini's findings. Mark Tester, research professor at the Australian Centre for Plant Functional Genomics, University of Adelaide, said, "The first thing that leaps to my mind is why has nothing emerged from epidemiological studies in the countries where so much GM has been in the food chain for so long? If the effects are as big as

SÉRALINI STUDY DESIGN AND FINDINGS

Séralini's study[3] tested the long-term effects of Monsanto's GM NK603 maize, which is engineered to survive being sprayed with Roundup herbicide, and Roundup. The study used 200 rats divided into ten groups, each of ten males and ten females. The GM maize alone was tested on three groups at 11%, 22% and 33% of the total diet. GM maize which had been sprayed with Roundup in the field was tested on three groups in the same proportions. Roundup alone, given in drinking water at three different doses, was tested on three groups. The lowest dose corresponded to contamination found in some tap water, the intermediate dose to the maximum level permitted in the USA in animal feed, and the highest dose to half the strength of Roundup as used in agriculture. Controls were fed a diet containing 33% non-GM maize and plain drinking water.

In treated males, the most commonly affected organs were the liver and kidneys, and deaths were mostly due to liver and kidney disease. Hepatic congestion and necrotic foci were 2.5–5.5 times more frequent in all treatment groups than controls. The activity of the liver enzyme gamma-glutamyl transferase was increased up to 5.4 times for the groups fed GM maize plus Roundup, a possible sign of toxicity.

For all treatments and both sexes, 76% of altered parameters were kidney-related. In treated females, sodium and chloride ions increased in urine. The same ions decreased in serum, as did levels of phosphorus, potassium, and calcium. Creatinine clearance in urine decreased in all treatment groups compared with female controls.

In females, the androgen/estrogen balance in serum was modified by GM maize and Roundup treatments. In males fed the highest Roundup dose, levels of estrogen more than doubled.

Up to 14 months, no animals in the control groups showed any signs of tumours, compared with 10–30% of treated females, except the group consuming the highest proportion of GM maize plus Roundup. By the 24th month, 50–80% of females in all treated groups had developed tumours, with up to three per animal, whereas only 30% of controls were affected.

Whereas 30% of control males and 20% of control females died before the mean survival time, up to 50% of males and 70% of females died prematurely in some groups containing GM maize.

Link to study: http://www.sciencedirect.com/science/article/pii/S0278691512005637

purported, and if the work really is relevant to humans, why aren't the North Americans dropping like flies?"[4]

This quote was cited uncritically in media articles worldwide.[6] Yet no reporter asked how many epidemiological studies have been carried out to examine the effects on humans of eating GM foods. The answer: none. Nor did they ask how such studies could be carried out in the country where most GM foods have been eaten for the longest time, the United States, given that GM foods are not labeled there and consumption cannot be traced.

Criticisms circulated by the Science Media Centre and quoted in the media were answered by Séralini's team in the journal that published his original research.[7] Criticisms were also addressed on a public information website, gmoseralini.org, set up by citizens and scientists who were concerned that important findings were being buried.

Subsequent investigations showed that most of Séralini's critics had conflicts of interest that went undisclosed in the Science Media Centre media releases and articles that quoted them.[8,9] Public interest scientific groups commented that double standards are used to evaluate studies on GM food safety, with those that find risk being subjected to relentless criticism, whereas those that conclude safety go unchallenged.[10,11]

The scientifically valid way to test Séralini's findings would be to repeat the study or to extend it into a full-scale carcinogenicity study, using larger groups of rats. But long-term studies like Séralini's have never been carried out by GM developer companies, nor are they required by regulators anywhere in the world. Studies that have found problems with GM foods have not been followed up. The preferred way is to discredit the researcher and the findings. This can include campaigns to persuade journal editors not to publish a paper or, if it is already published, to retract it.[12,13] Such a retraction campaign was waged against Séralini's study,[14] albeit unsuccessfully.

When are statistically significant findings not biologically relevant?

Séralini designed his 2012 study as a direct follow-up to Monsanto's own 90-day rat feeding study on the same GM maize, carried out in support of regulatory authorization. Statistically significant changes were found in the GM-fed rats, but the Monsanto authors claimed they were not biologically relevant.[15] The European Food Safety Authority (EFSA) agreed,[16] though biological relevance with respect to changes in GM-fed animals has never been defined.

Séralini's team obtained Monsanto's raw data, which had been kept hidden under commercial confidentiality agreements with regulators. The team's re-analysis, published in 2009, concluded that the data revealed signs of liver and kidney toxicity in the GM-fed rats. GM-fed rats showed increased liver weights and urine creatinine clearance, together with a reduction in blood creatinine and a decrease in blood urea nitrogen.[17]

Séralini's team decided to find out whether the initial signs of toxicity seen in Monsanto's 90-day study were biologically irrelevant, as Monsanto and EFSA claimed, or whether over time they might develop into serious pathology. They replicated Monsanto's study design but extended the length from 90 days to two years. The results were alarming. Signs of toxicity found in the 90-day study developed into severe organ damage, tumours, and premature death.[3] These effects had not shown up in Monsanto's 90-day test[15] because it was too short: the first tumour in Séralini's experiment only appeared four months into the experiment.[3]

Séralini's findings revealed that industry and regulatory claims of biological irrelevance of effects found in 90-day tests are invalid. They showed further that the regulatory system for GM foods is inadequate and cast into question the safety of all commercialized GM foods. Criticisms by some regulatory agencies of Séralini's findings[18,19] should be viewed with this fact in mind.

Safety testing and regulatory oversight

The rat feeding studies typically performed in support of regulatory authorizations for GMOs last for a maximum of 90 days, a sub-chronic period equivalent to only 7–9 years in a human.[20] The studies are designed and conducted by the same company that wishes to commercialize the GMO.

The US regulatory system is even weaker. The US food regulatory agency, the Food and Drug Administration (FDA), does not require safety tests at all. Nor does it require labelling for GM foods because it assumes that they are substantially equivalent to non-GM foods and Generally Recognised As Safe (GRAS).[21,22] Substantial equivalence has never been scientifically or legally defined.[23] GM foods cannot accurately be termed GRAS,[24] since GRAS status requires a scientific consensus of safety based on data, and no such consensus exists with relation to GM foods. The FDA allowed the first GM foods to be released onto world markets in spite of warnings by its own scientists that genetic engineering is different from conventional breeding and poses special risks, including the production of new toxins or allergens.[25,26,27,28,29,30]

No consensus of safety has emerged since. Reviews of the literature show that studies funded or carried out by the GM industry, or in which funding is undisclosed, tend to conclude safety, whereas studies carried out by scientists independent of industry are more likely to find hazards.[31,32,33]

What is the problem with GM foods?

The genetic engineering process is inherently imprecise and causes widespread disruption to the genome, which can lead to unintended effects. These can include the creation of novel toxins or allergens or altered nutrient value.[22,34,35,36]

A study on the GM insecticidal maize MON810 showed that its proteins were altered compared with those in the non-GM variety. Unexpected changes included the appearance of a new form of the protein zein, a known allergen that was not present in the non-GM variety.

Other proteins were present in both their natural forms and in truncated and lower molecular mass forms.[37] These findings suggest disruptions in gene structure and function in this GM crop.

Another study showed that Monsanto's GM herbicide-tolerant soy had 27% higher levels of an allergen and anti-nutrient, trypsin-inhibitor, than the non-GM parent variety.[38]

Overview of animal feeding studies with GM foods

A review of animal feeding studies with GM crops concluded that they cause toxic effects such as hepatic, pancreatic, renal, or reproductive effects and may alter the hematological, biochemical, and immunologic parameters (details in the sections below). The authors added that most of the studies were too short to enable the full range of toxic effects to be evaluated and called for long-term toxicity studies on GM foods before commercialization.[31]

A review of 19 animal feeding studies (including those of industry) on GM soy and maize found that GM-fed animals showed signs of toxicity. Rats fed GM Bt maize over three generations showed histopathological changes in the liver and kidneys, including congestion, cell nucleus border changes, and severe granular degeneration in the liver. Rats fed GM Bt maize for 90 days had a significantly lower albumin/globulin ratio, indicating a change in hepatic metabolism. The review authors noted that such effects may be markers of the onset of chronic disease, but that long-term studies would be required to assess this more thoroughly.[39]

The need for long-term safety testing of GM foods was highlighted by the French food safety agency ANSES, which is responsible for national authorizations of GMOs in France, in its criticism[40] of Séralini's study.[3] ANSES's literature search turned up only two long-term studies examining the health effects of GM foods.[40] One is only available in Japanese.[41] The other found problems. Mice fed GM soy over a 24-month period showed changes in the expression of proteins relating to hepatocyte metabolism, stress response, and calcium signaling, indicating more acute signs of ageing in the liver.[42]

A review of studies on GM foods by Snell et al (2011) concluded that they are safe,[43] but this cannot be justified from the data presented. Some of the studies examined did not look at health effects, but focused on parameters of interest to food producers, such as feed conversion in livestock. Some studies found toxic effects but these were dismissed as not biologically relevant, either by the authors of the original studies or by the authors of the review. Also, the review authors applied double standards, in that they accepted conclusions of safety at face value yet dismissed findings of risk on the grounds of methodological weaknesses. These weaknesses were, however, common to studies finding safety and those finding risk, as admitted by the review authors.

Studies on GM insecticidal crops

Most GM insecticidal crops are engineered to express a GM form of the Bt insecticidal toxin, derived from the from the naturally occurring soil bacterium *Bacillus thuringiensis*. GM Bt crops were commercialized on the basis of the assumption that the Bt toxin expressed in GM plants is the same as the 'wild' Bt toxin used as a biological pesticide by conventional and organic farmers. But this assumption is false.[39,44] The Bt toxins in GM plants are truncated or otherwise modified. There is at least a 40% difference between the toxin in Bt176 maize and natural Bt toxin.[39]

Such differences mean that humans and animals that eat Bt crops are eating an insecticide with no history of safe use in food.[44,45] Indeed, Bt176 maize was withdrawn by the developer Syngenta in the wake of accusations that it caused illness and deaths in cows,[46] though Syngenta denied the allegations.[47]

Another false assumption underpinning the release of GM Bt crops is that the toxin is broken down harmlessly in the digestive tract. Bt toxin from GM crops can survive the digestive process, as shown *in vitro* and *in vivo*.[48,49] Bt toxin protein has been detected in the blood of pregnant women (range of 0 to 1.50 ng/mL) and in the blood supply to their fetuses.[50] It is not known if the Bt toxin was of GM origin, if the protein was intact or fragmented, or if this dose could cause illness in humans. However, even fragments of a protein could cause allergies, autoimmune disorders and chronic disease,[51] and the onus is not on the public to prove that GM crops cause harm, but on industry to prove that they are safe prior to release. It is clear that the most basic safety tests were not done.

Weaning and old mice fed GM Bt maize for periods of 30 and 90 days respectively showed a disturbance in intestinal and peripheral immune response, namely alterations in the percentage of T and B cells and of CD4+, CD8+, γδT, and αβT lymphocytes. An increase of serum cytokines IL-6, IL-13, IL-12p70, and MIP-1β after Bt maize feeding was also found, an effect associated with allergic and inflammatory responses.[52] GM Bt potatoes caused the disruption, multinucleation, swelling, and increased degradation of ileal surface cells in rats fed over a two-week period.[53]

Laboratory studies in mice found that GM Bt toxin produces a potent immune response when administered intragastrically or by intraperitoneal immunization.[54,55] The Bt toxin protein was found to bind to the mucosal surface of the small intestine of the mice, which the authors said could lead to changes in the physiological status of the animals' intestine.[56] The Bt toxin protein also enhanced the immune response of the mice to other substances.[57]

GM peas engineered to contain a different insecticidal protein (α-amylase inhibitor) found that the insecticidal protein acted as a sensitizer in mice, prompting the mice to develop immune reactions to a protein from eggs. This is called immunological cross-priming.[58]

Recent attempts[59,60] to claim that a new study[61] resolves concerns raised by the first study[58] are unfounded, as it used a different methodology. In the first study, the mice were fed intragastrically, an approximation of human dietary exposure, and then tested for allergic reaction.[58] In the new study, mice were first intraperitoneally or intranasally immunized with the GM and non-GM test proteins, then fed intragastrically with GM peas and

non-GM beans containing the proteins, and then tested for allergic sensitization. The result: both GM peas and non-GM beans were found to be equally allergenic.[61] A question could be asked as to whether the initial immunization – not the usual way a human is exposed to food – was a predictable way to sensitize the mice to any food.

An *in vitro* test confirmed that Bt toxin proteins in GM crops are not inert in human cells. The Bt toxin protein Cry1Ab caused cell death in human embryonic kidney cells from 100 ppm.[45]

Studies on GM Roundup-tolerant soy

Mice fed GM soy showed changes in the constituents of pancreatic acinar cells and in the synthesis and processing of zymogen (an enzyme precursor), compared with controls fed non-GM soy.[62,63] The GM soy-fed mice had markedly reduced pancreatic levels of the enzyme α-amylase, which helps break down starch into sugars.[63]

A multigenerational study in rats found decreased weight, increased mortality, and decreased fertility in rats fed GM Roundup-tolerant soy.[64,65] The Russian researcher who carried out the study found her work subjected to a highly irregular review process in the pages of a scientific journal.[66] Whereas the review process was condemned in some media outlets,[67,68,69] her findings were never followed up.

GM Roundup-tolerant soy will necessarily contain elevated levels of Roundup herbicide. Far from being benign, Roundup has been linked in laboratory and epidemiological studies and clinical reports to serious health effects, including endocrine disruption, DNA damage, birth defects, cancer, and neurological disorders. Some toxic effects have been found at low doses comparable to those found in food and feed crops and drinking water.[3,70,71,72,73]

Case studies and treatments

Given the absence of epidemiological data on the effects of consuming GM foods, one of the best sources of information may be clinical case studies.

One case study involves a boy living in the US. He was eight years old in March 2012, when he began suffering severe gastrointestinal pain after eating. He was constipated and had blood in his stool. Tests for celiac disease proved negative. In October 2012 the boy's mother heard about GM foods and removed them from his diet. She also gave him a preservative-free probiotic. Within weeks, the gastrointestinal symptoms vanished. To date the boy remains healthy and symptom-free.[74]

Other case studies are presented in the documentary film, *Genetic Roulette: The Gamble of Our Lives*.[75] The film and its director are subject to the usual attacks directed at critics of GMOs, so members of the public are encouraged to reach their own conclusions. According to practitioners and patients interviewed in the film, symptoms that can improve or disappear when GM foods are removed from the diet include gastrointestinal disorders, food intolerances and allergies, immune responses, and asthma. Speed of recovery varies but full results are typically seen within six weeks.[75] Farmers interviewed in the film[75] and other media outlets[76] have reported improvements in the health of livestock after changing their diet from GM to non-GM, notably in gastrointestinal disorders, reproductive problems, and birth defects.

Conclusion

The evidence supports the American Academy of Environmental Medicine's (AAEM) statement on GM foods, which notes that they have not been properly tested for human consumption but that animal studies offer "ample evidence of probable harm". The AAEM recommends that physicians prescribe non-GM diets to patients.[77]

In practice this means avoiding processed foods and foods subject to genetic modification, including derivatives like maize starch and oils derived from GM soy and canola. Whole and organically grown foods cooked from scratch should be favored, as organic production excludes GM seeds and many synthetic pesticides. Probiotics and measures aimed at ameliorating leaky gut syndrome, such as minimizing intake of sugar and refined foods, may also be helpful.

Non-GMO shopping guides and mobile phone apps are available, and shoppers can seek foods carrying organic and "Non-GMO Project Verified" labels.

About the Author

Claire Robinson is research director at the food sustainability and science policy nonprofit Earth Open Source; co-author of the report GMO Myths and Truths (Earth Open Source 2012: http://bit.ly/ZILXBd); editor of GMOSeralini.org; and an editor at GMWatch.org.

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