Invited Editorial

Crop conundrum

Adrian C Dubock

The lead review "Risk assessment of genetically modified crops for nutrition and health" by Magaña-Gómez and Calderon de la Barca,[1] ends with a common plea: "more research is needed". It is valid to put both this plea and the justification for other similar research into perspective. How selective are the reviews that lead to the conclusion that more of such research is needed? What comparators are available? Why genetically modified (GM) crops particularly? And what political effect does the science promulgate; to what advantage and to what disadvantage is global society affected?

Magaña-Gómez and Calderon de la Barca[1] conclude that at a macroscopic, whole animal level, there is no provable adverse health effect of GM crops, but there is evidence that microscopic and molecular changes may have been induced in animal studies. It is implied that these may be important for safety. But what is the comparator basis for these studies?

Crops and plants, in general, are dynamic and complex. At different growth stages, in different environments, as well as in different varieties (e.g., there are more than 20,000 varieties of rice), there will be variations at the molecular and microscopic levels. Research into normal biological variation for any relevant crop species of the growth stages, environmental effects, and variety differences would be useful so that comparisons of the same data, which need statistical analysis anyway, from any GM crop plant could be made based on properly established, statistically valid, baseline data for that species. Yet such research would be very time-consuming, expensive, and unlikely to receive grant funding, so it will probably not be done. Yet, without having a very firm understanding of the breadth of this variation, a comparison of analytical data (chemical or histological) from any sample of a GM crop may only be a comparison with one part of the spectrum of normal variation in that species. Such a comparison is like comparing apples and pears: they are essentially different, which explains any differences.

A similar point can be made regarding the utility of animal studies for determining subtle changes that may be due to dietary components, i.e., they may not be very useful. "Normal" individuals of a species exist in many varieties, with many variations including in behavior, metabolism, disease susceptibility, and disease state. Think of humans. If we are really interested in evaluating microscopic, subtle changes to inform us of a potential for hazard in humans, will a 90-day rodent study, using standardized rodents, really inform us, however thoroughly it is executed? To do more is costly in terms of both time and money. To sacrifice animals for no purpose is ethically questionable as well as wasteful.

Conventional breeding has created plants that are potentially hazardous to humans: certain varieties of celery and potatoes are normally quoted as examples. Of course, these plants have not been developed further. The major concern for human hazard from genetically modified crops is the possibility that novel proteins may be introduced and ingested, and these may prompt potentially dangerous allergic reactions in man. However, sophisticated computer databases have been created that allow for searches of new protein structures to be made and compared against extensive databases of the structures of known human allergens, and these are used routinely as a proxy. The development of some potential GM products has been halted as a result, just as the development of some conventionally bred crop varieties has been halted.

Crop plants have been introduced as novel food to previously unexposed populations for thousands of years.[2] None of them has been tested for safety before being introduced to the new population. One example is the kiwifruit from New Zealand; originally from China, kiwifruit was introduced to Europe only in 1955. Potato, maize, and tomato are all examples of plants containing known allergens that have been introduced to other populations from their regions of origin, and all are nowadays commonly consumed as food

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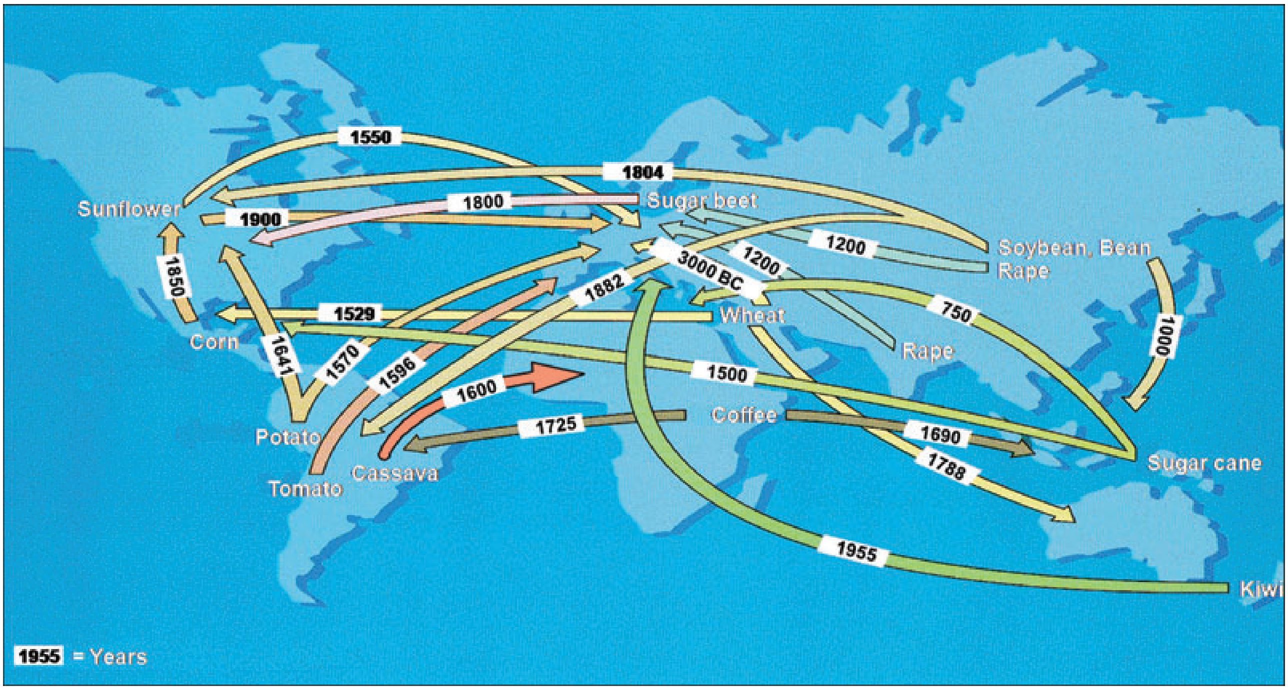

Figure 1 **Crops have been introduced as novel food to new populations for thousands of years.**

constituents in processed form (Figure 1). No harm has arisen.

The genetic nucleotide code for amino acids is universal among all organisms – plant, animal, and bacteria. There is also a growing understanding that the large degree of metabolic unity existing among organisms is based on the presence of homologous genes. This knowledge allows the rapid identification of genes controlling many useful traits – including protecting crops from biotic and abiotic stresses, as well as improved nutritional qualities – which have not been possible hitherto, as they cannot be achieved through conventional breeding.

So why single out GM crops for special analysis? Why not organically produced crops, for example? Aficionados of the latter often expect better nutrition from them: wouldn't it be interesting to search for the evidence behind the claim? Or why not examine crops produced by conventional breeding, especially when chemicals or irradiation are purposefully used to induce mutation? In those cases, more random gene mixing and random mutational change occurs than in the relatively precise technique of genetic modification in which unitary numbers of genes (usually much fewer than five) are introduced rather than the tens of thousands in "conventional" breeding. Similarly, why not review the effect on variation in animals of genetically engineered drugs? Most new drugs in the pipelines of industry are biological agents of one sort or another, and they are registered for use on both sides of the Atlantic.

Are there not more pressing needs towards which scarce science resources should be applied than GM crops? Does the cumulative scientific opinion of national and international scientific institutions and international organizations have no weight? They have commented that GM crops are safe to humans and the environment and there is no inherent risk from the technology (Table 1).[3–5]

In the review of Magaña-Gómez and Calderon de la Barca,[1] some importance is given to the research of Ewen and Pusztai[6] on potatoes and Losey et al.[7]on Monarch butterflies. Both groups concluded there were adverse effects of genetic modification. However, in both cases the experimental design did not support the conclusions reached by the authors, nor did it allow the research to be repeated by others. The quality of the science in both cases was widely discredited after publication, making any valid use of the results highly questionable.[8–11] This is not mentioned by Magaña-Gómez and Calderon de la Barca – there remains no substantiated negative health (or environmental) affect of the use of commercialized GM crops. Magaña-Gómez and Calderon de la Barca also make no differentiation between "products" at the experimental stage, and those that have been through a regulatory process and are commercially available. It should be noted that no commercial GM crops contain lectin and, despite the authors assertion to the contrary, "insect-resistant potato" is not "currently planted on millions of farmland hectares".

Table 1 **Impartial institutions have concluded genetically modified crops are safe to man and the environment and the technology poses no inherent risk.**

Institution	Country	Year
Nuffield Council on Bioethics	UK	1999
Organisation of Economic Co-operation and Development	International	2000
European Research Directorate	European Commission	2001
French Academy of Science	France	2002
French Academy of Medicine	France	2002
Director General, World Health Organisation	International	2002
International Council for Science	International	2003
Royal Society	UK	2003
United Nations, Food and Agriculture Organisation	International	2004
British Medical Association	UK	2004
Union of German Academies of Science & Humanities	Germany	2004
The American, Brazilian, Chinese, Indian, and Mexican Academies of Science		

Is it valid in seeking subtle impacts of GM crops to ignore the positive benefits and potential benefits of GM crops to the economy, the environment and, yes, human health?

For several years, the Italian government suppressed data from university trials it had organized of maize containing the specific, safe-to-humans, insecticidal gene "Bt".[12] The data from the suppressed trials demonstrated a significant yield increase (28–43% higher) for GM Bt-maize compared with the use of non-GM maize. The data also demonstrated a very significant reduction in fumonisin in the maize from 6000 parts per billion to less than 60 parts per billion. Fumonisins are human toxins from fungi that enter the crop through lesions caused by uncontrolled insect pests. The European standard currently allows 4000 parts per billion. In the year of the trial, more than half of the Italian maize crop was unfit for human consumption, but this was not true of the GM Bt. maize.

In the case of Golden Rice, which is rice bioengineered to express β-carotene in the endosperm, it is expected that a significant impact can be made in reducing morbidity and mortality due to vitamin A deficiency in poor populations where rice is the staple food.[13] Despite the validity of current interventions, around 6000 people die daily as a result of vitamin A deficiency as they cannot afford a suitably varied diet. This is a real and substantial health problem. It is not a potential one. It demands attention.

Excessive testing is not benign. Just conducting the tests prompts concerns: why would there be so much testing, if there was no reason to be concerned? And how great would changes have to be to imply hazard to man? We all eat, if we are wealthy enough, a variety of crop plants. We are not prevented by the generally accepted situation that 90% of known carcinogens are of plant origin. The "Precautionary Principle" originating from Europe appears to be more of a cloak for ideology or trade issues, than a principle. If applied uniformly, nothing new would ever be attempted! And even in Europe, it is not applied to, for example, bioengineered pharmaceuticals in the same way that it is to GM crops.

Agricultural biotechnology, in all its forms, including genetic modification, is scalable, requires little capital, is a continuation of the process of crop improvement started 10,000 years ago in Mesopotamia (now Iraq) and is very appropriate and sustainable for adoption by developing countries struggling for the dignity of self sufficiency in food production.

The time-limited (normally 20 years) and nationally determined monopoly granted for inventions by the patent system to encourage investment in and publication of research with industrial application is as relevant to biotechnology research as to other fields. Due to the passage of time, the earliest biotech patents that were commercially exploited have now expired and will continue to expire over time. The technology is thus available to all. Farmers may choose to buy the latest products, or not. There is no monopolistic commercial capture of the food supply as appears to be feared by many.

Agriculture is necessary in order for humans to produce the food they need. Agriculture is not "natural", nor is it static, and intensive agriculture protects biodiversity by focusing production on less land. Plant breeders, and farmers' use of seed, maintain variety separation of crop plants. There is no reason to fear gene flow from GMO crops to conventional crops any more than the flow of uncontrolled pests and diseases from organic to conventional agriculture. Crop plants have to be cultivated to survive: uncultivated fields become infested with weeds; natural lands do not become infested with crop plants. There is no special reason to fear loss of biodiversity in agriculture or uncultivated land through the use of GM crops.

Intensive agriculture with modern methods is sustainable. People in developing countries were spending

70% of their limited incomes on food even before the recent price hikes. They can't afford to be denied access to any technology that has the potential to increase crop productivity and food quality. Excessive caution about genetic modification slows adoption and is therefore life threatening. Freed of excessive regulation and suspicion, genetic modification combined with marker-assisted breeding has the potential to very rapidly introduce useful new traits into established varieties of sexually reproduced crop plants. Such traits, which are unachievable by conventional breeding, have the potential to significantly contribute to poverty alleviation and nutritional improvement in developing countries and also to mitigate climate change in both developing (e.g., drought tolerance) and industrialized (e.g., through reduced tractor fuel consumption) countries.

The additional capability that genetic modification of crops allows should be embraced with enthusiasm, not continually challenged by suspicion. Genetic modification technology is a useful complement to other agricultural technologies. All have great relevance to nutrition and health. As one British MP said recently: "about 300 million Americans have consumed food derived from GM crops, without a single tort in the most litigious society in history".[14]

Acknowledgment

Adrian Dubock is an independent consultant who specializes in agricultural development in developing countries. He has 30 years of global experience in the agricultural input business for Syngenta. For 15 years he was also a sheep farmer in the United Kingdom. He is a member of the Humanitarian Board for Golden Rice (http://www.goldenrice.org). He resigned as an author of the World Bank-led, International Assessment of Agricultural Science [knowledge] and Technology for Development project (IAASTD) because of the lack of recognition of the importance of all agricultural technology – not just biotechnology – for food productivity, especially in the poorest countries.

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