


Review on Genetic Engineering and Omitted Health Research

Mastewal Birhan , Muluken Yayeh and Amebaye Kinubeh

Department of Veterinary Paraclinical Studies, College of Veterinary Medicine and Animal Sciences, University of Gondar, Gondar, Ethiopia

Corresponding author's Email: maste675@gmail.com; ORCID: [0000-0002-0984-5582](https://orcid.org/0000-0002-0984-5582)

ABSTRACT

Central to the development of green lifestyles is the consumption of foods that by dint of their status as chemical free locally produced and/or free of genetically modified ingredients, reduce the environmental impact of food provision. Yet there are many other factors, such as health concerns, that may also encourage the consumption of 'green' foods. Commercialization of genetically modified organisms has sparked profound controversies concerning adequate approaches to risk regulation. Scientific uncertainty and ambiguity, omitted research areas, and lack of basic knowledge crucial to risk assessments have become apparent. A major conclusion is that the void in scientific understanding concerning risks posed by secondary effects and the complexity of cause-effect relations warrant further research. Initiatives to approach the acceptance or rejection of a number of risk-associated hypotheses are badly needed. Further, since scientific advice plays a key role in genetically modified organism's regulations, scientists have a responsibility to address and communicate uncertainty to policy makers and the public. Hence, the acceptance of uncertainty is not only a scientific issue, but is related to public policy and involves an ethical dimension.

Original Article

PII: S225199391800013-8

Rec.	22 Jul	2018
Rev.	15 Aug	2018
Pub.	25 Sep	2018

Keywords

Chemical,
Foods,
Genetically,
Health,
Organisms,
Risk

INTRODUCTION

The world has been flooded with a vast amount of the writings and actions of root-and-branch proponents and opponents of genetic modification. There has also been a proliferation of arguments about differing philosophies of regulation and labeling [1].

Biotechnology has been applied as one of the eco-techno-political technologies in the 21st century. Many countries have developed their technological strategies to improve their productivity in different fields. In developing countries scientific and technological bases are weak and infrastructures are not strong [2]. The formation of new biotechnology firms is mostly a strategic response rather than based on a real appreciation of environmental threats. It is maintained that the applications of this technology provide potential contributions to sustainable agricultural productivity and new inputs for resource-poor and small-scale farmers [3].

Since the second half of the 1980s, when the first genetically modified (GM) organisms were introduced for the industrial production of medicinal products, there has been a heated debate over the applications of gene technology. To date, however, the debate has failed to clarify an agreed direction of policy, and has instead run into stalemate. Sharply opposed parties of stakeholders and experts characteristically advocate conflicting opinions. For the moment, the public is left on the sidelines, while scientists, stakeholders, and other experts are in dispute [4].

Environmental factors including damage from insects and competition with weeds for resources necessary to support growth contribute to decreased yield from field crops. Historically, synthetic insecticides have been used for protection of plants from insect damage and herbicides have been used to control weeds. While they have been effective, more recent developments have applied the tools of biotechnology to produce genetically modified (GM) crops for insect and weed control. Early generation GM crops including insect resistant maize and herbicide tolerant soybeans express proteins from foreign sources that endow them with these particular phenotypes. They have been cultivated in the United States for nearly 20 years with significant

benefits including decreased use of pesticides and herbicides, yield increases, decreased labor costs and improvements in quality [5].

In recent years, the use and release of genetically modified organisms (GMOs) has been an issue of intense public concern and, in the case of foods, products containing GMOs or products thereof carry the risk of consumer rejection. The World Health Organization (WHO) defines GMOs as those organisms in which the genetic material has been altered in a way that does not occur naturally [6]. As genetically modified (GM) foods are starting to be present in our diet concerns have been expressed regarding GM food safety [7]. Although the WHO declares that the GM products that are currently on the international market have all gone through risk assessment by national authorities, the risk assessment of GM foods in general, and crops in particular for human nutrition and health, has not been systematically performed as indicated in the scientific literature [8]. Therefore, the aim of this review, I tried to summarize the current status, available evidence, and present several clinical and nonclinical data concerning mainly the use of genetically modified organisms and their impacts in the treatment of different industrial foods, highlighting both the opportunities and the limitations of genetic engineering and omitted health research.

DO WE KNOW THAT ANY GENETIC ENGINEERING FOOD IS SAFE FOR CONSUMPTION?

Based on the idea that any genetic information from any source can be expressed in any organism, genetic engineering has, for example, looked at improving the protection of agricultural crops. Other sought advantages include shortening the delay to obtain a new variety, improving the yield and quality of crops, producing high value-added molecules (like pharmaceuticals or vitamins or biopolymers for industry), and improving the nutritional quality of plants [9]. In general this process consists of three different steps:

1. Detection (screening of GMOs) in order to gain a first insight into the composition of the food and agricultural product.
2. Identification to reveal how many GMOs is present, and if so, whether they are authorized within the EU (or other countries with regard to their regulations). A prerequisite for the identification of GMOs is the availability of detailed information on their molecular make-up.
3. Quantification, in order to determine the amount of one or more authorized GMOs in a product or seed lot, and to assess compliance with the threshold regulation. For this approach it is necessary to get a better understanding of DNA/protein degradation during processing and of the robustness of the analytical methods [10].

Safety evaluation strategies

At an early stage in the introduction of recombinant-DNA technology in modern plant breeding and biotechnological food production systems, efforts began to define internationally harmonized evaluation strategies for the safety of foods derived from genetically modified organisms (GMOs) [11].

Two years after the first successful transformation experiment in plants (tobacco) in 1988, the International Food Biotechnology Council (IFBC) published the first report on the issue of safety assessment of these new varieties. The comparative approach described in this report has laid the basis for later safety evaluation strategies. Other organizations, such as the Organization for Economic Cooperation and Development (OECD), the Food and Agriculture Organization of the United Nations (FAO) and the World Health Organization (WHO) and the International Life Sciences Institute (ILSI) have developed further guidelines for safety assessment which have obtained broad international consensus among experts on food safety evaluation [12].

ADVANTAGES AND DISADVANTAGES

GM Crops

The main advantage of GM food crops is their potential promise of future food security, especially for small-scale agriculture in developing countries. The main arguments of GM supporters are safe food security, improved food quality, and extended shelf-life as the reasons why they believe in GM crops which will benefit not only both consumers and farmers, but also the environment [13].

As Belcher *et al* discuss, a critical question is what impact(s) biotechnology companies should take into their account. For example, in corn, the productivity impact is mainly yield increase, and in soybeans the GM

technology allows saving on inputs of chemicals and labor. Moreover, the companies claim that GM technology will promote food security while they are also healthier, cheaper, and more stable. Yet, the nutrients will have more quality and better taste. The issue is the impact of international regulations on the food situation in the developing countries. In these countries, approximately 800 million people remain seriously malnourished, including at least 250 million children [14].

One main debate and disagreement has already been made on the claim that biotechnology can potentially help developing countries to go for such advances as higher yields while shorter growing duration, asking for less chemical fertilizers, advanced pest management, higher drought resistance, and increased nutrients quality. Such advantages of GM crops would mitigate public hesitation about GM technology [15]. Some also acknowledged the potential of plant biotechnology to improve plant breeding and crop production in developing countries.

In 2006, global cultivation of genetically modified (GM) crops exceeded 100 million hectares for the first time. In the European Union (EU), the only GM crop that is currently cultivated is Monsanto's maize event MON810, which is resistant to the European and Mediterranean corn borer. Throughout 2006 and 2007, the area planted with GM maize almost doubled, reaching the 100 thousand hectare milestone, spread over six countries. Despite this enthusiasm, GM maize plantings still cover less than 2% of the total EU maize cultivation area. With this evolution, the question now arises of whether GM crops can 'coexist' with conventional and organic farming while still preserving freedom of choice for consumers [16].

The same processes are also wiping out small efficient family farms and replacing them with inefficient and unhealthy industrialized food systems under multi-national agribusiness corporations. Such corporations are supposed to increase production of food, increase efficiency of food production, improve the economic situation of farmers and improve patterns of food consumption. However, the evidences point to the opposite direction. In fact, the beneficiaries of such corporations are neither farmers nor governments of in the South, but making more money for the North, as Senator McGovern of the US Senate had stated, "Food security in private hands is no food security at all" because corporations are in the business of making money, not feeding people [17].

Nevertheless, the critics of genetic engineering of foods have concerns, not only for safety, allergenicity, toxicity, carcinogenicity, and altered nutritional quality of foods, but also for the environment. In this context, it would be interesting to note that the recent research has contested the claims of reduced pesticide use by genetically modified cotton (Bt cotton) due to the rise of secondary pests (other than the main cotton pest the bollworm).

Evolution of insect resistance threatens the continued success of transgenic crops producing *Bacillus thuringiensis* (Bt) toxins that kill pests. The approach used most widely to delay insect resistance to Bt crops is the refuge strategy, which requires refuges of host plants without Bt toxins near Bt crops to promote survival of susceptible pests [18].

Transgenic crops producing *Bacillus thuringiensis* (Bt) toxins kill some key insect pests and thus can reduce reliance on insecticides. Widespread planting of such Bt crops increased concerns that their usefulness would be cut short by rapid evolution of resistance to Bt toxins by pests [19]. However, economic performance is highly variable and seems dependent more on the market characteristics, support structures and culture of the systems in which Bt crops are deployed than on the Bt crops themselves. Given their specificity for key target pests and well demonstrated lack of impact on beneficial insects, Bt crops provide an important new platform for sustainable IPM systems, one that is compatible with a full range of other tactics [20]. These results were confirmed in a recent research, based on a survey of 1000 cotton farm households in China. It was then found that farmers have perceived a strong increase in secondary pests after Bt cotton was introduced [21].

Organic Farming

The recent growth in organic farming has given rise to the so-called "conventionalization hypothesis," the idea that organic farming is becoming a slightly modified model of conventional agriculture [22]. Concurrently, it avoids chemical [23], which are generally expensive for small-scale farmers who have a livelihood farming system and earn normally much less than large-scale farmers who can afford expensive technologies. Additionally, small farmers cannot easily eliminate the harmful effects of chemicals which normally need big funds to deal with. Yet, there is a fair amount of debate on whether or not it is a lower-cost technology [24], and promotes [25]. Another matter of debate is production costs which can potentially be increased by the adoption of, more specially, if major soil protection or restoration activities are needed. For instance, if farmers need to

control weeds mechanically, they may need bigger funds to buy or rent such vehicles than chemical ways. Although in other cases, they might be able to reduce the costs through biological ways of control [26].

COULD GENETIC ENGINEERING FOOD CAUSE ALLERGIES?

Safety Assessment of Proteins Used in GM Crops

Candidate proteins to be expressed in GM crops are compared and contrasted with proteins that are allergenic or toxic using a weight of evidence approach consisting of individual and independent studies. None of the individual studies or data is necessarily more or less important than the others when considered in the context of weight of evidence but typically numerous studies are conducted.

Allergenicity

In the US, it has been estimated that 6–8% of children and 1–2% of adults are allergic to one or more foods [27]. The percentage decreases with age as many people outgrow the allergy. The incidence of food allergy outside of the US is unknown. Based on the US population, it is also known that the majority of food allergies are attributable to a relatively small number of foods that include peanuts, soybeans, cow's milk, eggs, fish, shell fish, wheat and tree nuts. Many other foods have also been reported to cause allergic reactions though the frequency of these sensitivities is much lower [28].

Persons that are allergic to particular foods possess antibodies to certain proteins present within those foods and the primary method of treating food allergies is for the allergic person to simply avoid consuming them. Much is known about the particular proteins in foods to which persons are sensitive and they are often referred to as allergenic proteins. This is not necessarily a technically accurate appellation since it implies that these proteins present some risk of allergic reactions in anyone when in fact they only present a risk in persons that are sensitive to them. Nevertheless, key learning about these proteins have been applied to the safety assessment of foods from GM crops. In particular, safety assessments are designed to ensure that the developer did not select a protein to which a sensitive person could be exposed to unknowingly. Potential for allergenicity is assessed for proteins to ensure that they are not similar enough to cross react with the antibodies present in persons with food allergies.

The source of the proteins is an important criterion in selection of candidate proteins. This is one component of the safety assessment for individual proteins called History of Safe Use [29]. However, each situation needs to be considered on a case-by-case basis. For example, peanuts may not be the best source for proteins to be used in GM crops like maize or soybeans simply because peanuts are known to possess more than one allergenic protein [30]. Regardless of the identity of the individual protein there would likely be concerns that any protein from peanuts could possibly be allergenic. Alternatively, if a protein from peanuts were to be selected to be expressed in a GM peanut plant then no new hazard has been introduced with regard to potential allergenicity.

Toxicity

In addition to allergenicity, some proteins are known to exist in nature that is capable of causing adverse effects when consumed. Though many are found in venomous snakes and insects or are produced by pathogenic bacteria, there are some that are found in plants such as kidney bean lectin and ricin [31]. Accordingly, proteins used in GM crops have also been assessed for potential to cause adverse effects if for no other reason that they too are proteins. There are obvious overlaps in the methods used to assess the potential toxicity and allergenicity of proteins.

Specifically, consideration of history of safe use of the source of the protein, bioinformatics comparison to known protein toxins, and *in vitro* resistance to digestive [32]. The primary basis of these considerations being that proteins selected from sources that are not known to produce toxic proteins, are not similar in sequence to known protein toxins, and are readily degraded in the presence of digestive enzymes are unlikely to be toxins.

There are differences in the bioinformatics analysis compared with the allergenicity assessment to note. First, there are no predefined criteria that identify a "match" between two proteins such as the 35% identity over 80 amino acid sequences for allergenic proteins. Second, there is currently no annotated and updated database in which the sequence of protein toxins is maintained [33]. Rather, what is commonly conducted is a comparison to all known protein sequences in the NCBI BLAST database [34, 35] followed by manual inspection

to determine if sequence similarities are present. Consideration of these data provides strong evidence for whether the protein intended for use in a GM crop is likely to introduce a hazard [36].

CONCLUSION

It is indeed hard to give a straight answer or simple solution on how food insecurity is being solved. Due to the possibilities offered by GM technology in this new century, societies will need to make some important choices about the type of world that they wish to build up. The politicians in the developing countries are recently faced by a crucial question on how GM technology should be viewed in relation to off. It has been estimated that hunger affects an estimated 1 billion people many of whom live in countries with developing economies. Population growth and decreased availability of arable land will continue to confound this issue. Modern biotechnology has the potential to be a significant tool in fighting hunger as it has been well established to address agricultural problems such yield loss from insect infestation, competition with weeds, and even drought. Biotechnology has been used to improve the quality and yield of field crops in many parts of the world for more than 20 years. It is more specific and relatively fast in development compared with traditional breeding techniques. A comprehensive safety assessment has been conducted on GM crops before the products are commercialized that includes evaluation of proteins used in these crops for potential allergenicity and toxicity as well as analysis of the composition of the crop and often feeding studies in rodents and livestock species in support of demonstrating substantial equivalence.

DECLARATIONS

Authors' contributions

MB, MY and AK conceived the review, coordinated the overall activity, and reviewed the manuscript.

Acknowledgment

The authors' heartfelt thanks will also go to University of Gondar for recourse supporting.

Availability of data and materials

Data will be made available up on request of the primary author

Consent to publish

Not applicable.

Competing interests

The authors declare that they have no competing interests.

REFERENCES

1. Blanchfield, J., Genetically modified food crops and their contribution to human nutrition and food quality. *Journal of food science*, 2004. 69(1).
2. Hsu, Y.-G., J.Z. Shyu, and G.-H. Tzeng, Policy tools on the formation of new biotechnology firms in Taiwan. *Technovation*, 2005. 25(3): p. 281-292.
3. Huang, J., et al., Plant biotechnology in China. *Science*, 2002. 295(5555): p. 674-676.
4. Borch, K. and B. Rasmussen, Refining the debate on GM crops using technological foresight—the Danish experience. *Technological Forecasting and Social Change*, 2005. 72(5): p. 549-566.
5. Brookes, G. and P. Barfoot, Global impact of biotech crops: socio-economic and environmental effects, 1996-2006. 2008.
6. Organization, W.H., Foods derived from modern technology: 20 questions on genetically modified foods. Available here, 2002.
7. Dona, A. and I.S. Arvanitoyannis, Health risks of genetically modified foods. *Critical reviews in food science and nutrition*, 2009. 49(2): p. 164-175.
8. Domingo, J.L., Toxicity studies of genetically modified plants: a review of the published literature. *Critical reviews in food science and nutrition*, 2007. 47(8): p. 721-733.
9. Gachet, E., et al., Detection of genetically modified organisms (GMOs) by PCR: a brief review of methodologies available. *Trends in food science & Technology*, 1998. 9(11-12): p. 380-388.
10. Anklam, E., et al., Analytical methods for detection and determination of genetically modified organisms in agricultural crops and plant-derived food products. *European Food Research and Technology*, 2002. 214(1): p. 3-26.
11. Conner, A.J., T.R. Glare, and J.P. Nap, The release of genetically modified crops into the environment. *The Plant Journal*, 2003. 33(1): p. 19-46.

12. Kuiper, H.A., et al., Assessment of the food safety issues related to genetically modified foods. *The plant journal*, 2001. 27(6): p. 503-528.
13. Wisniewski, J.-P., et al., Between myth and reality: genetically modified maize, an example of a sizeable scientific controversy. *Biochimie*, 2002. 84(11): p. 1095-1103.
14. Liddle, B., Demographic dynamics and per capita environmental impact: Using panel regressions and household decompositions to examine population and transport. *Population and Environment*, 2004. 26(1): p. 23-39.
15. Soregaroli, C. and J. Wesseler, Minimum distance requirements and liability: implications for co-existence. 2005.
16. Demont, M. and Y. Devos, Regulating coexistence of GM and non-GM crops without jeopardizing economic incentives. *Trends in Biotechnology*, 2008. 26(7): p. 353-358.
17. Godfray, H.C.J., et al., Food security: the challenge of feeding 9 billion people. *science*, 2010. 327(5967): p. 812-818.
18. Tabashnik, B.E., et al., Insect resistance to Bt crops: evidence versus theory. *Nature biotechnology*, 2008. 26(2): p. 199.
19. Tabashnik, B.E., T.J. Dennehy, and Y. Carrière, Delayed resistance to transgenic cotton in pink bollworm. *Proceedings of the National Academy of Sciences*, 2005. 102(43): p. 15389-15393.
20. Fitt, G.P., Have Bt crops led to changes in insecticide use patterns and impacted IPM?, in *Integration of insect-resistant genetically modified crops within IPM programs*. 2008, Springer. p. 303-328.
21. Ho, P. and D. Xue, Ecological change and secondary pests in Bt cotton: a survey of 1, 000 farm household in China. *Int J Environ Sustain Dev*, 2008. 7(4): p. 396-417.
22. Best, H., Organic agriculture and the conventionalization hypothesis: A case study from West Germany. *Agriculture and human values*, 2008. 25(1): p. 95-106.
23. Mäder, P., et al., Soil fertility and biodiversity in organic farming. *Science*, 2002. 296(5573): p. 1694-1697.
24. Lampkin, N., *Organic farming*. 1990: Farming press books.
25. Hole, D., et al., Does organic farming benefit biodiversity? *Biological conservation*, 2005. 122(1): p. 113-130.
26. Closter, A., et al., *Organic farming and genetically modified crops in relation to food security*. Henning Høgh Jensen Publication, 2004.
27. Sampson, H.A., Update on food allergy. *Journal of Allergy and Clinical Immunology*, 2004. 113(5): p. 805-819.
28. Hefle, S.L., J.A. Nordlee, and S.L. Taylor, Allergenic foods. *Critical Reviews in Food Science & Nutrition*, 1996. 36(S1): p. 69-89.
29. Constable, A., et al., History of safe use as applied to the safety assessment of novel foods and foods derived from genetically modified organisms. *Food and Chemical Toxicology*, 2007. 45(12): p. 2513-2525.
30. De Jong, E., et al., Identification and partial characterization of multiple major allergens in peanut proteins. *Clinical and Experimental Allergy*, 1998. 28(6): p. 743-751.
31. Rossi, M., J. Mancini Filho, and F. Lajolo, Jejunal ultrastructural changes induced by kidney bean (*Phaseolus vulgaris*) lectins in rats. *British journal of experimental pathology*, 1984. 65(1): p. 117.
32. Delaney, B., et al., Evaluation of protein safety in the context of agricultural biotechnology. *Food and Chemical Toxicology*, 2008. 46: p. S71-S97.
33. Ladics, G.S., et al., Bioinformatics and the allergy assessment of agricultural biotechnology products: industry practices and recommendations. *Regulatory Toxicology and Pharmacology*, 2011. 60(1): p. 46-53.
34. Hileman, R.E., et al., Bioinformatic methods for allergenicity assessment using a comprehensive allergen database. *International archives of allergy and immunology*, 2002. 128(4): p. 280-291.
35. Altschul, S.F., et al., Basic local alignment search tool. *Journal of molecular biology*, 1990. 215(3): p. 403-410.
36. Gendel, S.M., Sequence analysis for assessing potential allergenicity. *Annals of the New York Academy of Sciences*, 2002. 964(1): p. 87-98.