GENETICALLY MODIFIED FOOD CROPS AND PUBLIC HEALTH

Cultivos alimenticios genéticamente modificados y salud pública

ORLANDO ACOSTA[1], Ph. D.; ALEJANDRO CHAPARRO[2], Ph. D.
Departamento de Ciencias Fisiológicas, Facultad de Medicina
/Instituto de Biotecnología, Universidad Nacional de Colombia,
Bogotá, Colombia. oacostal@unal.edu.co
Departamento de Biología, Facultad de Ciencias, Universidad Nacional
de Colombia, Bogotá, Colombia. achaparrog@unal.edu.co

ABSTRACT

The progress made in plant biotechnology has provided an opportunity to new food crops being developed having desirable traits for improving crop yield, reducing the use of agrochemicals and adding nutritional properties to staple crops. However, genetically modified (GM) crops have become a subject of intense debate in which opponents argue that GM crops represent a threat to individual freedom, the environment, public health and traditional economies. Despite the advances in food crop agriculture, the current world situation is still characterised by massive hunger and chronic malnutrition, representing a major public health problem. Biofortified GM crops have been considered an important and complementary strategy for delivering naturally-fortified staple foods to malnourished populations. Expert advice and public concern have led to designing strategies for assessing the potential risks involved in cultivating and consuming GM crops. The present critical review was aimed at expressing some conflicting points of view about the potential risks of GM crops for public health. It was concluded that GM food crops are no more risky than those genetically modified by conventional methods and that these GM crops might contribute towards reducing the amount of malnourished people around the world. However, all this needs to be complemented by effective political action aimed at increasing the income of people living below the poverty-line.

Key words: biofortification, genetically modified food, public health, risk assessment.

RESUMEN

El progreso de la biotecnología de plantas ha hecho posible ofrecer una oportunidad para desarrollar nuevos cultivos alimenticios con características deseables para el mejoramiento de la producción, la reducción del uso de agroquímicos y la incorporación de propiedades nutricionales en cultivos básicos. No obstante, los cultivos GM se han convertido en un objeto de intenso debate, en el cual los opositores argumentan que los cultivos GM representan una amenaza para la libertad individual, el medio am-

biente, la salud pública y las economías tradicionales. A pesar de los avances en la agricultura de los cultivos alimenticios, la situación actual a nivel mundial está caracterizada por una hambruna masiva y por una desnutrición crónica, lo cual constituye un importante problema de salud pública. Los cultivos GM biofortificados se han considerado como una estrategia importante y complementaria para suministrar alimentos básicos naturalmente fortificados a las poblaciones con desnutrición. Las recomendaciones de los expertos y las preocupaciones públicas han conducido al diseño de estrategias para la evaluación de los riesgos potenciales de la producción y el consumo de los cultivos GM. El objetivo de la presente revisión crítica es la exposición de algunos puntos de vista en conflicto sobre los riesgos potenciales de los cultivos GM para la salud pública. Se concluye que los cultivos alimenticios GM no son más riesgosos que aquellos modificados genéticamente con los métodos convencionales, y que estos cultivos GM podrían contribuir a la reducción de la población con desnutrición en el mundo, pero se necesita que esto sea complementado con acciones políticas efectivas dirigidas a incrementar los ingresos de la población que vive por debajo de la línea de pobreza.

Palabras clave: alimentos genéticamente modificados, biofortificación, evaluación de riesgos, salud pública.

INTRODUCTION

Farmers have successfully resorted to genetically improving their crops through deliberated plant breeding for thousands of years, although its scientific basis was not established until classical Mendelian genetics were rediscovered in the early twentieth century (Robinson, 1999; Uzogara, 2000). Such classical or conventional technology has been the major contributor towards maintaining food supplies during post-World War II decades, noticeably increasing crop yields, particularly seen in intensive agriculture of developed countries. For millennia, the traditional plant breeding practices of farmers have led to altering the genetic constitution and evolution of crops. In this sense, farmers have been considered to be the first genetic engineers (Jones, 1994; Prakash, 2001). The earliest evidence of agricultural practices dates from 10 thousand years ago in the part of the world now known as Iraq (Heiser, 1990).

Research concerning the molecular and genetic mechanisms underlying important agronomic traits has provided strong support for crop biotechnology in recent years. Advances accumulated in molecular and cell biology during the last three to four decades have revolutionised modern genetic improvement of crop cultivars. Recombinant DNA technology, DNA sequencing from genes, using DNA markers for constructing genetic maps, designing PCR-based methods for selecting and characterising genes, and DNA transfer technologies between different species have all laid the foundations for the modern production of the genetically-engineered plants and crops currently on the market (Conner & Jacobs, 1999).

The biotechnology industry (mainly based in developed countries) has rapidly developed food and agricultural products, besides other products in the fields of human health, industrial processing and bioremediation. Livestock resulting from biotechnology was

first reported over 30 years ago in the form of animal clones and later on as transgenic animals. Genetically modified (GM) animals have been produced to improve animal health, increase zootechnic performance, reduce the environmental impact of animal production or produce biopharmaceutical products. None of them has entered the market as food or fibre; however, livestock products from biotechnology are now challenging science, regulators and the public to move into food and fibre markets (Rexroad *et al.*, 2007; Kochhar & Evans, 2007).

Although the benefits of transgenic technology are potentially enormous, scientists, commerce, politicians, trade protectionists, environmentalists, religious rights' groups, consumers and the media are still involved in fierce debate about using this particular kind of agricultural biotechnology (Acosta, 2002; Margulis, 2006). Many potentially beneficial traits may be introduced into GM crops, such as enhanced pest- and disease-resistance and herbicide tolerance, reduced fertiliser and water requirements, enhanced nutritional value, extended shelf-life, improved flavour, modified aesthetic and ornamental characteristics, the elimination of naturally-expressed toxins and allergens, bioremediation and the production of pharmaceuticals (bio-factories) (Fischer & Emans, 2000; Singh *et al.*, 2006; Taylor *et al.*, 2006). This paper provides an overview concerning the debate regarding the safety of GM food crops. The material presented leads to the conclusion that the process used in producing GM food crops and current sound-science based methods used in assessing their safety make them no more risky for the public health than conventionally-bred crop varieties.

The Debate

Intense debate concerning GM crops has been prolonged in different sceneries during the last couple of decades, involving a wide variety of actors. It should be stressed that this debate be informed by sound-scientific data, information and knowledge to contribute to a productive GM crop debate; however, philosophical points of view are as important as scientific ones in such debate (Thro, 2004). Philosophical issues and value judgments have been recently addressed and discussed regarding the claim that environmental risks concerning GM and conventional crops are comparable on scientific grounds (Thompson, 2003). These value judgments (present in part of the discussion) incorporate assumptions associated with political, economic and ethical issues which would not be easily resolved by scientific experimentation. Even the politics of food safety (a very controversial field) incorporates philosophical problems associated with the way scientific and policy issues should interact (i.e. there is discussion about how food safety policy-making should be scientifically and democratically legitimated; Millstone, 2007).

Groups opposing GM crops have presumed that conventional crops do not represent risks for the environment and food safety and, as such, new crop varieties produced by conventional methods are not controlled by a regulatory environmental system. On the contrary, transgenic crops have been associated with negative and harmful effects on the environment and human health, no matter whether science-based evidence has been available or not. Those arguing for the comparability of environmental risks of GM and conventional crops have assumed that crops which have been genetically modified by either transgenic technology or conventional methods are similar in terms

of risks, traits and purposes (Thompson, 2003). In fact, transgenes incorporated into transgenic crops have produced traits which are essentially the same as those desirable agronomic traits which have been targeted by conventional breeding programmes. Crop development thereby becomes a continuous process of introducing novel traits where transgenic technology is a new stage following and coexisting with conventional crossbreeding. Assessment policy regarding environmental risks is thus being based on the product rather than the process (Brill, 1985; Brill, 1986).

The fears of the people opposing the technology producing GM crops are associated with a wider spectrum of issues (Uzogara, 2000; Prakash, 2001; Pengue, 2004; Singh *et al.*, 2006) including the feeling that transnational companies are more interested in increasing their profits than in protecting the environment or alleviating hunger, the possibility that transgenic crops may invade wild ecosystems with detrimental effects on biodiversity, the unfair competition with other agricultural systems such as organic, agro-ecological and traditional ones, the negative effects that GM food might produce on human health, the possible negative impact of GM crops on food supply safety, and a lack of trust in the agencies responsible for regulating GM crop biosafety. Critics of GM crops argue that transgenic technology has serious implications for farmers in developing countries as this foreign multinational technology may destroy farmers' competencies built around indigenous agricultural systems, thereby exacerbating social exclusion in the case of subsistence farmers (Hall *et al.*, 2008). They also warn that multinationals do not take into account that transgenic technology might have broad social and ethical implications. Controversy concerning GM crops also involves issues related to the globalisation of agro-food systems and its effects on food safety, social equity and rural agricultural systems (McAfee, 2008). In some countries (such as Mexico) this dispute has been extended to include regional economic integration which has been considered to implicate asymmetric and disadvantageous power relationships in opening up markets around the world. However, most public concerns about GM food crop safety are generally related to human health, consumer choice and environment (Uzogara, 2000; Singh *et al.*, 2006; Moyer & Anway, 2007).

Allegations regarding potential environmental harm have been based on possible cross-pollination of wild plants with GM pollen, killing beneficial insects and producing new weeds which are resistant to current control. However, the US EPA has concluded that the existent statutory and regulatory framework has suitably addressed environmental concerns raised by GM crops; the US FDA has recognised that food produced by transgenic technology is safe and, therefore, has considered that labelling this kind of food is not necessarily required (Moyer & Anway, 2007). US policy concerning GM crops (as opposed to that of the European Commission) states that GM crops should be allowed to prosper in the absence of scientifically-proven hazards. The debate also includes the use made by the USA of modern genetic engineering to achieve its goals in the plant-based bioeconomy, where plants are seen to be a source of fuel, energy and other industrial chemical precursors, besides traditional uses of agricultural crops for food, animal feed and fibres (Chapotin & Wolt, 2007).

Some non-GM movements have seemed to express their desire to change market structures and capitalism as a whole. Nevertheless, their tactics against transgenic crops and foods often strengthen and reproduce the very structures they are trying to

change rather than promoting sustainable agriculture. Roff, 2007, has advanced an interesting analysis of such contradictory behaviour by antibiotech activists; according to this analysis, many antibiotech groups have been promoting neoliberal logic as they have focused on the contemporary markets as the best way of ensuring alternative agriculture. Their tactics remain focused on what can be done at the commodity level. There is emergent discourse regarding individualism and consumer freedom as a means to interfere the practices of food manufacturers. This means that the more you buy the more pressure is placed on manufactures to change their practices. As a result, market-based activism provides a space for rent-seeking practices of food manufactures. Roff, 2007, emphasises that consumerism does not guarantee alternative sociologies, economies and agriculture espoused by current food movements.

Although the non-GM movement criticises the state to some extent, the most common tactics encourage consumers to act through their money in buying non-GM foods; this therefore indicates that desired changes come primarily from the market rather than the legislature. Neoliberalisation of antibiotech activism is transferring state and food manufacture responsibility to individual consumers; neoliberalising logic thus states that non-GM activism empowers the market rather than the state. The market thus becomes the final judge of social and environmental quality, reinforcing the ideology of competitive advantage and free market rationality (Roff, 2007). The state and manufactures are thus not responsible for food quality as they only respond to what consumers want (Roff, 2007).

Despite fierce opposition to GM crops (or partly as a consequence of such opposition), several countries have managed to develop science-based biosafety regulatory systems. Scientific bodies have recently proposed guidelines for assessing the nutritional value and safety of GM crop-derived feed and food (OECD, 2003; ILSI, 2003; 2004; EFSA, 2004); there is also a regulatory framework for GM crops and food encompassing principles of risk analysis, institutions, policy, laws and guidelines (Konig *et al.*, 2004). Effective risk assessment and monitoring mechanisms are essential prerequisites for any regulatory framework to properly address the potential risks of GM crops (Singh, *et al.*, 2006).

Regulations and restrictions on GM crops have been considered as obstacles which must be reduced to allow the world's population to take complete advantage of what such technology is offering (Potrykus, 2001; Pawlak, 2005). Some have concluded that unnecessary restrictions and regulations are still in force, partially due to demands from anti-genetically modified organism (GMO) organisations, such as Greenpeace, 2005, or they have been strongly influenced by consumer perceptions (Kleter *et al.*, 2001). Anti-GMO campaigns against poor and malnourished people using GM crops and food (even when multinational companies do not benefit) might be seen to be inconsistent with the interests of those whom non-GM activism tries to fight for (Potrykus, 2001). It should be stressed that the remarkable public debate and sound-scientific discussion on the safety of GM crops has resulted in introducing compulsory risk assessment of these crops; some accurate molecular tools have been produced for use in large-scale screening of GM crops as part of such assessment protocols (Made *et al.*, 2006; Jeong *et al.*, 2007). However, non-scientific criticism of GM crops will doubtless delay productivity-enhancing biotechnology applications being developed in less developed economies.

Although GM crops have been subjected to intense controversy they are now grown in a number of countries in which more than half the world's population lives. Ten years after the commercial introduction of GM crops their world-wide area had reached more than 102 million hectares (252 million acres) by 2006 and the number of farmers growing these crops had exceeded 100 million (ISAAA, 2006; Brookes & Barfoot, 2006). It seems to be that the obvious advantages of transgenic technology for improving agronomic performance and yield of crops have encouraged extensive GM crop growing. GM crops have therefore been the most rapidly adopted technology in the history of agriculture (Halpin, 2005). Although the USA is the leading country in transgenic technology research and development, more than half the 63 countries engaged in biotech research belong to the developing world (Acosta, 2000; Newell-McGloughlin, 2006), China being foreseen as the future leader in GM crops (Oliver & Hankins, 2007).

FOOD AND THE GLOBAL POPULATION

The world's population exceeded the 6 billion mark at the end of the twentieth century. This means that the global population more than doubled during the second half of the twentieth century. It has been predicted that the planet will have around 7.5 billion people on it by 2020, rising to 9 to 10 billion by 2050. Most of this growth is supposed to occur in poor countries, where 80% of the world's population is currently living. It has been estimated that demand placed on world agricultural production by 2050 will double, assuming moderately high income growth taken together with expected population growth (Johnson, 2000; United Nations, 2001; Ruttan, 2002).

However, rigorous investigation must be carried out within the context of producing enough food to feed the world to establish the relative contributions of all forms of available agriculture, including transgenic crops, organic agriculture, agroecology and other forms of traditional agriculture (Lacey, 2002). Some authors have anticipated that the supply of organic products will not be able to meet future demand, which would lead to such shortfall being filled by conventional non-GM crops at a cheaper price (Roff, 2007). This means that if the organic alternative is taken, then the increasing demand for large acreage crops would cause the weakening of conventional crops' quality standards (Roff, 2007). Although transgenic technology could contribute towards resolving crop deficiencies, it does not mean that all agriculture should become transgenic.

Resolving the low productivity, poverty and difficulties which resource-poor farmers are facing (mainly in developing countries) would require several strategies and policies. Hunger and poverty in developing countries may not be resolved simply by increasing world food production and productivity. In fact, today's world food production is greater than that required to feed all the people living on the earth, but there are more hungry people in the underdeveloped world today than there were in 1996. The number of undernourished people was estimated to be 820 million in 2003 and it has been increasing since then at the rate of four million per year (FAO, 2004). Although poverty in terms of household income has fallen worldwide since 1990 (except in sub-Saharan Africa) 2.8 billion people are currently living on less than two dollars a day and 1.3 billion are living in a situation of even more extreme poverty, surviving on the equivalent of less than one dollar a day; this means that about half the world's population is trying to survive below the poverty threshold of two

dollars a day (UNDP, 2006). Developing countries' hunger and poverty thus also involve environmental, demographic, social, economic, political and cultural factors which need to be addressed and resolved. Institutional factors are as important as transgenic technology performance (Raney & Pingali, 2007). Transgenic technology potential for providing enough, safe and effective food to alleviate hunger needs to be complemented with effective political action aimed at pursuing the moral obligation of providing the hungry with sufficient nourishment (Carter, 2007).

Some information indicates that per capita cereal grain production has been declining since 1984 due to rapid population growth and the per capita decline of cropland, irrigation and the use of fertilisers (Pimentel *et al.*, 2000). Increased food production to satisfy a growing world population should not be done at the expense of incorporating new land for agricultural purposes. Without disregarding some potential crop-producing land, an increase in food must come mainly from increasing the productivity of land currently being cultivated. Those countries at the technological frontier (which have reached their highest performance in terms of agricultural productivity) will thus probably have little difficulty in accomplishing the production levels needed to satisfy their slowly rising demand for food (Ruttan, 2002). On the other hand, advances in transgenic technology for countries which are far from approaching the scientific and technological frontiers of agricultural productivity could represent an opportunity for improving their rate of crop productivity. Pre- and post-harvest crop losses in tropical and subtropical developing countries caused by pests, disease, low quality soil and poor storage facilities are exacerbated by climatic conditions and a lack of economic resources for purchasing improved seed, fertilisers and insecticides. GM crops are therefore seen to be very promising in increasing agricultural productivity in developing countries, where transgenic technology can be applied to different crops without implying major changes in subsistence farmers' agricultural practices (Herrera-Estrella, 2000).

BIOFORTIFICATION

Improving food crops to provide better nutrition for humans and livestock has been a major long-term aim of traditional breeding programmes. Biofortification (an approach consisting of bred food crops producing high bio-available nutrient concentrations in some of their edible tissues) has been presented as a promising alternative for fighting malnutrition in poor countries. Iron, vitamin A, zinc and iodine deficiencies are of the greatest public health importance as they represent a serious threat to the health and productivity of more than one-half of the world's population, women and children being most exposed to such micronutrient deficiencies (Darnton-Hill, 1998; United Nations, 2004). Vitamin A deficiency (VAD) is one of the leading causes of micronutrient malnutrition in less industrialised countries, annually causing about half a million children to become partially or totally blind (Conway & Toenniessen, 1999; West, 2002) and claiming 3,000 lives every day (Raney & Pingali, 2007). The World Health Organisation (WHO, 1995) estimated that 254 million children were vitamin A deficient in 1995 and around 2.8 million children aged less than five were afflicted by xerophthalmia, a severe manifestation of VAD. A more recent study has indicated that around 127 million and 4.4 million preschool children were suffering from VAD and xerophthalmia, respectively (West, 2002). The study also found more than 7.2

million pregnant women affected with VAD in developing countries and another 13.5 million with low vitamin A status. About 45% of the children affected by VAD and xerophthalmia and the pregnant women having low or deficient vitamin A live in South and Southeast Asia (West, 2002) where rice is a staple crop.

Micronutrient intervention by fortifying staple foods has been found to be a major factor in reducing micronutrient deficiencies in developed countries (Darnton-Hill & Truswell, 1990; Nestel, 1993; Bower, 1996; Darnton-Hill, 1998) and, although fortification programmes have recently been successfully implemented in Latin-American countries (Darnton-Hill, 1998), both previous and recent experience in other developing countries has suggested that fortification programmes are not always suitable for such countries (Murphy, 1996; Darnton-Hill, 1998; Mayer, 2005). National governments and authorities are facing problems in deploying and maintaining efficient supplement and fortification programmes. The factors constraining developing fortification programmes have been classified as being technical, socio-economic, infrastructural and political (Darnton-Hill, 1998). Although breeding-based solutions to micronutrient deficiencies initially need substantial investment for their development, micronutrient-improved varieties can be grown and consumed during the years ahead without incurring greater additional cost (Nestel *et al.*, 2006). Even though this approach is cost-effective, conventional breeding methods have been unsuccessful in producing staple crops having high vitamin A content. Transgenic technology has recently been used for producing GM rice that produce high pro-vitamin A concentration, this being an example of direct benefit to the consumer by increasing micronutrient content in the crop edible parts. Staple mineral- and vitamin- dense foods represent a low-cost, sustainable strategy for reducing the percentage of micronutrient malnutrition.

Golden Rice, a variety of rice engineered to produce β-carotene (pro-vitamin A), has been further improved to produce 23 times more total carotenoids than the previous *Golden Rice* version produced in 2000 (Paine *et al.*, 2005). Despite the potential of this achievement as a viable and sustainable alternative contributing towards alleviating VAD in many poor countries (Mayer, 2007) antibiotech opponents have claimed that *Golden Rice* is not effective and superfluous (Greenpeace, 2005). Some *Golden Rice* critics argue that this GM crop might actually interfere with current vitamin A supplement and fortification programmes (Mayer, 2005); however, opponents of GM technology often ignore the great number of people who are not receiving the benefits of these programmes. It is well documented that even in countries having ongoing supplement and fortification programmes (i.e. India) about 57% of children aged less than six are affected by sub-clinical VAD (Mayer, 2005). On the contrary, economic analysis of *Golden Rice* is based on anticipated profits of several billion US dollars for South-eastern Asian countries (Anderson *et al.*, 2004), whereas scientific data does not predict any harmful effects for human beings or any deleterious consequences for the environment (Lu & Snow, 2005).

Another example of directly improving food micronutrients comes from *Iron Rice* which is a GM rice having increased iron content obtained by inserting a gene from the *Aspergillus niger* fungus into the rice genome (Prakash, 1997; Lucca, 1999). This transgene encodes phytase, an enzyme which degrades the phytate present in rice seed endosperm; this enzyme releases and makes phosphorous, calcium and other mineral

micronutrients available. A heat-stable form of *Aspergillus fumigatus* phytase has also been engineered which can break down the phytate ingested from other food sources (Prakash, 1997). Transgenic soybean production has been also described, expressing phytase through inserting a liner construct lacking selectable markers and other vector sequences (Gao *et al.*, 2007); phytase activity has thus been increased 2.5 times, compared to an untransformed plant. GM rice having increased iron concentration has also been produced by transferring the soybean ferritin gene which encodes an iron-binding protein (Goto *et al.*, 1999). Iron deficiency causes anaemia in child-bearing aged women and in young children. This condition makes pregnant women more susceptible to stillborn, underweight children and to mortality at childbirth. According to Conway & Toenniessen, 1999, anaemia has been found to be a factor accounting for more than 20% of maternal deaths in Asia and Africa after mothers have given birth. Pro-vitamin E availability in vegetable oils is relatively low, compared to potential availability. Tocochromanols (tocotrienols and tocopherols) are lipophylllic antioxidants, especially accumulating in oilseeds. Vitamin E is present in the form of tocotrienols and tocopherols which have differential vitamin E activities. Most plant seeds have higher γ-tocopherol content than α-tocopherol, the latter having ten times more vitamin E activity than the former (Bramley *et al.*, 2000; Schneider, 2005). Two *Arabidopsis thaliana* genes encoding methyltransferases (VTE3 and VTE4) have been combined into the soybean genome to increase soybean vitamin E activity. The seeds from the resultant GM soybean exhibited more than 95% α-tocopherol content (Van Eenennaam *et al.*, 2003), corresponding to 8-fold pro-vitamin E content. A strategy has been reported recently for engineering commercial oilseed thereby producing oils having highly enhanced tocochromanols and vitamin E content (Karunanandaa *et al.*, 2005). An F2-seed was obtained from crossing transgenic high tocochromanol soybean with transgenic high α-tocopherol soybean; this had vitamin E activity 11-times higher than that of an average wild soybean. Biofortification of currently accepted food crops, together with transgenic technology and conventional breeding, could offer a sustainable alternative to malnutrition affecting many millions of people (mainly children) around the world. Biofortification through GM crops represents a potential complement to current supplement and fortification programmes and campaigns.

ASSESSING GM FOOD CROP SAFETY
Genetic engineering allows the transfer of known encoding or non-encoding DNA across species thereby leading to intended genetic food crop modification. Such modifications are more specific, controlled and rapid than those obtained via conventional breeding and selection methods. However, inserting foreign genes into the plant genome could also have unintended and unexpected pleiotropic effects on the host, leading to changes in the expression level of some genes (and their corresponding proteins) which are unrelated to the desired modification (Wal, 2001; Rischer & Oksman-Caldentey, 2006). However, unintended modification of gene expression in food crops can occur in any kind of traditional breeding; concerns about potentially unintended modifications should not therefore be restricted to GM food crops (Bernstein *et al.*, 2003).
Assessment strategies and guidelines related to the safety of GM crop-derived food have been based on the principle of substantial equivalence which requires comparing

the GM crop to an appropriate reference crop, usually the conventionally-bred parent crop (OECD, 1993; Konig *et al.*, 2004). The aim of GM crop safety assessment is essentially to compare GM crop safety with that of conventionally-bred varieties. Such comparison allows significant differences to be identified in terms of morphological and agronomical characteristics and chemical composition. The conventional counterpart is generally assumed to be safe, according to its history of human consumption. The food safety standard for GM food crops is that these foods must be at least as safe as food derived from conventional crops. GM crop-derived food is assessed by following some steps including characterising the parent crop and any hazards related to it, characterising the donor organism from which the transgene has been derived and the transformation procedures, characterising transferred transgene products (protein and metabolites) to establish their potential toxicity and allergenicity and identifying any targeted or unintended change produced in the food or edible parts of the GM crop (Konig *et al.*, 2004; Hothorn & Oberdoerfer, 2006).

So-called first generation GM crops (EFSA, 2004; ILSI, 2004) have been characterised by input traits which are assumed to produce no substantial changes in their composition as compared to their isogenic counterparts within the framework of substantial equivalence (OECD, 1993). These input traits have included tolerance to herbicides or resistance to insects. On the other hand, so-called second generation GM crops (ILSI, 2004) have been genetically modified to express output traits such as greater concentration of amino acids, fatty acid, vitamins and lower allergen content or substances making nutrients unavailable (Flachowsky & Bohme, 2005). These crops have received increasing scientific support for preventing and treating disease (Newell-McGloughlin, 2006). The first generation GM crops engineered with input traits to provide improved agronomic performance and economic and environmental benefits have been associated with farmers' interests. However, there is an increasing trend towards producing second generation GM crops by transferring value-added output traits, mainly benefiting consumers and processors. Promising markets for nutraceuticals (functional foods) and bioreactors for producing valuable proteins, pharmaceutical products and other compounds fall within this second generation of GM crops (Mascia & Flavell, 2004; Newell-McGloughlin, 2006; Sardana *et al.*, 2007; Stoop *et al.*, 2007).

International panels of experts have considered that transgenic technology is not inherently risky as all DNA is chemically and structurally the same (irrespective of its origin) (Royal Society, 1998; Royal Society, 2002). Human beings (as thermodynamically open and non-equilibrium systems) take energy and matter from the outer environment, foreign DNA being part of food derived from living matter. The passage of food DNA fragments across the intestinal wall is a natural and physiological phenomenon, mainly when DNA is at high concentrations in the food. Transferring DNA between different species has also been a major driving force in the evolution of living organisms. Given that livestock consume substantial amounts of GM crop-derived plant feed, public concern about the consumption of animal products containing transgenic DNA and protein have led to investigations related to their fate within the gastrointestinal tract of livestock and the possible accumulation of transgenes and their encoded proteins within tissues. Transgenic protein has not been detected in any animal tissue or product when using DNA- and protein-based assays (Alexander *et al.*, 2007). On the other hand, small

fragments of endogenous DNA from high-copy number chloroplast genes have been detected in tissues from pigs, ruminants and poultry. Endogenous and transgenic DNA fragments from low-copy genes have been detected in animal tissues, but in lesser amounts than that detected in the case of high-copy genes. Passage of plant DNA fragments, endogenous or not, across the intestinal barrier does not appear to have had adverse effects on livestock (Alexander *et al.*, 2007; Ramessar *et al.*, 2007). It has been estimated that the proportion of GM DNA content in typical livestock diets represents about 0.00042% of total dietary DNA intake (Beever & Kemp, 2000), practically all of it being hydrolysed to small fragments and ultimately converted into individual non-coding monomers.

Proteins expressed by GM crops have raised some concern as they may be involved in food allergies. Assessing allergenicity to GM foods and novel proteins has included decision trees using clinical and laboratory methods leading to scientific evaluation of the potential allergenic risks of GM crops prior to their sale (FAO/WHO, 2001; Metcalfe, 2003; Acosta & Guerrero, 2007). One main approach has been to assess whether an introduced protein has been encoded by a gene taken from a source known to be allergenic. Transgenic technology uses well-characterised transgenes encoding proteins which can be examined for their structural similarity and sequence homology to known allergen amino acid sequences obtained from allergenic food proteins. Serological assays have been conducted for detecting human specific IgE antibodies against food allergens which can be made to react with a GM food crop to look for allergens. It has thus been possible to detect a positive reaction between human IgE and protein from transgenic soybean modified with a Brazil nut-derived gene (Nordlee *et al.*, 1996). As expected, this GM soybean was not marketed. Assessing allergenicity to GM crops has also involved physicochemical and biochemical assays relating protein stability to heat, acid and digestive enzymes. Moreover, transgenic technology has been useful in producing hypoallergenic crops by interfering with the expression of genes encoding major allergens (Bhalla & Singh, 2004; Acosta & Guerrero, 2007). Genetic engineering has also enabled improving food and feed protein quality by incorporating genes encoding non-allergenic proteins containing essential amino acids (De Lumen, 1997; Roller & Hallander, 1998; Chakraborty *et al.*, 2000).

StarLink corn produced by the Aventis Corporation was approved by the US EPA as animal feed; however it was confirmed in 2000 that this GM crop had contaminated human food. Many consumers reported allergic symptoms deriving from their contact with StarLink following media coverage of this incident. This corn, containing Bt (*Bacillus thurigiensis*) insecticide protein Cry9C, had not been approved for human consumption due to the heat stability of this protein compared to other Bt proteins, suggesting that the Cry9C protein might be an allergen for humans (Bucchini & Goldman, 2002). The US FDA, US EPA and US Department of Agriculture Food Safety and Inspection Service provided assistance for obtaining information about exposure to StarLink and its potential adverse effects (Bernstein *et al.*, 2003). After examining a group of patients showing symptoms consistent with allergic reactions, the CDC (Centers for Disease Control & Prevention) could not demonstrate that the Cry9C protein was indeed the product responsible for the adverse health reaction. No IgE from patients was found to be reactive with the Cry9C in protein ELISA tests (CDC, 2001).

Plant transgenic technology commonly uses antibiotic and herbicide resistance selectable marker gene systems, thereby leading to GM plant production. Although there is no justification in terms of safety, public perception about antibiotic resistance selectable markers has partly promoted the search for marker-free transformation systems. A recent review on the use of these selectable markers discussed the currently available scientific literature in detail; this overwhelmingly supports the conclusion that there is no scientific basis against the use and presence of antibiotic resistance selectable marker genes in GM plants (Ramessar *et al.*, 2007). Within the context of using proteinase inhibitors, transgenic expression of cystatin (a cystein proteinase inhibitor) confers partial resistance to plant nematodes. Cystatins occur naturally in rice, maize, potato tubers, human saliva and egg-white. It has been concluded that an engineered rice cystatin has no toxicity for humans arising from its expression in roots (Atkinson *et al.*, 2004).

A recent study of GM wheat could be illustrative of a scientific approach to the alleged substantial equivalence of GM and non-GM crops (Shewry *et al.*, 2007). A detailed and systematic comparison of GM composition and performance with that of conventional lines of wheat was conducted in field and glasshouse conditions. It was concluded that transgene expression in the lines being studied was intrinsically as stable as that of the corresponding endogenous genes; both GM and control lines showed similar stability in agronomic performance. Gene expression and metabolite profiles of GM and control lines also reinforced the idea that GM wheat can be produced which is substantially equivalent to conventional wheat. This does not mean that all GM crops are substantially equivalent to their conventional counterpart, and the case by case protocol continues being valid.

More than 18 studies involving feed from GM crops used in nutrition for many farm animals have been conducted since 1997. In a recent report, Flachowsky *et al.* (2007) advanced results from studies on GM crop-derived feed which were in agreement with more than 100 international experiments. They showed that GM crops had no substantial changes made to their composition and they did not significantly differ in their nutritional attributes from those of their isogenic counterparts. Moreover, recombinant DNA was not found in any organ or tissue samples obtained from animals fed with feed from first or second generation GM crops; a proposal was submitted for nutritional assessment of second generation GM crops (Flachowsky & Bohme, 2005; Flachowsky *et al.*, 2007).

The safety of Roundup Ready corn (a glyphosate herbicide-tolerant GM corn) was assessed in a 13-week study of feeding rats. Herbicide tolerance was produced by inserting the transgene from *Agrobacterium* sp. strain CP4 which expresses the CP4 EPSPS enzyme (5-enolpyruvylshikimate-3-phosphate synthase), which is not inhibited by glyphosate. Comparison between rats fed diets containing the GM corn and control rats fed corn grain from conventional varieties led to confirming that the Roundup Ready corn grains were as safe and nutritious as conventional corn grain (Hammond *et al.*, 2004). Additional studies have shown the safety of CP4 EPSPS protein (Ramessar *et al.*, 2007).

Bt Rice has been engineered to express cry genes providing resistance to major lepidopteran insects affecting rice. Such genetic modification has the potential for reducing chemical insecticide applications, decreasing yield loss and reducing mycotoxin levels

which are a consequence of larval attacks (Papst *et al.*, 2005). Bt rice KMD1 (expressing Cry1Ab protein and exhibiting high levels of resistance to at least eight different insect pest species) was submitted to a comparative 90-day safety assessment study in an animal model (Wistar rats; Schrøder *et al.*, 2007). No adverse or toxic effects were observed during the study after comparing haematological and biochemical parameters and examining a large number of organs. A few parameters were significantly different, but remaining within the normal reference limits for rats of this kind and age. A gene encoding *Galanthus nivalis* snowdrop lectin (GNA lectin) has been inserted into a number of different food crops including rice, wheat, potatoes and sugarcane (Stoger *et al.*, 1999; Setamou *et al.*, 2002; Poulsen *et al.*, 2007) to confer resistance to several insect pest species (Powell *et al.*, 1998). A 90-day feeding study was conducted for comparing the safety of a new GM rice variety expressing GNA to its parental variety (Poulsen *et al.*, 2007). The results of this study revealed several significant differences between rats fed diets with GM and parental rice; they were probably related to GNA lectin content, but none of the effects were considered to be adverse. However, the authors concluded that the design of this 90-day study including one control group and one group given the GM food was not enough for assessing the safety of this GM food crop.

GM crop-derived food ingredients are found in thousands of food products consumed worldwide (Prakash, 2001). Science-based reasoning and accumulated research regarding crop improvement have allowed the scientific community to support GM crops. There is scientific confidence that GM crops do not represent greater risks than those already present in conventional agriculture and that any new risk posed by GM crops could be identified, managed and prevented (Prakash, 2001). In fact, GM crops are subjected to rigorous testing within a regulatory framework developed for supervising their commercialisation. Obviously, risks from GM crops must be identified, measured and balanced against the enormous benefits that this technology can offer to a growing world population.

There are specific regulations for the agronomic coexistence of GM crops and their conventional relatives to prevent cross-fertilisation between GM and non-GM crops during their production. Such regulations involve defining isolation distances which may differ, depending on the scientific criteria defined for a particular agricultural context (Tolstrup *et al.*, 2003; Sanvido *et al.*, 2008).

RISKS INVOLVED IN CONVENTIONALLY-PRODUCED FOOD CROPS

GM crop critics commonly ignore the fact that conventionally bred varieties contain proteins and metabolites which are eventually harmful for humans. Indeed, several conventional crop varieties have been removed from the market due to the severe toxic effects produced on humans. In the case of allergy to food, about 6-8% of children and 2-3% of the adult population present allergic reactions to food (Young *et al.*, 1994; Munoz-Furlong *et al.*, 2004; Acosta & Guerrero, 2007). Most food allergies are induced by peanuts, milk, eggs, tree nuts and fish and crustaceans, although more than 160 foods and food-related substances have been identified as allergic reaction inducers (Metcalfe *et al.*, 1996). All known food crop allergens are contained in conventionally modified crops. By contrast to GM crops, conventional crops have not been routinely tested for toxic or allergic effects on consumers prior to their commercial release,

disregarding that traditionally-bred food may contain natural toxins, anti-nutrients and carcinogenic compounds.

Assessing the risk of GM plants using conventional methods has been essentially derived from incidental records (Hodgson, 2001). It has been well-documented for a long time that plants' secondary metabolites can be toxic for humans and animals. Thus, any genetic modification caused by transgenic or conventional breeding technology could be seen to be a potential hazard in terms of concentration changes of these secondary compounds. Without disregarding the case by case principle for risk assessment, conventional varieties produced by traditional breeding seem to show a greater probability of producing toxic effects on humans. For instance, toxic glycoalkaloids are present in potatoes but their concentration in tubers from most varieties is not harmful for humans (Friedman & McDonald, 1997). Nevertheless, there are a number of reported cases of humans having been poisoned by the high glycoalkaloid content of conventional potato varieties (Friedman & McDonald, 1997). For example, the Lenape variety of potato developed by conventional *Solanum tuberosum* and *S. chacoense* breeding was withdrawn from the market (Sinden & Webb, 1972) after its commercial release in 1967 (Akeley *et al.*, 1968) due to illness caused by ingesting its tubers which contain high glycoalkaloid levels (Zitnack & Johnson, 1970). A popular potato variety (Magnum Bonum) was also withdrawn from the market in Sweden for similar reasons (Hellenas *et al.*, 1995). Glycoalkaloid aglycone proportions in potato have been shown to depend on interspecific somatic hybrid genome constitution (Laurila *et al.*, 2001; Laurila *et al.*, 2001a). New and possibly toxic glycoalkaloid aglycones can be produced in such somatic hybrids, even though they have not been found in any of the parental lines. These new compounds have apparently resulted from bringing together substrates and enzymes which have not previously been in contact. For example, inter-specific somatic hybrids between *Solanum brevidens* and *S. tuberosum* have been found to contain the toxic steroidal alkaloid demissine. A hypothesis has been advanced that a hydrogenase present in *S. brevidens* normally produces tomatidine from teinamine; however, in the new cellular environment created by somatic hybridisation, this enzyme produces demissine from solanidine, a substrate found in *S. tuberosum* but not in *S. brevidens* (Laurila *et al.*, 1996). Conventional plant breeding methods can lead to other unintended results. Celery contains furanocoumarins which are mutagenic, carcinogenic and reproductive toxicants, and can also cause contact dermatitis. A new celery variety was conventionally developed and selected for its resistance to *Fusarium,* but the high content of linear furanocoumarins causing severe contact dermatitis in field workers became apparent when this variety was almost ready for commercial release (Trumble *et al.*, 1990; Diawara & Trumble, 1997). The cases referred to above show that conventional genetic modification of crops might produce unexpected and unintended effects, although it is well recognised that traditional plant breeding has contributed to agriculture by producing many safe food crops and has also successfully removed toxic elements from several foods (Uzogara, 2000). Prakash (2001) has stressed that solanine found in tomatoes and potatoes can cause spina bifida and that phyto-hemagglutinin from kidney beans is toxic. African cassava contains cyanogenic glucosides which can produce limb paralysis when consumed before proper processing; peach seeds are also very rich in cyanogenic glucosides. Many foods in our daily diet naturally contain thousands of

compounds, many of them being carcinogenic or hazardous when tested at high doses in lab animals. It has been reported that roasted coffee contains more than 1,000 different chemicals and that after testing 27 of them, 19 were found to be carcinogens for rodents (Ames & Gold, 1997). None of these food crops, and many others, has been subjected to mandatory testing for risk assessment.

Despite the risks associated with food derived from new varieties produced by traditional plant breeding, these food products have been readily and widely accepted as part of the human diet for many years. Any genetic manipulation by traditional plant breeding or genetic engineering methods inherently has the potential risk of producing new food hazards which can arise from the products encoded by the inserted transgenes or the introgressed chromatin fragments from wild species into the new cultivars. In both cases, the secondary pleiotropic effects leading to unintended modifications of gene expression cannot be ruled out. Therefore, the risks associated with inserting new genes through genetic engineering must be considered within the same context of introgressing large DNA sequences by traditional breeding (Conner & Jacobs, 1999). However, conventionally introgressed genes are numerous and their functions remain essentially unknown, whereas transgenes are controlled by their nature, making them more reliable in terms of obtaining the desired outcome.

CONCLUSIONS

Despite the rapid increase in areas cultivated with GM crops and the widespread adoption of GM food and feeds, there still remain public concerns about the safety of GM crops and their potential impact on public health. Although no correlation between public perceptions and the scientific data available to date has been established, intense public and scientific debate regarding the safety of GM crops has led to implementing mandatory risk assessment of novel GM crops. Rather than causing new food safety problems, food crops developed until now have shown their potential for improving the nutritional quality of food and feed. Developing more nutritious food by using transgenic technology may contribute towards reducing the number of undernourished people in the world; however, policies and strategies aimed at increasing the income of people living below the poverty line must also be developed. A growing world population critically needs the effective contribution of science and technology for increasing the global food supply. Non-scientific disputes concerning GM crops could result in serious consequences for agricultural policy, food security and world trade.

Genetic modification through conventional plant breeding is essentially random and imprecise, taking up to two decades for producing a commercially valuable new variety. Genetic modification through transgenic technology (which uses molecular biology tools) is more powerful and precise in achieving the desired goals than conventional breeding. Crops and foods produced using transgenic technology have been available on the market for more than a decade and no harmful effects have been detected to date. Regulatory agencies have adopted the principle of substantial equivalence to ensure the food safety of GM crops and, to date, no adverse effects have been presented in animals or humans after consuming GM food crops approved on the basis of this principle. This does not mean that GM crops are necessarily risk-

free. In terms of food safety, they must be addressed within the same context of food crops genetically modified by traditional crossbreeding. There is no food (natural or genetically modified) which is absolutely free of risk. It has been well-documented that all technologies bring benefits and risks to the environment and that no technology is absolutely safe; GM food crops therefore appear to be no more risky for public health than conventionally-bred crop varieties.

Some expressions of neoliberalisation from the non-GM movement have been identified during the debate. One such expression is exemplified by current activism's strong market focus. Another aspect associated with non-GM activism tactics is the strong commitment to individual consumer's rights and power. Emphasising individual freedom of choice, alternative food activism seems to be working to change the world by shopping and, as Roff, 2007, states, using the market will not change the way the market works.

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