SPECIAL GUEST EDITOR SECTION

Impact of Foods Nutritionally Enhanced Through Biotechnology in Alleviating Malnutrition in Developing Countries

G. SARWAR GILANI
Nutrition Research Division, Food Directorate, Health Products and Food Branch, Health Canada, Government of Canada, 251 Sir Frederick Banting Dwy, Ottawa, ON, Canada K1A 0L2
ANWAR NASIM
National Commission on Biotechnology, Government of Pakistan and COMSTECH Secretariat, 3 Constitution Ave, G-5/2, Islamabad-4400, Pakistan

According to United Nations (UN) projections, the world's population will grow from 6.1 billion in 2000 to 8 billion in 2025 and 9.4 billion in 2050. Most (93%) of the increase will take place in developing countries. The rapid population growth in developing countries creates major challenges for governments regarding food and nutrition security. According to current World Health Organization estimates, more than 3 billion people worldwide, especially in developing countries, are malnourished in essential nutrients. Malnutrition imposes severe costs on a country's population due to impaired physical and cognitive abilities and reduced ability to work. Little progress has been made in improving malnutrition over the past few decades. The Food and Agriculture Organization of the UN would like to see more nutrient-rich foods introduced into these countries, because supplements are expensive and difficult to distribute widely. Biofortification of staple crops through modern biotechnology can potentially help in alleviating malnutrition in developing countries. Several genetically modified crops, including rice, potatoes, oilseeds, and cassava, with elevated levels of essential nutrients (such as vitamin A, iron, zinc, protein and essential amino acids, and essential fatty acids); reduced levels of antinutritional factors (such as cyanogens, phytates, and glycoalkaloid); and increased levels of factors that influence bioavailability and utilization of essential nutrients (such as cysteine residues) are advancing through field trial stage and regulatory processes towards commercialization. The ready availability and consumption of the biofortified crops would have a significant impact in reducing malnutrition and the risk of chronic disease in developing countries.

According to projections of the United Nations (UN), the world's population will grow from 6.1 billion in 2000 to 8 billion in 2025 and to 9.4 billion in 2050 (1). Most of the increase (93%) will take place in developing countries. The amount of arable land/capita has been shrinking since the middle of the 20th century, and the drop projected for the next 50 years means that many developing countries will no longer be able to feed themselves. The challenge to governments presented by continual rapid population growth is not limited to food. It also includes education, health, housing, and employment.

Large numbers of people in developing countries exist on simple diets composed primarily of a few staple foods (cassava, wheat, rice, and maize) that are poor sources of some macronutrients (such as essential amino acids and fatty acids) and many essential micronutrients, such as minerals (iron and iodine) and vitamins (vitamin A).

The magnitude of micronutrient malnutrition in developing countries over the past few decades has not been reduced in spite of major international efforts and investments that have been put into tablet-, capsule-, and injection-based approaches linked to health care and social welfare systems (2).

Biofortification of staple crops through modern methods of biotechnology has the potential to be a powerful complement to traditional plant breeding methods to help offset essential nutrient deficiencies and improve human health through elevated levels of essential nutrients, reduced levels of toxic factors and antinutrients that impact bioavailability and utilization of nutrients, and increased levels of factors that enhance bioavailability of essential nutrients (3).

A number of these crops, developed with a focus on improving nutritional quality, have reached the field trial stage and/or are advancing through regulatory processes towards commercialization. Some examples of the crops nutritionally enhanced through biotechnology include cyanogen-free cassava (4); nutritionally enhanced rice with an elevated level

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Corresponding author's e-mail: Sarwar_Gilani@hc-sc.gc.ca

Table 1. Ten largest countries ranked according to population size in 1998, with projections to 2050[a]

Rank	Country	Population 1998, million	Country	Population 2050, million
1	China	1255	India	1533
2	India	976	China	1517
3	United States	274	Pakistan	357
4	Indonesia	207	United States	348
5	Brazil	165	Nigeria	339
6	Pakistan	148	Indonesia	318
7	Russia	147	Brazil	243
8	Japan	126	Bangladesh	218
9	Bangladesh	124	Ethiopia	213
10	Nigeria	122	Iran	170

[a] Ref. 1.

of β-carotene (5), increased levels of iron and zinc (6), an elevated level of cysteine residues to enhance iron bioavailability, and a decreased level of phytates to improve iron and zinc bioavailability (7); nutritionally improved potatoes with elevated levels of total protein and essential amino acids (8), reduced glycoalkaloid (a toxic factor) content and high starch to absorb less fat during frying (9); nutritionally enhanced oilseeds to provide healthier oils, including *Brassica juncea*, containing high levels of very long chain polyunsaturated fatty acids such as arachidonic acid (AA) and eicosapentaenoic acid (EPA; 10), which are essential for maintaining membrane structure, growth, and optimal development of brain and retina; and tomatoes and soybeans with increased antioxidant contents (9).

The objective of this paper is to discuss the impact of foods nutritionally improved through biotechnology in potential alleviation of malnutrition in developing countries.

Projected Population Growth and the Magnitude of Malnutrition

According to the estimates of the UN, some developing countries are projected to triple their populations by 2050 (Table 1). For example, Ethiopia's current population of 62 million will more than triple by 2050. Pakistan's population is projected to increase from 148 million to 357 million, surpassing that of the United States. Nigeria, meanwhile, is projected to go from 122 million currently to 339 million, giving it a higher population in 2050 than that for the whole of Africa in 1950. The rapid population growth in developing countries creates major challenges for governments regarding food and nutrition security. Providing food to this population will require an astonishing increase in agricultural production.

The World Health Organization (WHO; 11) has estimated that more than 3 billion people worldwide are malnourished, including widespread deficiencies of macro- and micronutrients. It has been estimated that 250 million children are at risk for vitamin A deficiency (causing irreversible blindness in up to 500 000 annually), 1.5 billion people are at risk for iodine deficiency (causing goiter and mental retardation), and 2 billion people are at risk for iron deficiency (with children and women of reproductive age particularly vulnerable), causing impaired physical and cognitive development, reduced work capacity and productivity, overall lowered resistance to disease, and increased morbidity and mortality (11, 12).

Worldwide, the largest numbers of people suffering from micronutrient malnutrition live in South Asia, including India, Pakistan, and Bangladesh (13). Micronutrient malnutrition, especially vitamin A deficiency, iodine deficiency disorders, and iron deficiency anemia (IDA), are serious public health problems in these countries. For example, the prevalence of IDA could be as high as 74% in children below 3 years of age, 85% in expectant mothers, and 90% among adolescents in India (14).

Impact of Hunger and Malnutrition Throughout the Life Cycle

The vicious cycle of malnutrition around the world results in millions of lives affected by death and disability (15). Every year, more than 20 million low birthweight (LBW) infants are born in the developing world. In some developing countries, including India and Bangladesh, >30% of all children are born underweight. From the moment of birth, the scales are tipped against them, and the cycle of malnutrition continues through childhood, adolescence, and old age. LBW babies face increased risk of dying during infancy, of stunted physical growth and cognitive functions during childhood, of reduced working capacity and earnings as adults and, if female, of giving birth to LBW babies themselves.

Nutritionally Enhanced Genetically Modified (GM) Rice

Rice is central to food security in the world, as it is the main source of caloric intake for about half of the world's population and is the predominant staple food for 34 countries in Asia, Latin America, and Africa (7). Rice, particularly in its milled form, is relatively poor in most nutrients except carbohydrates (16). Therefore, current attempts at improving the nutritional value of this staple food through biotechnology are justified.

Lucca et al. (7) introduced a ferritin gene from *Phaseolus vulgarus* into rice grains, increasing their iron content up to 2-fold. To increase bioavailability of iron, the same researchers also introduced a thermo-tolerant phytase from *Aspergillus fumigatus* into the rice endosperm and increased the phytase level by about 130-fold, giving phytase activity sufficient to completely degrade phytic acid (an inhibitor of iron bioavailability) in a simulated digestibility experiment. Moreover, cysteine peptides, which are

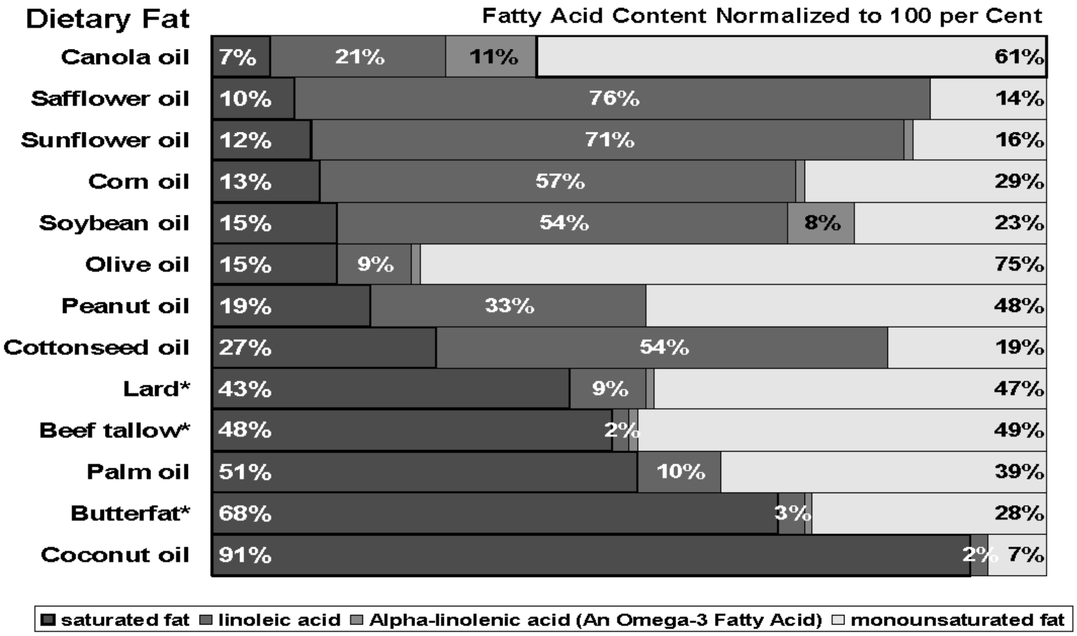

Figure 1. Fatty acid composition of some common oils and fats. * = Cholesterol content (mg/Tbsp): Lard 12; beef tallow 14; butterfat 33. No cholesterol in any vegetable oils.

considered major enhancers of iron bioavailability, were overexpressed by about 7-fold. The nutritionally enhanced rice, with higher iron content and rich in phytase and cysteine peptides, has great potential for improving iron nutrition in developing countries where iron deficiency is so widespread.

β-Carotene, a precursor of vitamin A (retinol), does not occur naturally in the endosperm of rice. Ye et al. (17) developed transgenic rice that produces grain with yellow-colored endosperm [*Golden Rice* (GR)]. Biochemical analysis confirmed that the yellow color represented β-carotene (provitamin A). The reported level of β-carotene in 1 g of the transformed rice was 1.6 μg, which would supply 15–20% of the recommended daily allowance (RDA) for vitamin A. Scientists at Syngenta (5) have developed a new generation of GR that uses an enzyme from maize to dramatically increase grain carotenoid levels over 20-fold, containing up to 37 μg carotenoids/g seed. The new lines, known as GR 2, are quite exciting from the perspective of combating vitamin A deficiency in developing countries. Truly significant levels of vitamin A equivalents can be delivered even to small children by the consumption of GR 2. It has been estimated that 50% of the 300 μg RDA for vitamin A for a 1–3 year old child could be met by 72 g dry GR 2 (18). A typical child's portion for rice is 62 g, which is consumed more than once a day in many developing countries. These estimates were based on a 12:1 factor for the conversion of β-carotene to vitamin A. Full potential of GR 2 would only be confirmed through human studies to assess bioavailability, conversion factors, and the minimum intake of dietary oils required for absorption of lipophilic carotenoids. The development and delivery of GR to developing countries are described in detail in the accompanying paper by Mayer (19) in this *Special Guest Editor Section*.

High-Protein GM Potatoes

Based on regional and country balance sheets, dietary surveys, and protein and amino acid composition data, there are very significant differences in protein and essential amino acid availabilities between the developed regions and the South Asian countries like India, Pakistan, and Bangladesh (102 versus 42–58 g/day; 20). Protein digestibility and quality of mixed diets in developing countries are also considerably lower than those in developed regions (20, 21).

Nutritional improvements in the potato crop, which ranks fourth in terms of total global food production, could potentially be a cheaper alternative to more expensive and

Table 2. Vegetable oil production, consumption, and imports in Pakistan expected in 2001–2002[a]

Amount	1000 Metric tons	% of Pakistan oil consumption
Total production	534	—
Total imports	1420	—
Total consumption	1955	—
Palm oil imports	1160	59
Soybean oil imports	250	13

[a] Ref. 24.

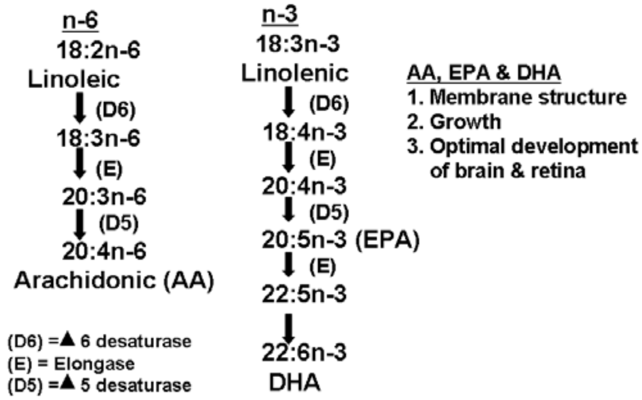

Figure 2. Metabolism of linoleic and linolenic acids.

poorly digestible legumes and pulses in alleviating protein and essential amino acid deficiencies in developing countries.

Transgenic potatoes containing the *AmA1* gene from the amaranth plant have been developed to produce about 33% more protein and substantial amounts of essential amino acids including lysine (8), which is deficient in many developing countries where diets heavily based on cereals are consumed. The protein-rich potatoes are in the final stages of testing in India. The potato is not the first protein-enriched GM crop. Strains of GM maize rich in lysine have already been created. The development and testing of high-lysine maize are described in detail in an accompanying paper by Glenn (22) in this *Special Guest Editor Section*.

GM Vegetable Oils with Desirable Fatty Acid Profiles

Fatty acid profiles of some of the commonly consumed dietary oils and fats are shown in Figure 1. Among vegetable oils, coconut oil and palm oil contain the highest levels of saturated fatty acids. According to the recommendations of the American Heart Association, high consumption of saturated fats such as animal fats and vegetable oils rich in saturated fatty acids is a major contributor to heart disease (23).

Palm oil and coconut oil, which are high in saturated fatty acids, are most frequently consumed in South Asian countries. For example, about 59% of Pakistan's oil consumption is met by imports of palm oil (Table 2; 24). It is also unfortunate that Pakistan is a country that already has a very high incidence of cardiovascular disease. There is evidence to suggest that South Asians, including Pakistanis, are genetically more susceptible to cardiovascular disease (25). Surveys in Pakistan indicated that >20% of the population is affected by cardiovascular disease. Therefore, efforts need to be made to find means to reduce consumption of palm oil and other saturated fats in Pakistan to stem the rising tide of cardiovascular disease.

Using the safety assessment guidelines and regulations, a number of oils extracted from GM canola, soybean, and flaxseed have been approved for human use in Canada and the United States. The imports of safe and nutritionally desirable oils such as canola and soybean would provide short-term approaches to ensure greater availability and utilization of the healthy oils. The increased production of oilseeds using safe and approved biotechnology principles and practices could lead to long-term strategies in making Pakistan self-sufficient in edible oils.

Canola oil, which is unique among all the edible fats, contains a very low level of saturated fatty acids (Figure 1). Moreover, canola oil contains a relatively high level of monounsaturated fatty acids and intermediate levels of polyunsaturated fatty acids with an appropriate ratio of the omega-6 and -3 fatty acids (26). This ratio is important for maintaining a balance in the production of eicosanoids of the omega-6 and -3 fatty acids, which in turn is required to maintain a balance between bleeding and clot formation.

Linoleic acid (18:2n-6) is the parent fatty acid of the omega-6 family, while α-linolenic acid (18:3n-3) is the parent fatty acid of the omega-3 family. Humans and animals have the capacity to convert the 2 essential dietary fatty acids into a series of longer-chain polyunsaturated fatty acids via a biosynthetic process that involves several desaturation and chain-elongation steps (Figure 2). Linoleic acid is converted to AA (20:4n-6), the most important fatty acid of the omega-6 series, while α-linolenic acid is converted to EPA (20:5n-3) and docosahexaneoic acid (DHA; 22:6n-3), the most important fatty acids of the omega-3 series. These longer-chain polyunsaturated fatty acids such as AA are required for maintaining the fluidity of the membrane structure and for growth (26). Similarly, DHA is needed for the optimum growth of the brain and the retina of the eye during early stages of human development. However, the bioconversion of linoleic and α-linolenic acids to AA and DHA, respectively, is very small. Therefore, the inclusion of a dietary source such as fatty fish or fish oil supplements becomes necessary to obtain sufficient amounts of these very long-chain polyunsaturated fatty acids, as vegetable oils do not contain them.

Recently, scientists from Canada were able to use stepwise metabolic engineering to produce high yields of very long-chain polyunsaturated fatty acids, AA and EPA, in *B. juncea* seeds (10). Moreover, they reconstituted the DHA biosynthetic pathway in plant seeds, demonstrating the feasibility of large-scale production of this nutritionally important omega-3 fatty acid in oilseed crops.

Safety Assessment of Nutritionally Improved GM Crops

Several international organizations including the Food and Agriculture Organization (FAO) of the UN, WHO, the Codex Alimentarius Commission, and the Organization for Economic Cooperation and Development have agreed that the concept of substantial equivalence is a powerful tool for assessing the safety of GM food/feed crops (27). This concept is used to identify similarities and differences between the new crop and its conventional counterpart, and the comparison aids in the identification of potential safety and nutritional issues.

There is international scientific consensus that the introduction of the first generation of agronomic-trait GM crops introduced no unique food safety concerns, and no evidence of harm has been reported from those GM crops which have been approved for use (9). The GM crops permitted for food use and traded on the international market include herbicide- and insect-resistant maize (*Bt* maize), herbicide-resistant soybean, rape (canola), and insect- and herbicide-resistant cotton (primarily a fiber crop, although refined oil is used as food; 9).

However, additional assessment of the second generation of GM crops with improved nutritional value, which are currently under development and/or testing, will be required. Stability and effects of postharvest factors, bioavailability, exposure assessment, and upper safe limits of nutrients and bioactive components will need to be investigated. The International Life Sciences Institute, a nonprofit worldwide scientific foundation, has developed comprehensive recommendations for assessing safety and nutritional quality of foods and feeds nutritionally improved through biotechnology (3). More recently, the Codex Alimentarius Commission has established a "Task Force on Safety Assessment of Foods Derived from rDNA Plants for Nutritional or Health Benefits" to provide guidance on this topic.

Conclusions

Availability of the nutritionally improved GM foods to consumers in developing countries would have a significant positive impact in improving their nutritional health. The FAO has strongly supported promotion of the production and consumption of micronutrient-rich foods as the only true solution to micronutrient deficiency problems.

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