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Biotechnology for reduction of micronutrient malnutrition

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Major advances have occurred in food production and agriculture during the past 30 years in countries like India as a result of the widespread adoption of benefits of the Green Revolution. The numbers of people who are food-deprived globally has dropped dramatically with the increase in the availability of cereals, although food insecurity is still a major problem in the developing world. The key to these dramatic gains of the Green Revolution is development and distribution of high-yield seeds and necessary inputs such as fertilizers and irrigation to make them grow to their full potential. Conventional methods of selective breeding and crossing of different varieties produced hybrids with desirable characteristics, led to increased productivity and incomes, and brought down the food prices. The Green Revolution of the latter half of the 20th century has led to the Gene Revolution with the recent advances in agricultural biotechnology. Transgenic crop technology is spreading faster than any other agricultural technology; though the furor about 'terminator' genes has died down, controversies about the potential risks of biotechnology persist, such as gene flow (the escape of inserted transgenes into related crops or wild plants), the emergence of resistant pests, and fears that eating genetically modified foods might affect the health of consumers[1]. The U.S. and Canada grow bulk of transgenic crops 60 percent by area cultivated but developing countries accounted for 38 percent in 2006, almost all of it in Argentina, Brazil, India and China. Transgenic crops have the potential to alleviate some of the concerns we have had with intensive agriculture with regard to the environmental problems and, by further increasing food productivity yet again, they may herald a doubly green revolution[1].

The poor quality of cereal-based diets and lack of diversity in the habitual diet contributes to deficiencies of micronutrients a global problem of 'hidden hunger', much bigger than hunger itself, which imposes enormous costs on societies in terms of ill health, lives lost, reduced economic productivity and poor quality of life. There are nearly 2 billion people who suffer nutritional deficiencies of micronutrients such as iron, zinc and vitamin A. While a number of nutritional interventions such as supplementation and food fortification as well as promotion of dietary diversity have been successful to some extent in reducing the problem of micronutrient malnutrition, agricultural biotechnology provides yet another opportunity for sustainable strategies to meet this challenge by developing cereal varieties with not only higher yield potential and stability, but also with improved nutritional content[2]. Various conventional approaches and tools of biotechnology are being employed in the development of crop varieties with higher yields and higher content of micronutrients. There are compelling global health and nutritional considerations to persuade plant breeders that micronutrient density traits should be their principal objective, which is targeted to the developing world. Current evidence strongly supports the contention that there is enough diversity within the genomes of staple plant foods to accomplish this task. Success in doing this would dramatically contribute toimproving the health and livelihoods of people in developing countries in a sustainable manner, thereby contributing greatly to furthering national development efforts in these countries.

Shifting emphasis from quantity to quality from yield to nutritional content

The post-war agricultural revolution commonly referred to as the 'Green Revolution' has been responsible for an extraordinary period of growth in food crop productivity in the developing world over the past 40 years[3]. It brought high-yielding, semi-dwarf wheat and rice varieties, developed through conventional plant breeding methods, to millions of small-scale farmers, initially in Asia and Latin America, but later in Africa as well. The major breakthroughs in yield potential that kick-started the Green Revolution in the late 1960s came from conventional plant-breeding approaches that initially focused on raising the yield potential of the major cereal crops. For example, yield potential in irrigated wheat has been rising at the rate of one percent per year over the past three decades, an increase of around 100 kg/hectare/year[4]. The gains achieved

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during the early decades of the Green Revolution were extended in the 1980s and 1990s to other crops and to less favoured regions. Essentially, no research or elite germ plasm was available for many of the crops grown by poor farmers in less favourable agro-ecological zones (such as sorghum, millet, barley, cassava and pulses) during the early decades of the Green Revolution, but since the 1980s modern varieties have been developed for these crops and their yield potential has improved[3]. In addition to the continuing progress in the yield of cereal crops, conventional plant breeders continue to have successes in many related fields. These include the development of crops with durable resistance to a wide spectrum of insect pests and diseases, plants that are better able to tolerate a variety of physical stresses such as drought and salinity, and crops that require a significantly lower number of days of cultivation. All these developments basically contribute to increases in quantity of cereal grain or crop yield globally. However, in recent years this emphasis on quantity has shifted, and increasing efforts are being made to enhance the taste and nutritional qualities of cereal grains.

The approaches for improving the quality of food crops have varied from those focused mostly on methods that are biotechnology-driven and resort to the use of transgenics, to those that have relied almost entirely on classical plant breeding techniques. The former is more recent and driven by science and the private sector, while the latter has a long history with varietals chosen by the small farmer for their special characteristics and have contributed much to the preservation of plant diversity in the world. Increasingly, there has emerged a hybrid method, with biotechnology contributing to the identification of desirable qualitative traits (using markers), which are then bred by classical methods. This last approach has enormous potential, because it sidesteps the issues related to safety (both with regard to health and environmental concerns). It also has the added advantage that it enables the combination of characteristics that have been hitherto favoured for the purpose of increasing yield i.e. quantitative traits, while at the same time addressing the need for better nutritional and related characteristics, i.e. qualitative traits.

The problem

The Green Revolution followed by the recent advances in crop sciences have contributed to increasing crop yields, and thus, to the availability of food to tackle the problem of global hunger. Hunger worldwide is now estimated to affect over 854 million people, most of them (820 million) in the developing world[5]. Globally, the prevalence of vitamin and mineral deficiencies is remarkably high (Table 1). Micronutrients including vitamins, minerals and trace elements are essential chemical compounds that are present in small amounts in food and fulfill many important functions in our body.

It is estimated that one-third of the world's people do not attain their physical and intellectual potential because of micronutrient deficiencies[6]. Estimates based on data from more than 80 countries in the developing world indicate that iodine deficiency disorders (IDD) in pregnancy cause almost 18 million babies every year to be born mentally impaired. IDD is estimated to lower the intellectual capacity of people in almost all the nations by as much as 10-15%. Iron deficiency anaemia (IDA), at the age of 6-24 months is impairing the mental development of 40- 60% of the developing world's children. Severe iron deficiency anemia (IDA) is responsible for the deaths of more than 60,000 young women every year during pregnancy and childbirth. IDA in adults is estimated to contribute to productivity losses of up to 2% of the GDP of these nations. Vitamin A deficiency (VAD) on the other hand, compromises the immune status of approximately 40% of the developing world's under-5-year-old children and is the cause of approximately one million deaths of young children each year. It is also important to recognise that the prevalence of multiple micronutrient (two or more) deficiencies occurs in 50% of the children in whom any deficiency is present, and this adds to the immeasurable burden on individuals, health and social services, education systems and families. Further, it is becoming apparent that other micronutrient deficiencies like zinc and folate deficiency are widespread enough to be considered as being of sufficient public health importance in view of both health and associated economic consequences. The economic and social costs of 'hidden hunger' can be fathomed only by recognizing that micronutrient deficiencies affect cognitive and physical development and decrease school performance in children, compromise work output, productivity and earning capacity of adults, impair immunity and increase susceptibility to infectious diseases, and increase mortality, particularly among vulnerable groups such as pregnant women and children.

More than two billion people in developing countries are victims of this insidious form of hunger due to the poor quality of food and lack of diversity in the habitual diet. Deficiencies of micronutrients are common in populations that consume largely cereal-based monotonous diets. Cereals do not contain carotenoid compounds (precursors to vitamin A) in the grain. Consequently, VAD often occurs where the diet is monotonous and relies heavily on only cereal staples. The amount of bioavailable iron is dependent on the content and source of iron in the diet and on iron absorption during the digestive process. The absorption of dietary iron of vegetable origin is relatively low, and this is considered to be a major factor in the causation of iron-deficiency anaemia. Also, cereals are high in phytic acid, which is a potent inhibitor of iron absorption. Foods that enhance non-haem iron absorption such as fruits and vegetables rich in ascorbic acid are often not consumed in adequate amounts in developing countries. Haem iron, which is relatively well absorbed by the human

Table 1. Estimated global impact of micronutrient malnutrition

Micronutrient Deficiency	Estimated impact
Vitamin A deficiency	140 million pre-school children affected with VAD[1] Contributes to 1.15 million deaths in children every year[2] 4.4 million children suffer from xeropthalmia[1] 6.2 million women suffer from xerophthalmia[1]
Iron Deficiency	2.0 billion women (96 million of them pregnant)[2] 67,500 maternal deaths per year from severe anaemia[2]
Iodine deficiency	1.98 billion at risk with insufficient or low iodine intakes[3] 15.8% of population worldwide have goitre[3] 17.6 million infants born mentally impaired every year[2]
Folate deficiency	Responsible for 200,000 severe birth defects every year[2]

1. SCN (2004) *Fifth report on the world nutrition situation: Nutrition for improved development.*
2. UNICEF/Micronutrient Initiative (2004) *Vitamin and Mineral deficiency: A World progress report.*
3. WHO (2004) *Iodine status worldwide*

intestine, is found primarily in animal products such as meat. Often, animal source foods are limited in most diets in developing countries, because of high cost and limited availability. IDA is exacerbated since haem iron-rich foods are often a negligible part of a typical diet in a developing country.

The solutions

Strategies to combat micronutrient deficiencies are probably among the most cost-effective of all health interventions. The World Bank[7] estimated that deficiencies of the three major micronutrients i.e. Vitamin A, iodine, and iron alone could contribute to reducing as much as 5 percent of gross domestic product (GDP) in developing countries, whereas the cost of addressing these deficiencies comprehensively and sustainably would be less than one-third of a percent of GDP. The World Health Organisation[8] estimated that, while 3.7 million deaths per year in children are attributable to underweight, deficiencies of vitamin A, iron and zinc each caused an additional 750,000 850,000 deaths. Effective nutritional interventions, including breastfeeding, complementary feeding and micronutrient supplementation, can reduce child mortality significantly and save 2.4 million children's lives each year.

Nutritional interventions

The time-tested strategies universally promoted have hitherto focused on nutrient supplementation and fortification with micronutrients of commonly consumed foods. Supplementation and fortification however, only address the symptoms and not the underlying causes of micronutrient deficiencies. Other complementary interventions include the treatment of parasitic infestations, which very often are important contributors to micronutrient deficiencies such as that of iron. The alternative is to advocate and support sustainable interventions that alter behaviour, such as *nutrition education* and the *promotion of dietary diversity* and investments in home vegetable gardens, which will contribute to dietary diversification. While these strategies have been tried with varying degrees of success and continue to play an important role in addressing the immediate needs of vulnerable segments of the population, (e.g. supplementation of infants and children alongside universal immunization programmes or the provision of micronutrient supplements to pregnant women) increasingly more emphasis is being placed by international agencies on food fortification strategies[9] since they can be categorized as food-based approaches and hence, probably sustainable in the long term.

Agricultural biotechnology solutions

It is obvious that improving and enhancing the nutritional quality of cereal grains by increasing their micronutrient content would be a sustainable and more effective approach, given that a major proportion of the diet of vulnerable populations in the developing world are cereal-based. For example, rice alone contributes to 23% of the calories consumed worldwide, and countries that rely on rice as the main staple often consume up to 60% of their daily calories from this cereal[10]. The International Conference on Nutrition (ICN) Declaration[11] had advocated a strategy to combat 'hidden hunger' that stated: "Ensure that sustainable food-based strategies are given first priority, particularly for populations deficient in vitamin A and iron, favouring locally available foods and taking into account local food habits." Supplementation was to be progressively phased out as soon as micronutrient-rich food-based strategies enabled adequate consumption of micronutrients. It has been pointed out that a sustainable solution to the problem of malnutrition can come only when it becomes possible to improve the content of the missing micronutrients in the major staple crops[12].

In agriculture, biotechnology- or molecular biology-based approaches are used primarily in one of two ways:

- genetic engineering to create transgenics or genetically modified organisms (GMO) by manipulating, deleting or inserting genes in order to change the organism; and
- marker-assisted selection to speed up conventional crop and animal breeding. Both can and have played a role in providing biotechnology-based solutions to improve the nutritional quality of agricultural products.

Genetic engineering

The production of "Golden Rice" was a major event in the use of genetic engineering to deal with the problem of addressing food security for developing countries from a qualitative perspective, given that the major forms of micronutrient malnutrition are "iron, iodine and vitamin A deficiency". In addition to the range of nutritional interventions hitherto promoted, biotechnology using genetic engineering provided a window of opportunity to tackle this global problem in a more sustainable manner by altering the nutritional quality of staple crops that constitute the bulk of the staple diet in developing countries. Using the example of rice, the necessary genes for improving the availability of carotenoids (vitamin A precursors) are not available in the rice gene pool; hence genetic engineering was an approach that was potentially very attractive. Since rice endosperm does not contain any provitamin A, the initial objective was to introduce the entire biochemical pathway for its synthesis. Several years of research culminated in the production of 'Golden Rice' by a group of Swiss transgenics researchers working with daffodil genes. The endosperm of Golden Rice contained substantially higher levels of provitamin A, visible as "golden" colour of different intensities in different lines[13,14]. The best provitamin A line had 85% of its carotenoids as beta-carotene. Other lines had less beta-carotene, but high levels of lutein and zeaxanthin, both of which are of nutritional importance because they have other positive nutritional effects[13]. The first-generation Golden Rice, with a gene from daffodil and a common soil bacterium, drew considerable criticism as a technological solution to a problem associated with poverty and hunger. It was argued that Golden Rice would encourage people to rely on a single food rather than the promotion of dietary diversification. Detractors also noted that a normal serving of Golden Rice contained only a small fraction of the recommended daily allowance (RDA) of beta-carotene[1]. Golden Rice 2 was developed by replacing the daffodil gene with an equivalent gene from maize. This modification increased the amount of beta-carotene approximately 20-fold, so that~ 140 grams of the rice would provide a child's RDA for beta-carotene.

Another approach with similar objectives was to increase the availability of iron while reducing the inhibitor content or adding a resorption-enhancing factor. Only 5% of the iron in the rice plant is in the seed and hence, an attempt was made to create a sink for iron storage within the endosperm by expressing a ferritin gene from *Phaseolus*, resulting in a 2.5-fold increase in endosperm iron content. Feeding studies with peptides from muscle tissue had shown that cystein-rich polypeptides enhance iron resorption. A metallothionin-like gene from Oryza achieved a 7-fold increase in endosperm cystein[15]. Since interference with the phosphate storage could affect germination, expression of the phytase gene had to be achieved in such a manner as not to interfere with germination. The enzyme was, therefore, excreted into the extra-cellular space, and one transgenic line that was developed expressed the phytase to levels 700-fold higher than endogenous phytase. However, the transgenic enzyme in this line did not refold properly after cooking; it had lost its thermo tolerance and was hence ineffective. New transgenic plants are being developed, aimed at targeting the enzyme to phytase storage vesicles so as to reduce the phytate content directly and thereby overcome the loss of enzyme during cooking. These three genes that influence iron availability and absorption are being combined with the provitamin A genes by crossing[15]. It is now well recognised that vitamin A-deficiency indirectly interferes with iron resorption, since higher intakes of beta-carotene (converted to retinol after ingestion) may promote absorption of iron and vice versa. The FAO, along with its partner in International Atomic Energy Agency as well as other investigators, have approached this problem differently. Their aim is to induce mutations using nuclear techniques[16] to produce strains of cereals with higher yields of micronutrients or low phytic acid content, thereby improving the bioavailability of these nutrients in cereals. Raboy[17] has developed low phytic acid (or lpa) mutant varieties of maize, rice and barley using similar techniques. The phytic acid content of lpa seeds is reduced by 50-80 percent as compared to non-mutant seeds. The total amount of phosphorus remains the same; phytic acid is replaced with inorganic phosphorus, which does not bind a range of trace minerals, thus making the nutrients available for absorption.

Marker-assisted selection and breeding

A careful examination of the composition of nutrients in a variety of crops demonstrates a wide genetic variation in the nutrient content of a range of food crops such as rice, cassava, beans and maize (Table 2) which contribute to the vast biodiversity in the plant kingdom. A similarly wide range in the micronutrient content of a single staple such as rice (Table 3) is also evident among the varieties of rice grown throughout the world[18]. Conventional plant breeding has not only demonstrated the existence of substantial and useful genetic variation that exists in the germ plasm of key crops, but also that it can be a valuable means by which varietals can be chosen and cross-bred to improve and enhance their nutrient content. Since plant breeding takes a long time, using molecular biological markers to identify traits can speed up the process. This approach, while falling under the broad rubric of agricultural biotechnology, is distinct from genetic engineering in that it involves looking at genes and not modifying or changing them. In this case, molecular biology is aiding the process of plant breeding by speeding up the identification of varietals with special characteristics with the assistance of markers, thus ensuring the outcomes of crossing different strains.

A strategy of breeding plants that enrich themselves and load high amounts of minerals and vitamins into their edible parts has the potential to substantially reduce the recurrent costs associated with fortification and supplementation. But this will be successful only if farmers are willing to adopt such varieties, if the edible parts of these varieties are palatable and acceptable to consumers, and if the incorporated micronutrients can be absorbed by the human body[19]. According to Bouis, if a plant breeding strategy to combat micronutrient deficiency is to work and be universally adopted, particularly in developing countries, five crucial questions need to be first addressed.

They are:

- ➢ Is it scientifically feasible to breed micronutrient-dense staple food varieties?
- ➢ What are the effects on plant yields and will farmers adopt such varieties?
- ➢ Will micronutrient-density change the characteristics of The food that are important to consumers?.
- ➢ Will the extra micronutrients in staple foods be bioavailable to humans?
- ➢ Are there other cheaper or more easily sustainable strategies for reducing micronutrient malnutrition?

Thus, the ICN goal of promoting sustainable 'food-based strategies' to enable adequate consumption of micronutrients in the developing world can be achieved by the introduction of 'bio-fortified' crops, which are varieties bred for their qualitative aspects and not merely to improve yields. The feasibility of plant breeding approaches for improving the micronutrient content of staple crops is real[20]. This is an approach that uses both classical plant breeding and modern biotechnology. Breeding programmes can readily manage nutritional quality traits, which, for some crops, are highly heritable, simple to screen, and offer the possibility of increasing the content of several micronutrients in the same variety. The desirable traits are sufficiently stable across a wide range of growing environments. In addition, these traits for quality and high nutrient content can be combined with the traits for which staples are specifically bred i.e., superior agronomic characteristics and high yields. Biotechnology, on the other hand, offers a repertoire of techniques, in particular the use of marker techniques, which will help scientists to better understand and identify the genes responsible for high nutrient content. Help to the identification of the relevant markers will enable marker-assisted selection to facilitate transfer of these desirable traits through conventional plant breeding.

Table 2: Genetic variation in concentrations of iron, zinc, beta?carotene, and ascorbic acid found in germplasm of five staples, (mg/kg of dry weight)[4]

	Iron Conc. (mg/kg)	Zinc Conc. (mg/kg)	Beta-carotene *** (mg/kg)	Ascorbic Acid (mg/kg)
Rice, brown	6-25	14-59	0-1	-
milled	1-14	14-38		-
Cassava: root	4-76	3-38	1-24*	0-380*
Cassava: leaves	39-236	15-109	180-960*	17-4200*
Bean	34-111***	21-54	0	-
Maize	10-63	12-58	0-10	-
Wheat	10-99**	8-177**	0-20	-

Notes: * fresh weight basis; ** including wild relatives, *** range for total carotenoids is much greater.
[4] Source: International Center for Tropical Agriculture, 2002.

Table 3: Varietal differences in nutrient composition of rice

Nutrient	Range	Average	Highest nutrient content	Lowest nutrient content
Protein (n=1339)	5.55 – 14.58 g/100g	8.55	Indica CR1707 (Costa Rica)	Indica Rd 19 (Thailand)
Iron (n=95)	0.70 – 6.35 mg/100g	2.28	Long grained[a] red (China)	Undermilled Red[a] (Philippines)
Zinc (n=57)	0.79 – 5.89 mg/100g	3.34	Ganjay Roozy (IRRI)	Long grain[a] Fragrant (China)
Calcium (n=57)	1.0 – 65.0 mg/100g	26	ADT-21, red (India)	Brown Japonica[a] (Korea)
Thiamin (n=79)	0.117 – 1.74 mg/100g	0.475	Juchitan A-74 (Mexico)	Glutinous rice[a] special grade (China)
Riboflavin (n=80)	0.011 –0.448 mg/100g	0.091	Tapol Dark Purple (Philippines)	Mun-pu red (Thailand)
Niacin (n=30)	1.97 – 9.22 mg/100g	5.32	Long grained[a] purple (China)	Glutinous round[a] grained (China)

[a] These data come from Food Composition Tables, and do not strictly represent rice varieties
Source: Kennedy and Borlingame, 2000

There is considerable progress in this new area of biofortification, and the good examples are iron-rich rice (International Rice Research Institute, Philippines), quality-protein maize (International Maize & Wheat Improvement Centre, Mexico), high-carotene sweet potato (International Potato center, Peru), and high-carotene cassava (International Center for Tropical agriculture, Colombia)[21]. The major advantage of the 'biofortification' approach is that this strategy does not depend on the change in behavior of either the producer (farmer) or the consumer. Already existing high-yielding varieties can be used, which are being widely cultivated and consumed. The increase in nutrient content is a natural variation, and hence breeding specifically for these qualities need not necessarily alter appearance, taste, texture or cooking qualities, thereby having no impact on consumer behaviour. Combining nutritional quality traits with those for high yield or pest- or drought-resistance ensures ready adoption by the farmer, and market success. An added advantage is the increasing recognition that high levels of trace minerals in seeds also aid plant nutrition and may thus contribute to better growth and yields of staple crops. Because trace minerals are important not only for human nutrition but also for plant and animal nutrition, plant breeding has great promise for making a significant, low-cost, sustainable contribution to reducing micronutrient deficiencies even among livestock and other agricultural food products[23]. It may thus have other important spin-off effects for environmentally beneficial increases in farm productivity in developing countries and may thereby contribute to agricultural trade from the South.

Cost-benefits of agricultural biotechnological approaches

The World Bank[7] estimates that, at the levels of micronutrient malnutrition existing in South Asia, 5 % of gross national product is lost each year due to deficiencies of just three nutrients: iron, vitamin A and iodine. In a hypothetical country of 50 million persons burdened with this rate of malnutrition, deficiencies in these three nutrients could be eliminated through fortification programmes costing a total of US $25 million annually, or 50 cents per person per year. The monetary benefit of this $25 million investment is quite high in terms of increased productivity - estimated at $20 per person per year, or a 40-fold return on an investment of 50 cents. These benchmark numbers will be used later in this paper as a basis of comparison with the benefits of a plant breeding strategy. A calculation of benefitcost ratios for biofortification plant breeding has been made by Bouis[23]. Expressed in present values, the costs are ~ US $13 million and the benefits are ~ $274 million, giving a benefit-cost ratio of over 20, which is quite favourable despite the very conservative assumptions made, and despite the long time-lag between investments and benefits. This last point highlights an essential difference between investments in standard fortification programmes and biofortification through plant breeding strategies. Standard fortification programs must be sustained at the same level of funding year after year. If investments are not sustained, benefits disappear. Such investments apply to a single geographical area, such as a nation-state. By contrast, research investments in plant breeding have multiplicative benefits that may accrue to a number of countries. Moreover, these benefits are sustainable since, as long as an effective domestic agricultural research infrastructure is maintained, breeding advances typically do not disappear after initial investments[24].

Improvements in other qualities of food that may benefit agricultural trade from developing countries

Qualities of food other than its nutrient content are also traits that producers, marketers and consumers look for. While producers and marketers favour traits that ensure long shelf life, appearance and safety of products, consumers go for the organo-leptic qualities like taste, texture and cooking characteristics. Biotechnology offers the potential to enhance and select for several positive qualities of agricultural products that consumers look for and thus promote agricultural trade. A survey of the biotechnology-related activities in this area that are already in progress in different regions in the world indicates that wide ranges of problems are being tackled. These include improving shelf-life and appearance of fruits, vegetables and flowers. Examples are papaya (shelf life), tomato (appearance and shelf life by delayed and improved ripening), potatoes (by increasing starch content and enhanced bruise resistance); orchids (by improved colour and shelf life); palm oil (improved quality); oil seeds (improvement in fatty acid composition - high lauric acid in rapeseed, high oleic acid in soya); cocoa (improved butter content and flavour); cassava (change in starch quality); and soybeans (stripping of allergenic genes). Other areas in which biotechnology is playing an important role are: reduction of toxicants (linamarin in lima beans, lotoaustralin in chick peas, solanine in potatoes, and cyanogenic glycosides in cassava); reduction of anti-nutritional factors (lectins and protease inhibitors); enhancing health promoting substances i.e. phytochemicals like lutein in tomatoes; and even foods like bananas and potatoes being engineered for pharmaceutical products or for vaccines against infections, as recently reported[25].

Summary and conclusions

A sustainable approach to reducing micronutrient malnutrition among vulnerable populations in developing countries is to enrich major staple food crops with micronutrients through plant-breeding strategies assisted by biotechnology, offering direct and indirect benefits to producers and consumers in developing countries[24]. Investment in breeding nutrient-dense staple foods can make a major contribution to reducing micronutrient deficiencies, and at the same time address the global problem of hunger. Because of the inherently wide variation in the micronutrient content of the available staple crops and the inherent compatibility of high yields and trace mineral density, success in increasing the mineral content of staples can be achieved in the short-run through conventional plant-breeding techniques. Plant breeding is a new strategy for improving nutrition, and it is essential to make these early, nutritionally improved varieties available to farmers for commercial production. Furthermore, doing so would also improve crop productivity. When micronutrient-dense seeds and grains are planted in micronutrient-poor soils, the farmer adopts the micronutrient-enriched seeds once they are developed. Any resulting improvements in micronutrient status must be measured to demonstrate the feasibility and practicality of plant breeding for improving micronutrient nutrition[26]. The time has come to invest in agricultural technologies to find sustainable solutions to micronutrient malnutrition. Plant breeding is one such technology that should be adopted by the world's agricultural community and should be supported by the world's nutrition and health communities.

Biotechnology not only offers the opportunity to increase crop yields and thereby increase the availability of food (quantity), but also has the enormous potential to improve the quality of staple foods and thus contribute to better nutrition of populations. The production of "golden rice" was a major event in the use of biotechnology to address the problem of micronutrient malnutrition by bringing about a qualitative improvement in the nutrient content of a cereal. Sustainable solutions can come only when it is possible to improve the content of the missing micronutrients in the major staple crops. Promoting sustainable 'food-based strategies' to enable adequate consumption of micronutrients can thus be achieved by the introduction of 'bio-fortified' crops which are varieties bred for their qualitative aspects and not merely to improve yields. The feasibility of plant breeding approaches worldwide for improving the micronutrient content of staple crops is real. This is an approach that uses both classical plant breeding and modern biotechnology. Plant breeding has already demonstrated the existence of substantial and useful genetic variation that exists in the germ plasm of key crops. Breeding programmes can readily manage nutritional quality traits, which for some crops are highly heritable, simple by screening, with the possibility of increasing the content of several micronutrients in the same variety. The desirable traits are sufficiently stable across a wide range of growing environments and, in addition, these traits for quality and high nutrient content can be combined with the traits for which staples are specifically bred, i.e. superior agronomic characteristics and high yields. Biotechnology offers a repertoire of techniques and helps in the identification of the genes responsible for high nutrient content, thereby making marker-assisted selection possible. This approach will facilitate transfer of these desirable traits through conventional plant breeding. However, nutrient content is not the only trait producers and consumers look for in a globalised world of increasing agricultural trade. While producers and marketers would favour traits that ensure long shelf-life, appearance and safety of products, consumers also go for the organo-leptic qualities like taste, texture and cooking characteristics. Biotechnology offers the potential to enhance and select for several other positive qualities of agricultural products. Given the importance of agricultural trade for developing countries, the judicious use of biotechnology may further the economic development of the developing countries while helping to tackle the problem of malnutrition in their midst.

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