

Symposium: Food Fortification in Developing Countries

Biofortification of Staple Food Crops^{1,2}

Penelope Nestel,³ Howarth E. Bouis, J. V. Meenakshi, and Wolfgang Pfeiffer*

*HarvestPlus, International Food Policy Research Institute, Washington DC and *HarvestPlus, Centro Internacional de Agricultura Tropical, Cali, Colombia*

ABSTRACT Deficiencies of vitamin A, iron, and zinc affect over one-half of the world's population. Progress has been made to control micronutrient deficiencies through supplementation and food fortification, but new approaches are needed, especially to reach the rural poor. Biofortification (enriching the nutrition contribution of staple crops through plant breeding) is one option. Scientific evidence shows this is technically feasible without compromising agronomic productivity. Predictive cost-benefit analyses also support biofortification as being important in the armamentarium for controlling micronutrient deficiencies. The challenge is to get producers and consumers to accept biofortified crops and increase their intake of the target nutrients. With the advent of good seed systems, the development of markets and products, and demand creation, this can be achieved. *J. Nutr.* 136: 1064–1067, 2006.

KEY WORDS: • *biofortification* • *staple food crops* • *plant breeding* • *iron* • *zinc* • *vitamin A*

Micronutrient malnutrition affects more than one-half of the world's population, especially women and preschool children (1). Reaching the Millennium Development Goals (2) to reduce the under-5 child mortality ratio by two-thirds and the maternal mortality ratio by three-quarters between 1990 and 2015 will require additional technologies and approaches to improving nutritional status, which is an important determinant of these mortalities. Biofortification of staple food crops is a new public health approach to control vitamin A, iron, and zinc deficiencies in poor countries. This paper gives a brief overview of this technology and asks 6 key questions: Is breeding for high nutrient content scientifically feasible? Will farmers adopt the new seeds? What is the target breeding level? What is the impact on nutritional status? Is it cost-effective? Will consumers accept the biofortified foods?

Biofortification. Biofortification is the development of micronutrient-dense staple crops using the best traditional breeding practices and modern biotechnology. This approach has multiple advantages. First, it capitalizes on the regular daily

intake of a consistent and large amount of food staples by all family members. Because staple foods predominate in the diets of the poor, this strategy implicitly targets low-income households. Second, after the one-time investment to develop seeds that fortify themselves, recurrent costs are low, and germplasm can be shared internationally. This multiplier aspect of plant breeding across time and distance makes it cost-effective. Third, once in place, the biofortified crop system is highly sustainable. Nutritionally improved varieties will continue to be grown and consumed year after year, even if government attention and international funding for micronutrient issues fade. Fourth, biofortification provides a feasible means of reaching undernourished populations in relatively remote rural areas, delivering naturally fortified foods to people with limited access to commercially marketed fortified foods that are more readily available in urban areas. Biofortification and commercial fortification, therefore, are highly complementary. Finally, breeding for higher trace mineral density in seeds will not incur a yield penalty (3,4). In fact, biofortification may have important spin-off effects for increasing farm productivity in developing countries in an environmentally beneficial way. Mineral-packed seeds sell themselves to farmers because these trace minerals are essential in helping plants resist disease and other environmental stresses. Moreover, a higher proportion of seedlings survive, initial growth is more rapid, and ultimately yields are higher.

Biofortification requires that agricultural research make direct linkages with the human health and nutrition sectors (5). This requires a multidisciplinary research approach, a willingness among scientists to communicate across disciplinary boundaries, and innovative funding strategies to support the research and ultimate dissemination of the biofortified seeds. In the HarvestPlus biofortification program, the major functional activities include plant breeding at the Consultative Group on International Agricultural Research centers and National Agricultural Research and Extension Services for common

¹ Presented as part of the symposium "Food Fortification in Developing Countries" given at the 2005 Experimental Biology meeting, April 5, 2005, in San Diego, CA. The symposium was sponsored by the American Society for Nutrition and the Society for International Nutrition Research and was supported in part by an educational grant from Akzo Nobel, Inc. The proceedings are published as a supplement to *The Journal of Nutrition*. This supplement is the responsibility of the editors to whom the Editor of *The Journal of Nutrition* has delegated supervision of both technical conformity to the published regulations of *The Journal of Nutrition* and general oversight of the scientific merit of each article. The opinions expressed in this publication are those of the authors and are not attributable to the sponsors or the publisher, editor, or editorial board of *The Journal of Nutrition*. Guest editors for the symposium are Jere D. Haas and Dennis D. Miller, Cornell University, Ithaca, NY. *Guest Editor Disclosure:* Jere Haas and Dennis Miller have no relationships to disclose.

² The HarvestPlus program is funded by the Bill and Melinda Gates Foundation, the World Bank, US Agency for International Development, UK Department for International Development, and the Danish International Development Agency.

³ To whom correspondence should be addressed: E-mail: p.nestel@cgiar.org.

bean, cassava, maize, rice, sweet potato, and wheat to develop varieties that combine the best nutritional and agronomic traits in each crop; food science and human nutrition research to measure the retention of nutrients in processing and cooking, screening of promising lines for micronutrient bioavailability, and efficacy studies involving human subjects to evaluate nutritional impact of the most promising lines intended for release; application of novel advances in biotechnology, genomics, genetics, and molecular biology to identify and understand plant biosynthetic genes and pathways of nutritional importance, including those for nutrient absorption enhancers and inhibitors, as breeding for these may also be a viable option; applying the above knowledge in marker-assisted selection for conventional breeding of crops and in the initial development (but not release) of transgenic lines; impact and policy research to 1) target regions where biofortification will have the greatest benefit and measurement of program impact and to 2) understand economic and social factors that determine the dietary quality of the poor and their micronutrient status, as well as policy advocacy based on that research; reaching and fully engaging the end users through improving seed dissemination systems, market and product development, and demand creation; and coordinated communication activities to provide support to internal project collaborators and external audiences, including donors, the academic and development communities, public officials, and the general media.

Is breeding for high nutrient content scientifically feasible? The potential to increase the micronutrient density of staple foods by conventional breeding exists (3,4,6): adequate genetic variation in concentrations of β -carotene, other functional carotenoids, iron, zinc, and other minerals exists among cultivars, making selection of nutritionally appropriate breeding materials possible. Also, micronutrient-density traits are stable across environments. In all crops studied, it is possible to combine the high-micronutrient-density trait with high yield, unlike protein content and yield, which are negatively correlated; the genetic control is simple enough to make breeding economic. Therefore, it will be possible to improve the content of several limiting micronutrients together, thus pushing populations toward nutritional balance.

To date, orange-flesh sweet potato lines with high levels of β -carotene (over 200 $\mu\text{g/g}$) have been identified, and beans with improved agronomic traits and grain type and 50–70% more iron have been bred through conventional means. Because of regulatory and political restrictions on the use of transgenic approaches, and because significant progress can be made through conventional breeding, 85% of HarvestPlus resources are currently devoted to conventional breeding. Transgenic approaches are in some cases necessary and, in some cases, potentially advantageous compared with conventional breeding. The best-known example is Golden Rice; β -carotene has not been identified in the endosperm of any rice variety, and an advanced transgenic line containing 37 $\mu\text{g/g}$ carotenoid, of which 31 $\mu\text{g/g}$ is β -carotene, is now available (7).

Ongoing transgenic research is exploring the use of an endosperm-specific promoter to deposit iron within the endosperm of rice so that it is not milled away (8). This approach is necessary because most of the iron in rice grains is deposited in the aleurone layer, which is removed when rice is milled to produce polished rice, a practice widely used in many countries (9).

Can we get farmers to adopt? Will yields and profitability be compromised? To work, the biofortification strategy requires widespread adoption by farmers. Farmers' criteria for changing varieties include food and income security, risk factors that are balanced against increased farm revenue through increased production or improved production efficiency and economics as

a consequence of adopting a new technology. Added economic value from improved end-use quality is also likely to be essential for adoption. This means that crop- and environment-specific traits relevant to adoption have to be considered in the breeding strategy for biofortified crops and end-product definition. For example, seed zinc concentration in wheat is closely related with stand establishment and final grain yield in zinc-deficient soils (10).

Two factors are critical to farmer adoption, namely whether the trait is visible and infrastructural development. The former includes color changes associated with high provitamin A concentrations or changes in dry matter content. Adoption of biofortified crops with visible traits will require that both producers and consumers actively accept the sensory change in addition to equivalent productivity and end-use features. Crops with invisible traits, such as higher concentrations of iron or zinc, do not require behavior change per se because the augmented levels will not result in sensory changes. Thus, productivity and improved end-use features such as flour quality are very important. In terms of infrastructure development, in Asia, for example, market networks and information flow operate reasonably efficiently, and once a new improved variety is released, it is rapidly taken up, as evidenced in the Green Revolution. In contrast, infrastructure in Africa is poor. Consequently, significant assistance will be needed to determine, understand, and identify the actions needed to overcome constraints to farmer adoption. This will include the use of farmer participatory breeding methods to identify the locally adapted biofortified genotypes that best suit producer-consumer needs, ensuring good access to planting material through the development of seed systems and the development of markets for both the harvested biofortified crop(s) and any processed products made from them, such as complementary foods.

What is the target breeding level? The critical information needed to set the target breeding level and thus determine the likely contribution to nutritional status is retention of the nutrient following processing and cooking, bioconversion/bioavailability, and nutrient requirements. HarvestPlus is currently collecting data on all these parameters, and data for provitamin A in sweet potato are used here for illustrative purposes. True retention of β -carotene in medium-sized orange-fleshed sweet potato, variety Resisto, was 88–92% for medium-sized roots of similar size and 70–80% when roots of different sizes were boiled together (11); thus, an average of 80% is assumed. The accepted bioconversion rate for β -carotene to retinol is 12:1, and the vitamin A estimated average requirements (EARs) for children are 210 μg retinol activity equivalents (RAE)/d for 1- to 3-y-olds and 275 μg RAE/d for 4- to 8-y-olds (12), and an average of 250 RAE/d is assumed. An average of 500 μg RAE/d is assumed for all other age groups.

In setting the target level, a liberal or conservative contribution can be assumed, depending on whether people are dependent on sweet potato as their sole source of β -carotene or if they eat a mixed diet. In the former case, sweet potato will have to supply 100% of the EAR, whereas 50% can be used for the latter. Unpublished data suggest it is possible for children and women to consume up to 200 g and 400 g sweet potato each day, respectively. Assuming these daily intake levels need to supply 100% of the EAR, the target breeding level will be 75 $\mu\text{g/g}$ β -carotene. To provide 50% of the EAR requires 37 $\mu\text{g/g}$ β -carotene. Varieties having 100 $\mu\text{g/g}$ β -carotene at harvest exist. However, they tend to have a low dry matter, and African consumers prefer sweet potato with a high dry matter (13).

What is the impact on nutritional status? Orange-fleshed sweet potato varieties that are naturally rich in β -carotene can be an excellent food source of provitamin A. A randomized

controlled study showed that feeding β -carotene-rich sweet potato, which provided about 830 μg RAE/100 g cooked root, to primary school children improved vitamin A liver stores as measured by the modified relative dose-response test (14).

To prove the concept that high-iron rice can improve the iron status of women of reproductive age, a double-blind intervention study was carried out in the Philippines. Undermilled iron-enhanced rice, which provided an additional 1.41 mg of iron/d, representing a 17% increase in dietary iron in the diets of these women, was efficacious in improving serum ferritin concentrations and body iron levels in nonanemic subjects compared with the locally used rice (15).

How cost-effective is the biofortification strategy? The principal cost components for biofortification relate to the research needed to develop biofortified varieties and implementation. Because an international agricultural research system is in place to develop modern varieties of staple foodstuffs, the research costs are essentially the incremental costs of enhancing micronutrient density. These research costs are likely to be the single largest cost component of biofortification and are a one-time investment, incurred at the outset. It is estimated that costs associated with plant breeding will average about \$400,000 per year per crop over a 10-y period, globally. Once biofortified varieties have been developed, in-country trials and local adaptation research costs are incurred, after which routine maintenance breeding to ensure the trait remains stable is put in place. Where systems for dissemination of modern varieties are in place, such as in South Asia, implementation costs are nil or negligible. Where such systems are underdeveloped, as in parts of sub-Saharan Africa, additional costs are incurred in establishing seed multiplication and delivery systems and creating both markets and consumer demand.

Quantification of the potential health benefits of biofortification has been done using the Disability-Adjusted Life Years (DALY) framework (16), in which the current burden of micronutrient malnutrition is quantified as the number of DALYs lost. The percentage reduction in this burden that can be attributable to biofortification is computed by considering current intake levels of the staple food, the additional amount of micronutrient it is likely to contain, and the percentage of the population that will consume the biofortified food. Placing a dollar value on DALY benefits is always problematic, and a uniform but arbitrary \$500 and \$1000 per DALY to value benefits have been used by HarvestPlus. This represents the range limits of per capita incomes in most of the developing world.

Applying the above cost-benefit framework to HarvestPlus target crops and countries suggests that the benefits far outweigh the costs; biofortification is a worthwhile investment even where the calculated benefits do not include the enhanced incomes that may result after adopting agronomically superior biofortified varieties. For example, the dissemination of β -carotene-enhanced orange-fleshed sweet potato in Uganda is likely to cost less than US\$5 per DALY saved, assuming coverage is between 25% and 50% (David Yanggen, International Potato Center, personal communication, May 2005). Vitamin A supplementation is estimated to cost US\$12 per DALY saved, but this assumes a 75% coverage rate (17).

Can we get consumers to adopt? The success of HarvestPlus is dependent on biofortified crops being available to consumers in a sustainable manner; thus, biofortified crops must be incorporated into existing marketing chains or new market opportunities developed. To achieve this, the HarvestPlus strategy centers on facilitating the dissemination of biofortified varieties and creating the demand for these varieties by linking producers and consumers through product and market development. The strategy focuses on engaging and developing the capacity of users

(producers, consumers, and processors/retailers) and diffusers (people in organizations and institutions that interact directly with enablers to move a technology to implementation) to adopt the new technology and, at the same time, transfer knowledge to and create awareness of the new technology among enablers (people working in organizations and institutions who can create a favorable environment for the adoption, dissemination, and increased consumption of biofortified crop varieties).

Diagnostic research is planned to identify how communication tools can be used to enhance behavior change in terms of increased consumption of the biofortified crop, after which basic strategies will be developed to initiate or build on desired behavior changes at different levels in the production-marketing-consumption chain. For example, to what extent does awareness need to be raised to change knowledge, attitudes, and beliefs about the role of, for example, orange-fleshed sweet potato to control vitamin A deficiency? Do practices need to be altered or new skills taught? Do people need to be motivated or provided with encouragement or reinforcement? Parameters for active behavior change will differ according to crop and target area, depending on whether and to what extent the trait is visible, as this may influence acceptance. Yellow corn, for example, is available in maize-growing countries in Africa, but there is a well-established strong cultural consumer preference for white maize for human consumption. If crops are new or nontraditional, color preferences are frequently not established. For crops with invisible traits, informing the consumer that new and nutritionally improved varieties are available will be important to avoid misperceptions that their food has been altered in an unauthorized or unacceptable way for nonnutritional purposes without their knowledge.

Summary. Based on micronutrient deficiency rates, there is compelling evidence that biofortification can be a key objective for plant breeders, in addition to the traditional objectives of disease resistance, yield, drought tolerance, etc. Scientific evidence shows that biofortification is technically feasible. Breeding for a micronutrient concentration that can have biological impact, without compromising agronomic traits, has been demonstrated for crops such as sweet potato. Predictive cost-benefit analyses have shown biofortification to be important in the armamentarium for controlling micronutrient deficiencies. The challenge is to get consumer acceptance for biofortified crops, thereby increasing the intake of the target nutrients. With the advent of good seed systems, the development of markets and products, and demand creation, this can become a reality.

LITERATURE CITED

1. United Nations System Standing Committee on Nutrition (SCN). 5th Report on the World Nutrition Situation Nutrition for Improved Development Outcomes. SCN, Geneva; 2004.
2. United Nations Development Programme. Human development report 2003: the millennium development goals: a compact among nations to end human poverty. UNDP, New York; 2003.
3. Graham RD, Welch RM. Breeding for staple-food crops with high micronutrient density: Agricultural Strategies for Micronutrients. Working Paper No 3; 1996. International Food Policy Research Institute, Washington, D.C.
4. Graham R, Welch R, Bouis H. Addressing micronutrient malnutrition through the nutritional quality of staple foods: principles, perspectives, and knowledge gaps. *Adv Agron.* 2001;70:77-142.
5. Bouis HE. Micronutrient fortification of plants through plant breeding: can it improve nutrition in man at low cost? *Proc Nutr Soc.* 2003;62:403-11.
6. Graham RD, Senadhira D, Beebe SE, Iglesias C, Ortiz-Monasterio I. Breeding for micronutrient density in edible portions of staple food crops: conventional approaches. *Field Crops Res.* 1999;60:57-80.
7. Paine JA, Shipton CA, Chaggar S, Howells RM, Kennedy MJ, Vernon G, Wright SY, Hinchliffe E, Adams JL, et al. A new version of Golden Rice with increased pro-vitamin A content. *Nat Biotechnol.* 2005;23:482-7.

8. Goto F, Yoshihara T, Shigemoto N, Toki S, Takaiwa F. Iron fortification of rice seed by the soybean ferritin gene. *Nat Biotechnol.* 1999;17:282–6.
9. Gregorio GB, Senadhira D, Htut H, Graham RD. Breeding for trace mineral density in rice. *Food Nutr Bull.* 2000;21:382–6.
10. Cakmak I, Kalayc M, Ekiz H, Braun HJ, Kılınç Y, Yılmaz Y. Zinc deficiency as a practical problem in plant and human nutrition in Turkey: A NATO-science for stability project. *Field Crops Res.* 1990;60:175–88.
11. van Jaarsveld PV, De Wet M, Harmse E, Nestel P, Rodriguez-Amaya DB. Retention of β -carotene in boiled, mashed orange-fleshed sweetpotato. *J Food Compos Anal.* 2005; in press.
12. Institute of Medicine. Dietary reference intakes for vitamin A, vitamin K, arsenic, boron, chromium, copper, iodine, iron, manganese, molybdenum, nickel, silicon, vanadium, and zinc. National Academy Press, Washington, D.C; 2001.
13. Tomlins K, Rwiza E, Nyango A, Amour R, Ngendello T, Kapinga R, Rees D, Jolliffe F. The use of sensory evaluation and consumer preference for the selection of sweetpotato cultivars in East Africa. *J Sci Food Agric.* 2004;84:791–9.
14. van Jaarsveld PJ, Faber M, Tanumihardjo SA, Nestel P, Lombard CJ, Benadé AJS. β -Carotene-rich orange-fleshed sweetpotato improves the vitamin A status of primary school children assessed by the modified-relative-dose-response test. *Am J Clin Nutr.* 2005;81:1080–7.
15. Haas JD, Beard JL, Murray-Kolb L, del Mundo A, Felix A, Gregorio G. Iron-biofortified rice increases body iron in Filipino women. *J Nutr.* 2005;135:2823–2830.
16. Stein A, Meenakshi JV, Qaim M, Nestel P, Sachdev HPS, Bhutta ZA. Analyzing the health benefits of biofortified staple crops by means of the disability-adjusted life years approach: a handbook focusing on iron, zinc and vitamin A. International Food Policy Research Institute (IFPRI) and International Center for Tropical Agriculture (CIAT), Washington, D.C. and Cali; 2005.
17. Jamison DT, Mosley WH, Measham AR, Bobadilla JL. Disease control priorities in developing countries. World Bank and Oxford University Press, Oxford, UK; 1993.