Symposium: Plant Breeding: A New Tool for Fighting Micronutrient Malnutrition

Breeding Strategies for Biofortified Staple Plant Foods to Reduce Micronutrient Malnutrition Globally[1]

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ABSTRACT One sustainable agricultural approach to reducing micronutrient malnutrition among people at highest risk (i.e., resource-poor women, infants and children) globally is to enrich major staple food crops (e.g., rice, wheat, maize, beans and cassava) with micronutrients through plant-breeding strategies. These target groups are dependent on these staples for their sustenance. Available research has demonstrated that micronutrient-enrichment traits are available within the genomes of these major staple food crops that could allow for substantial increases in the levels of Fe, Zn and provitamin A carotenoids (as well as other nutrients and health-promoting factors) without negatively impacting crop yield. Furthermore, Fe- and Zn-dense seeds can increase crop yields when sowed to soils deficient in these nutrients ensuring their adoption by farmers in these regions once they are developed. Importantly, micronutrient bioavailability issues must be addressed when using a plant-breeding approach to eliminating micronutrient malnutrition. The reduction of antinutrient substances that inhibit micronutrient bioavailability or the increase in substances that promote micronutrient bioavailability from staple plant foods are both options that could be pursued in breeding programs, although care needs to be taken not to compromise agronomic performance and sufficient attention paid to possible beneficial roles of compounds which reduce the bioavailability of trace minerals. 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 that should be supported by the world's nutrition and health communities. J. Nutr. 132: 495S–499S, 2002.

KEY WORDS: • *micronutrient malnutrition* • *trace minerals* • *agricultural productivity* • *bioavailability* • *sustainability*

Micronutrient-enriched staple plant foods, either through traditional plant breeding methods or through molecular biological techniques, are powerful intervention tools that target the most vulnerable people (resource-poor women, infants and children (1,2). These tools should be fully exploited by the nutrition and public health communities to combat micronutrient malnutrition (3). Biofortifying crops that feed the world's poor can significantly improve the amount of these nutrients consumed by these target populations (4). Additionally, increasing the micronutrient metals stored in seeds and grains of staple food crops increases the yield potential of these crops when they are sown to micronutrient-poor soils (5). Much of the developing world has significant areas of such soils (6). Enhancing seeds with micronutrient metals will act as an incentive to farmers affected by micronutrient-poor soils to adopt seeds that are micronutrient-enriched for use in their cropping systems (3).

Genetically modifying plants in ways that will increase the density of Fe and Zn in edible portions of seeds and grains requires that several barriers to metal accumulation within the plant be overcome (7). Therefore, the physiological processes controlling metal accumulation by plants is discussed below. Furthermore, because plant foods contain substances (i.e., antinutrients and promoters; **Tables 1** and **2**) that influence the bioavailability of these nutrients to humans, it is necessary to demonstrate the efficacy of micronutrient enrichment of plant foods toward meliorating the nutritional health of targeted populations. (Bioavailability is defined as the amount of a nutrient that is potentially available for absorption from a meal and once absorbed, utilizable for metabolic processes in the body.) This requires that the bioavailability of Fe, Zn and provitamin A carotenoids in select micronutrient-enriched genotypes of staple plant foods must be determined before advancing genotypes (3).

Physiological bases for micronutrient accumulation

The physiological basis for micronutrient efficiency in crop plants and the processes controlling the accumulation of mi-

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TABLE 1

Antinutrients in plant foods that reduce Fe and Zn bioavailability and examples of major dietary sources (3)

Antinutrients	Major dietary sources
Phytic acid or phytin	Whole legume seeds and cereal grains
Fiber (e.g., cellulose, hemicellulose, lignin, cutin, suberin, etc.)	Whole cereal grain products (e.g., wheat, rice, maize, oat, barley and rye)
Certain tannins and other polyphenolics	Tea, coffee, beans, sorghum
Oxalic acid	Spinach leaves, rhubarb
Hemagglutinins (e.g., lectins)	Most legumes and wheat
Goitrogens	*Brassicas* and *Alliums*
Heavy metals (e.g., Cd, Hg, Pb, etc.)	Contaminated leafy vegetables and roots

cronutrients in edible portions of seeds are not understood with any certainty. Because of space limitations and the complexity and volume of literature available, these subjects will not be covered in this short review. For an in-depth discussion of these topics, the reader is referred to the following references (5,7–10). A brief outline of the processes that determine micronutrient element concentrations in edible plant tissues follows.

There are several barriers to overcome in genetically modifying plants to accumulate more micronutrient metals (e.g., Fe and Zn) in their edible parts (7). These barriers to micronutrient metal uptake and distribution in plants are the result of tightly controlled homeostatic mechanisms that regulate metal uptake and distribution in plants, allowing adequate but nontoxic levels of these nutrients to accumulate in plant tissues. The first and most important barrier to micronutrient uptake resides at the root-soil interface (i.e., the rhizosphere). To increase micronutrient metal uptake by roots, the available levels of the micronutrient in the root-soil interface must be increased to allow for more absorption by root cells. This could be enhanced by stimulating certain root-cell processes that modify micronutrient solubility and movement to root surfaces, such as by stimulating the rate of root cell efflux of H^+, metal-chelating compounds and reductants, and by increasing root absorptive surface area such as the number and extent of fine roots and root hairs. Second, the root-cell plasma membrane absorption mechanisms (e.g., transporters and ion channels) must be sufficient and specific enough to allow for the accumulation of micronutrient metals once they enter the apoplasm (i.e., the intercellular free space between cells) of root cells from the rhizosphere. Third, once taken up by root cells, the micronutrients must be efficiently translocated to edible plant organs. For seeds and grains, phloem sap loading, translocation and unloading rates within reproductive organs are important characteristics that must be considered in increasing micronutrient metal accumulation in edible portions of seeds and grains (11). Finally, to be effective, the forms that the micronutrient metals are accumulated in edible portions of seeds must be bioavailable to people that eat the seeds (5,11).

Breeding for micronutrient enrichment: the question of yields

The genetic potential for increasing the concentrations of bioavailable Fe, Zn and provitamin A carotenoids (as well as Se and I) in edible portions of several staple food crops, including rice, wheat, maize, beans and cassava, is discussed by Graham et al. (3) and is reviewed by Gregorio in this volume.

The effects of breeding for micronutrient-dense staple seeds and grains on crop yields have been addressed in a number of recent reviews (8,12–14). Briefly, increasing the micronutrient stores in seeds increases seedling vigor and viability, which enhances the performance of seedlings when seeds are planted in micronutrient-poor soils. This improved seed vigor allows for the production of more and longer roots under micronutrient-deficient conditions, allowing seedlings to scavenge more soil volume for micronutrients and water early in growth, an advantage that can lead to improved yields compared with seeds with low-micronutrient stores when grown under micronutrient deficiency stress. **Figure 1** presents an example of such enhancement of crop productivity through micronutrient enrichment of seeds. In the experiment depicted, micronutrient-enriched wheat grain were sown to farmers' fields having micronutrient-poor soils in three farming regions of Bangladesh. Seven of the nine farms had significant increases in wheat grain yield when produced from micronutrient-enriched grain compared with control or farmers' grain not so enriched, clearly showing the advantage of using micronutrient-enriched grain on wheat productivity in these regions of Bangladesh.

Many of the countries where micronutrient deficiencies in humans are a problem are also countries that have large areas of micronutrient-poor/deficient soils (6). Thus, improving seed vigor with respect to micronutrient stores should be very beneficial to agricultural production in these countries. Additionally, disease resistance and stress tolerance are improved in micronutrient-dense seeds, which would also aid agricultural production in target countries (5,11). Thus, selecting for these traits in staple food crops is a win-win opportunity. It has the potential to enhance crop yields without additional farmer

TABLE 2

Examples of substances in foods that promote Fe, Zn and vitamin A bioavailability and major dietary sources (3)

Substance	Nutrient	Major dietary sources
Certain organic acids (e.g., ascorbic acid, fumarate, malate and citrate)	Fe and/or Zn	Fresh fruits and vegetables
Hemoglobin	Fe	Animal meats
Certain amino acids (e.g., methionine, cysteine, histidine and lysine)	Fe and/or Zn	Animal meats
Long-chain fatty acids (e.g., palmitate)	Zn	Human breast milk
Fats and lipids	Vitamin A	Animal fats, vegetable fats
Selenium	I	Sea foods, tropical nuts
Iron, zinc	Vitamin A	Animal meats
β-carotene	Fe	Green and orange vegetables
Inulin and other nondigestible carbohydrates (prebiotics)	Ca, Fe, Zn	Chicory, garlic, onion, wheat, Jerusalem artichoke

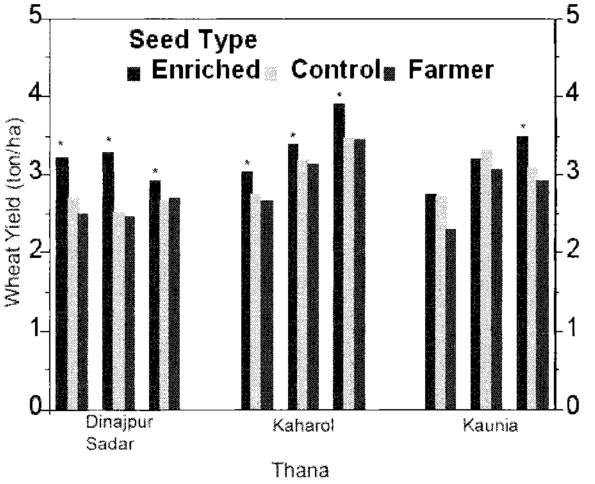

FIGURE 1 Effects of micronutrient enrichment of wheat grain on wheat grain yields harvested from nine farms in three districts (i.e., Thanas) in Bangladesh. Asterisks indicate significant difference from control and farmers' grain. The enriched and control grain were produced on an experimental farm. The enriched grain was generated from foliar applications of micronutrients to mother plants during their reproductive growth. Unpublished data from John Duxbury (Department of Crop and Soil Sciences, Cornell University, 2000).

inputs and to improve their nutritional quality at the same time.

Bioavailability issues

Determining the bioavailability of micronutrients in plant foods to humans is complex. A myriad of factors interact to ultimately determine the bioavailability of a particular micronutrient to an individual eating a mixed diet within a given environment (15). Because of this complexity, the data obtained using various bioavailability model systems are always ambiguous (16,17). Only data obtained on reducing the prevalence of micronutrient deficiencies among those afflicted using feeding trials in test populations under free living conditions can delineate the actual efficacy of using micronutrient-enriched varieties of plant foods as an intervention tool. However, it is impractical to test the bioavailability of selected micronutrients in numerous genotypes of staple plant foods that can be generated in plant-breeding programs in this way (3,8).

Micronutrient inhibitor and promoter substances. Plant foods (especially seeds and grains) contain various antinutrients (Table 1) in differing amounts depending on both genetic and environmental factors that can reduce the bioavailability of dietary nonheme Fe, Zn and other nutrients to humans (18). Dietary substances that promote the bioavailability of Fe and Zn in the presence of antinutrients are also known whose levels are also influenced by both genetic and environmental factors (Table 2). Current plant molecular biological and genetic modification approaches now make it possible to reduce or eliminate antinutrients from staple plant foods or to significantly increase the levels of promoter substances in these foods (19). Given these options (i.e., to decrease antinutrients or to increase promoters in staple plant foods), which is the wisest path to pursue?

Plant breeders could breed for genotypes that contain lower concentrations of antinutrients or molecular biologists could alter plant genes in ways that reduce or even eliminate antinutrients from plant food meals. However, doing so is not without risk and should be done with caution because many antinutrients are major plant metabolites that may play important roles in plant metabolism, in plant abiotic stress resistance and in plant resistance to crop pests or pathogens. Additionally, some of the antinutrients, such as phytate and polyphenols, may play important beneficial roles in human diets by acting as anticarcinogens or by promoting health in other ways, such as decreasing the risk of heart disease or diabetes (20–22). Thus, plant breeders and molecular biologists should be aware of the possible negative consequences of changing antinutrients in major plant foods before they attempt to alter food crops in this manner (8,23).

Other substances, as shown in Table 2, promote the bioavailability of micronutrients in plant foods to humans even in the presence of antinutrients in those foods. Many of these compounds are normal plant metabolites and only small changes in their concentration may have significant effects on the bioavailability of micronutrients (24). Therefore, it is highly recommended that plant breeders and molecular biologists closely scrutinize the strategy of increasing promoter substances in food crops when attempting to improve food crops as sources of micronutrients for people (23).

Bioavailability enigmas. Anomalies in some studies of the effects of various dietary factors on micronutrient bioavailability suggest that some aspects of the current dogma concerning the mechanisms of action of some antinutrients in plant foods on Fe and Zn bioavailability are not fully understood. Under some experimental conditions, antinutrients, such as phytic acid, do not have large negative effects on Fe and Zn bioavailability in human subjects. The reasons for these anomalous findings are unknown. For example, **Table 3** lists some data reported by Morris and Ellis (25) from a study with humans fed either low- or high-phytate muffin diets. As expected, the subjects fed the dephytinized muffins remained in positive Fe balance for the entire period that they were fed the dephytinized muffins. Interestingly, subjects fed the high-phytate diet during the first 5 d were in negative Fe balance (as expected), but by study d 10, these same subjects demonstrated positive

TABLE 3

Apparent iron absorption in men fed whole bran muffins or dephytinized bran muffins (25)

Whole bran muffin		Dephytinized bran muffin	
5 d	10 d	5 d	10 d
	(Fe, mg/d)[1]		
	Subjects 1–5[2]		
−3.0 ± 1.1	2.2 ± 0.4	1.3 ± 2.5	2.8 ± 1.1
	Subjects 6–10[2]		
−0.3 ± 2.5	3.5 ± 0.9	0.0 ± 1.6	1.1 ± 1.8
	All subjects		
−1.6 ± 1.6	2.9 ± 0.7	0.7 ± 1.6	2.0 ± 1.1

[1] Intake minus fecal excretion, means ± SD, 10 subjects total.

[2] Subjects 1–5 consumed whole bran muffins for the first 15 d then consumed dephytinized bran muffins. Subjects 6–10 consumed the muffins in the reverse sequence.

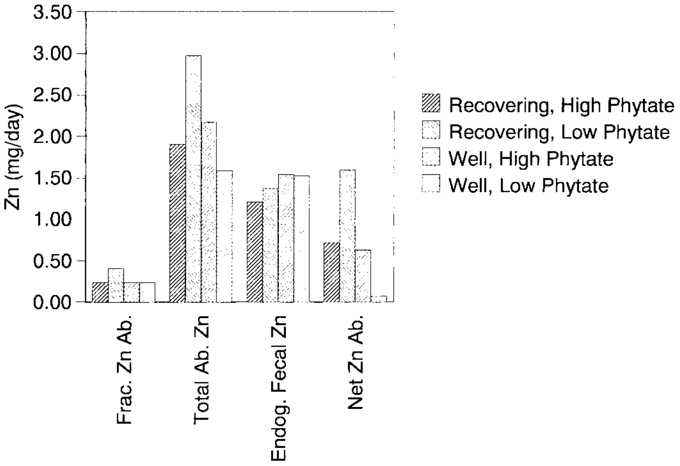

FIGURE 2 Effects of dietary phytate reduction (through phytase treatment of corn and soy flours) on Zn bioavailability to Malawian children recovering from tuberculosis or well children fed a corn, soy porridge meal served five times daily. Frac. Zn Ab. = fractional absorption of Zn; Total Ab. Zn = total absorbed Zn; Endog. Fecal Zn = endogenous fecal Zn; Net Zn Ab. = net absorbed Zn. Oral and intravenous doses of stable isotopes of Zn were used to determine Zn homeostasis values from analyses of urine and stool samples. Data from (27).

Fe balances (which was not expected), suggesting that there must have been some adaptation to the high-phytate meals in these test subjects. Others have reported similar results from balance studies to those of Morris and Ellis (26).

Figure 2 presents some recent findings reported by Manary et al. (27) concerning phytate action on Zn bioavailability in the human gut (i.e., precipitation of Zn as a Zn-phytate complex in the lumen of the small intestine making it unavailable for absorption). They studied the effects of phytate on Zn homeostasis in four groups of children: two groups recovering from tuberculosis (27) were fed high-phytate and low-phytate diets and two groups that were well but in the hospital for elective surgery and other treatments were fed high-phytate and low-phytate diets. As expected, in the children recovering from tuberculosis fed meals high in phytate, fractional Zn absorption, total Zn absorption and net Zn absorption were significantly reduced, while endogenous fecal Zn decreased compared with those fed low-phytate diets. However, unexpectedly, for the well children fed a high-phytate diet, more phytate had no effect on fractional Zn absorption, while total Zn absorption and net Zn absorption were higher, compared with well children fed the low-phytate diet. A major difference between the recovering children and the well children was the fact that the recovering children had received four potent antibiotics for over 60 d, whereas the well children received none. This suggests that the activity of microorganisms in the gut may have a large influence on the effects of phytate in meals on Zn bioavailability. Possibly, certain microorganisms in the gut may have active phytases that hydrolyze phytate making it inactive toward Zn absorption from the gut. If this is found to be the case, the composition of the diet and how it affects the microorganism population in the gut may be an important factor in determining the effects of phytate on Fe and Zn bioavailability. Further studies are needed to clarify this possibility.

CONCLUSION

There is very compelling global human health and nutritional evidence to convince plant breeders that micronutrient density traits should be primary objectives in their work targeted to the developing world. Furthermore, doing so should also improve crop productivity when micronutrient-dense seeds and grains are planted to micronutrient-poor soils, thus ensuring farmer adoption of the micronutrient-enriched seeds once they are developed. Current evidence strongly supports the contention that there is enough genetic diversity within the genomes of staple plant foods to accomplish this task. Succeeding in doing this would dramatically contribute to improving the health, livelihood and felicity of numerous resource-poor, micronutrient-deficient people in many developing countries and would contribute greatly to sustaining national development efforts in these countries. Finding sustainable solutions to micronutrient malnutrition will not be forthcoming in the foreseeable future if we do not begin to adopt agriculturally based tools, such as plant breeding, in this important global crisis in human health and well-being.

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