Nutritionally enhanced cereals: A sustainable foundation for a balanced diet

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Three nutrients, iron, zinc and pro-vitamin A, are widely deficient in humans, especially among low socio-economic groups in developing countries, but they remain significant concerns in industrialized countries as well. Cereals provide the majority of the intake of these nutrients in low-income families. Moreover, these three nutrients may interact synergistically in absorption and function to such an extent that there are potentially huge advantages in providing all three together in the one staple food. Because of this, they may be more bioavailable to deficient individuals than current thinking allows. To do so would provide a sound basis on which to build a better balanced diet for nutritionally compromised individuals. Genetic variation in nutrient composition exists in cereals and can be exploited in conventional breeding programmes and through gene technology. Cultural techniques, including fertiliser technology and organic farming, have also impacted upon the nutrient composition of cereals. Human iron and zinc intake can be doubled at least, and essential carotenoid intakes can be increased dramatically. Preliminary feeding trials with nutrient-dense grains have been encouraging. Moreover, nutrient-dense seeds also produce more vigorous seedlings and higher grain yield in soils where these nutrients are poorly available, so that to a significant extent agronomic and health objectives coincide. New varieties are rapidly adopted, especially where there are yield advantages, ensuring maximum impact without new inputs. This approach is potentially more sustainable than fortification and supplementation programmes because intake is continuous, which is especially important for zinc because it is needed almost daily.

Key words: iron, zinc, vitamin A, phytate, fertilizer, plant breeding, farming system.

Introduction

During the push of the 'Green Revolution' towards food security through increasing the yield of staples, little thought was given to human health and the nutritional value of diets. Diets throughout the world changed, resulting in a dramatic increase in iron deficiency, following the breeding of new cereal varieties in which the contents of iron and other micronutrients were largely overlooked.

The current agricultural paradigm, which takes into account the sustainability of natural resources, still fails to address the nutritional quality of the food its systems develop.

We propose that nutritionally enhanced cereals can form the basis for a food-based solution to the nutritional needs of the population and this paper will look at how this might be approached in relation to micronutrient deficiencies.

The need for a sustainable balanced diet

The need to address micronutrient deficiencies has been brought into sharp focus by statistics of the World Health Organization and the World Bank,[1,2] with micronutrient malnutrition diminishing the health, productivity and well-being of over half of the global community. The most important micronutrients, in order of numbers of people known to be affected by deficiency, are iron (3 billion deficient), iodine (2 billion at risk of deficiency) and vitamin A (230 million children are deficient). To this group we add zinc which is, in the opinion of specialists in zinc nutrition, as important as iron deficiency.[3] Other micronutrient minerals that should be considered for nutrient balance include selenium, copper, boron, manganese, chromium and lithium. In addition, we need to consider vitamins (e.g. vitamin E, folic acid and vitamin C) and other dietary substances that affect human health and nutritional status through their influence on bioavailability of nutrients.

It is more than the extent of these deficiencies that makes them important. Deficiencies of iron, zinc, vitamin A and iodine not only compromise the immune system, but can irreversibly retard brain development *in utero* and in infancy. This means that deficiency of any of these in a pregnant or lactating woman can result in subclinical mental retardation in children so that they never achieve their genetic potential. Such children may be less fit to control their environment and to provide for their own food security in later life, to compete for better education and for higher level jobs within their society. They are therefore more likely to be nutrient deficient too, giving rise to a higher chance of another generation of less fit and less adaptable individuals. An example of how economic and social development rely on good nutrition is given by Hetzel.[4] He records two separate instances of how treatment of a village with iodine not only eliminated cretinism, goitre and other health manifestations of the deficiency, but also led to improved social and economic development compared to a control village. This included the adoption of new agricultural technology. Poverty and malnutrition tend to perpetuate themselves and contribute to the high population growth rate that is associated with unsustainable food security.

The impact of micronutrient malnutrition is primarily seen among women, infants and children from impoverished

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families in developing countries;[5,6] however, micronutrient deficiencies are not restricted to developing countries, with Australia recording up to 5% anaemia overall and almost a staggering 10% in teenage girls.[7] Additionally, 41% of all poor, pregnant African-American women in the United States are anaemic.[8] The problem is, therefore, qualitatively the same within both industrialized and developing countries and we argue that the sustainable solution is also the same: through a food system that delivers all required nutrients in adequate amounts.

Supplementation with essential nutrients by injection or pills can be an effective and economically viable way of alleviating deficiencies. However, almost without exception, supplementation has failed through a lack of adequate infrastructure and education in developing countries and public perception in developed countries. In addition, these programmes generally focus on individual micronutrients, foregoing increased health benefits that can be achieved by taking into account valuable interactions that have the ability to improve health over and above that achievable by single micronutrients.

Therefore, a food-based system of dealing with micronutrient deficiencies as a whole rather than on an individual basis is the only sustainable solution to this insidious problem affecting both rich and poor nations.

Nutrient interactions and bioavailability

In the prevention or correction of nutrient deficiencies, the nutritional value of a diet can not be determined based on the concentration of individual nutrients, as interactions between nutrients and with antinutrients affect bioavailability, which is the degree to which a nutrient is absorbed from the diet. Interactions are recognized when the response of an individual to a nutrient is not constant but varies depending on the level of another nutrient or antinutrient in the diet. Because the issues of nutrient bioavailability in food are complex, an alliance with human nutritionists can be the only way for agricultural scientists to take on nutritional quality as a specific objective for a food-based system and succeed.

Anti-nutrients

An antinutrient is a substance occurring in the diet which acts antagonistically towards one or multiple nutrients, reducing bioavailability. This is usually done through complex formation which reduces nutrient absorption.

Phytate

Phytic acid and its salt, phytate, are important antinutrients to trace element absorption. Phytic acid converts dietary calcium into insoluble and, therefore, unabsorbable calcium phytate. This precipitate, in turn, binds to zinc and iron, rendering these trace elements also unabsorbable.

Phytate is an organic form of phosphorus that is especially high in cereal grains comprising 70–90% of the total phosphorus in the whole grain, depending on the species.[9] Although variation in phytate exists between species, very little intraspecific variation has been found.[9–11] Phytate concentrations do vary, however, in response to cultural techniques; for example, irrigation and fertilizer application.[10–12] This indicates that it is possible to reduce levels of phytate in grain, but not through traditional breeding methods.

In wheat, 87% of the phytate in the grain is present in the aleurone,[9] which results in much of the phytate being removed by milling, although along with a large proportion of iron and zinc.

There are many other antinutrients including tannins and antivitamins;[13] however, these are of lesser importance in cereals.

Nutrient interactions involving iron, zinc and vitamin A

Iron, zinc and vitamin A are nutrients of interest because they are among the most widely deficient in human populations[2,3,5,14] and their density can be increased in staples by plant breeding. The potential for synergistic interactions among these three nutrients is shown in Fig. 1. Each side of the triangle represents the first order interaction of a pair of nutrients, and there is the potential for a second order interaction among all three nutrients. In terms of nutrition and health, the essential roles (main effects) of these three nutrients, represented by the apices of the triangle, are well known and do not need to be repeated here.

Zinc–vitamin A interactions

Evidence of interactions between vitamin A (retinol) and zinc has emerged in the late 20th century (discussed elsewhere[15,16]). In their summary figure, Christian and West[15] indicate a role of zinc in the synthesis of retinol-binding protein (RBP), which is involved in releasing vitamin A from the liver, and in increasing lymphatic absorption of retinol and its inter- and intracellular transport. In return, vitamin A promotes the synthesis of a zinc-dependent binding protein and thereby the absorption and lymphatic transport of zinc. The interaction of delivering these two essential nutrients together to patients deficient in both was shown by Udomkesmalee and coworkers.[17] They observed the strong synergistic effects of adding both nutrients together on conjunctival parameters and RBP. They concluded that the dual treatment was so effective that supplementation with as little as twice the recommended daily allowance of both together

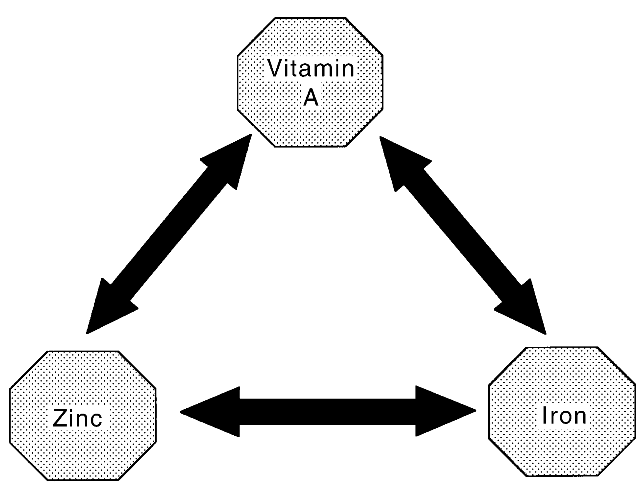

Figure 1. Potential synergistic interactions among vitamin A (VA), zinc and iron.[42] Interactions between zinc and vitamin A are already well established, as are the interactions between vitamin A and iron. Reprinted with permission.

was sufficient to normalize the deficiencies. We note here that plant breeding can also double the normal daily dose of these nutrients compared to that delivered by today's staples.

Iron–zinc interactions

Interactions of the mineral–mineral type among chemically similar members of the transition metal series have been characterized in both plants and animals much earlier than the zinc–vitamin A interaction.[18] Both synergistic and antagonistic interactions occur, but the competition between Fe^{2+} and Zn^{2+} for the bond with plasma transferrin is an antagonistic interaction that is well documented.[19] However, this effect is not as likely to be significant if the subject is deficient in these nutrients and less probable when iron and zinc are given as food rather than as soluble supplements. Recently, evidence of synergy in the absorption generated by genetically different beans was identified (J. King, pers. comm., 1999). The iron absorbed by young women fed one of two beans of similar iron density was greater in the beans with the higher zinc density. This could not be explained alternatively by the levels of phytate or tannins. Such a synergistic effect strongly indicates that breeding for staples that are dense in both iron and zinc is required in order to effectively address iron-deficiency anaemia.

Vitamin A–iron interactions

A seminal paper by Hodges and coworkers brought this important interaction into focus.[20] They showed that humans kept on a vitamin A-deficient diet became anaemic despite adequate iron intake. The anaemia responded to vitamin A and not to iron supplementation. Since then, numerous studies have confirmed the effect, both in experimental animals[21] and in human populations in a number of countries.[22,23] The animal studies confirmed an effect of vitamin A on blood formation, and human studies the effect of vitamin A on iron transport in blood. Several supplementation studies established that dual supplements of iron and vitamin A were more effective than if either was alone.[24]

Interest in this interaction has been rekindled by the recent work of Garcia-Casal and coworkers. They showed that 500 IU of vitamin A or β-carotene (a precursor to vitamin A) added to a 0.1 kg meal of cereal (wheat, rice or maize) doubled the iron absorption from the gut of human subjects in Venezuela.[25] Earlier work suggests that this effect occurs in the presence of non-haeme, phytate-bound iron and may be due to reduction and/or chelation of iron by the carotenoid, hence enhancing transport of iron from the lumen of the gut to the mucosal cell membrane.[26–28] It appears that in the presence of high levels of phytate and tannins in the diet, vitamin A or β-carotene will enhance the bioavailability of iron in humans,[25] but in the absence of phytate, no enhancement was found.

A putative second order interaction

Although the proof may be technically difficult, a three-way interaction in which the response to one nutrient depends on the levels of the other two nutrients can be predicted. Such synergistic three-way interactions are well known in plants. Given the synergies in all three first order interactions, an individual deficient in all three nutrients can be expected to respond dramatically to a relatively small supplementation of the three nutrients given together, until normal homeostasis is reached. This is because absorption efficiency is likely to be very high for each in the presence of the other synergists, and with more of each nutrient available to catalyse the primary functions of the others, deficiency symptoms will be quickly suppressed. This principle is consistent with other findings[17] that only a relatively small combined supplement of zinc and vitamin A was needed to normalise the diagnostic indices.

Nutritional enhancement of cereals

In order to deliver enhanced nutrition within a food-based system, it is necessary to increase the nutritional value (i.e. increase nutrient loading and reduce the amount of antinutrients) of the food consumed. By nutritionally enhancing cereals, severe deficiencies can be eliminated in developing countries where largely cereal-based diets are consumed. However, in industrialized countries like Australia, where cereals constitute a lower percentage of the total diet, nutritionally enhanced cereals could be important amongst women and children in lower socio-economic groups and in reducing subclinical deficiencies among those who choose poor diets.

There are two distinct ways in which the nutritional value of cereals can be enhanced. The first is through breeding, utilizing the genetic variation available, and the second is through cultural methods, including fertilizer technology and, possibly, organic farming.

Breeding

Exploiting the genetic variation in crop plants for micronutrient density is one of the most powerful tools we have to change the nutrient balance of a given diet on a large scale. We have found four- or five-fold variation between the highest and lowest micronutrient concentrations in the grain of several hundred accessions from the germplasm banks of the major cereals.[29] The highest micronutrient densities, which are approximately double that of popular modern cultivars and indicating the existing genetic potential, can be successfully combined with high yield.

Unlike mineral micronutrients, preformed vitamin A is not obtainable from plants; however, its precursors, the provitamin A carotenoids, are and some of these are found in high levels in yellow maize, sorghum and pasta wheats, higher still in cassava and sweet potato but at low levels in other staples such as wheat, rice and potato. Therefore, the source for a food-based solution to vitamin A deficiency can be via carotenes rather than vitamin A itself.

Plant breeding

Plant breeding involves the selection of superior varieties of a species for crossing to improve a desired trait, here being micronutrient density.

Rice is inherently low in iron and milling removes half or more of that, hence making rice the poorest of all the cereals in iron. The progress in the rice breeding project is particularly encouraging in improving iron content. Iron density in rice varied from 7 to 24 mg/kg and zinc density from 16 to 58 mg/kg. A benchmark was established in that nearly all the widely grown 'Green Revolution' varieties were similar, about 12 and 22 mg/kg for iron and zinc, respectively. The best varieties discovered in the survey of the germplasm collection were, therefore, twice as high in iron and 1.5 times as high in zinc as today's most widely grown varieties. High iron and, to a lesser extent, high zinc concentration were subsequently shown to be linked to the trait of aromaticity and have been combined with high yield. Most aromatic rices, such as jasmine and basmati types, are high in both iron and zinc (Table 1) and in most other minerals.[29–31]

Gene technology
Gene technology involves the identification and insertion from another source, or deletion of a gene in order to improve the desired trait, in this case micronutrient density.

Little definitive information on the genetics of inheritance of carotenoid content in plants is available, except in carrots where three major genes controlling primary colour classes have been described,[32] with three basic biosynthetic enzymes involved.[33] In tomato, seven major biosynthetic steps, and more than 20 genes, have been well characterized in the synthesis of carotenoids.[34] Hauge and Trost described a major gene for carotene content in maize, and designated it the Y (yellow) locus that is incompletely dominant.[35]

Ingo Potrykus and colleagues have reported producing yellow endosperm transgenic rice grain containing 1.6 μg/g β-carotene by completing the biosynthetic pathway to β-carotene.[36] The resulting transgenic rice line synthesized enough β-carotene in its grain-endosperm to meet part of the vitamin A requirements of people dependent on rice as a staple in South Asia.

Recently, yellow rice was discovered in the International Rice Research Institute germplasm bank that may supply the missing genes through conventional plant breeding. On the advice of Prof. Lita del Mundo (University of the Philippines, Los Baños, Philippines), a search was made for Amarillo (Spanish for yellow) and two entries were found, one from the Philippines and one from Cuba. The high performance liquid chromotography analyses of the pigments in these lines are under way. The endosperm is vitreous and appears to have pigment through half of the endosperm of one line and 90% of the other, the rest in each case being white, chalky 'belly'. If so, further enhancement of expression should be possible and incorporation into the new high-iron, high-zinc, high-yielding variety should not take more than two to three years.

Table 1. Concentrations of iron and zinc (mg/kg, dry weight) in aromatic rice cultivars in comparison with non-aromatic types when grown, in a study typical of many comparisons, at the International Rice Research Institute, Los Baños, Philippines in 1996. Modified from references.[29,30]

	Fe	Zn
Aromatic		
Ganje Roozy	18.1	36.6
Banjaiman	18.1	33.3
CT 7127	17.1	32.4
Lagrue	19.0	34.8
Non-aromatic		
Bg 379-2	11.3	20.5
BG1370	11.5	19.5
UPLRi 7	10.8	20.9
Tetep	10.7	24.1

Bread and durum (pasta) wheats and a range of vegetables and fruit were analysed for carotenoid content (Fig. 2). While the amounts in wheat are perhaps 20 times less than in fruit and vegetables, the greater consumption of staples would make them more equal suppliers of carotenoids in the diet. If all carotenoids present in the carotenoid-dense lines of durum wheat were present as β-carotene rather than being oxidized to non-provitamin A carotenoids, this would be enough to supply the daily dietary requirement (1–2 mg/kg of wheat product). This could be possible using gene technology by down-regulating the carotene hydroxylase enzyme that oxidizes the carotenes to xanthophylls during grain maturation. However, the xanthophylls are now also implicated in eye health along with the carotenes.[37]

Cultural methods

Fertilizer technology
Fertilizer technology and use is widely understood and appreciated in modern agriculture so it can be a major vehicle for change in plant mineral content and food quality. The density of several micronutrients can be usefully enhanced by application of the appropriate mineral forms.[38,39] These micronutrients are zinc (Table 2), iodine, selenium, copper and nickel. However, because of their rapid oxidation in soil and low mobility in phloem, soluble iron and manganese fertilizers are ineffective in increasing these concentrations in plants, especially in the seeds that develop months after application. Foliar applications of iron are also of limited value. The vitamins in plants are not required as fertilizers because they are synthesized *de novo* by the plant. Thus, for many of the mineral nutrients of concern, fertilization is a useful strategy but, particularly for iron and the vitamins, it is not.

Organic farming
Organic farming is not a single cultural technique but is a whole system of farming. It is characterized by the absence

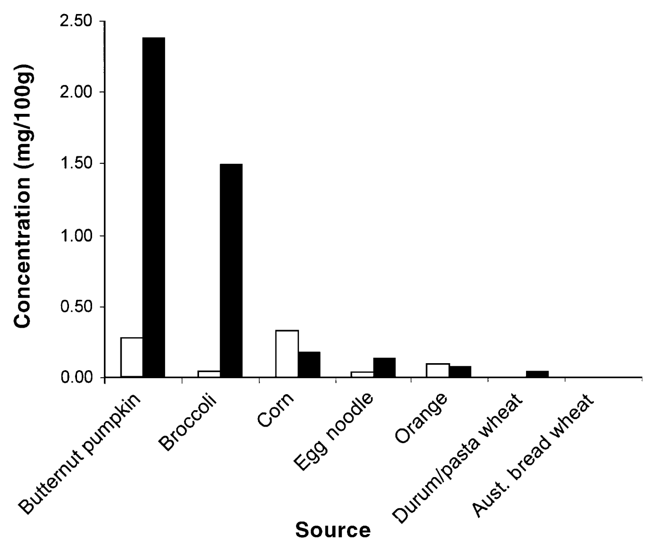

Figure 2. Carotenoid content of fruit, vegetables and wheat showing only lutein and zeaxanthin, which are not precursors to vitamin A. (■) Total lutein (mg/100 g); (□) total zeaxanthin (mg/100 g). Australian bread wheat has a lutein content of 0.01 mg/100 g. Modified from Graham and Rosser.[42]

Table 2. Zinc concentrations (mg/kg, dry weight) in the grain of wheat cultivars grown on zinc-deficient soil in South Australia, with and without zinc fertilizer added to the soil at sowing. Modified from Graham *et al.*[40]

Cultivar	Zinc concentration (mg/kg)	
	–Zn	+ Zn
Excalibur	7.6	25.3
Warigal	13.0	26.0
Kamilaroi	8.8	23.4
LSD (0.05)	3.4	

of pesticides and soluble fertilizers plus adjusted cultural techniques to compensate for the absence of these inputs. Like conventional farming, organic farming practices vary greatly from farm to farm. However, we have found, through an extensive comparison of organic and conventionally grown wheat in South Australia, that there are some reasonably consistent differences in mineral nutrient composition that are independent of yield. These include organic grain containing higher levels of zinc and lower levels of phosphorus, reflected in lower levels also of phytate phosphorus (Table 3). In a much more intensive, mostly single-site comparison of organic and conventionally grown wheat in New South Wales, Derrick reported similar nutrient results, although he did not investigate phytate.[41] These results indicate that organic farming has the potential to increase zinc and reduce phytate levels in cereal grains.

Conclusion

Micronutrient malnutrition is a leading health-care issue in the world today and, although much more detectable in developing countries, is also present but not widely appreciated in Australia and other industrialized countries. Although supplementation can be used to overcome deficiency, we propose that a food-based system can be just as effective and has greater sustainability.

Interactions between nutrients and the effect of antinutrients on uptake of the micronutrients must be taken into account when approaching this problem as they have the potential to affect bioavailability.

Table 3. Nutrient concentrations (mg/kg, dry weight) in the grain of wheat grown in 'across the fence' field trials on organic and conventional farms near Wolseley, South Australia, in 1997 (three farms, five varieties) and 1998 (two farms, four varieties) averaged across varieties*

		Organic	Conventional	
Zinc				
	1997	26.8	21.4	$P < 0.05$
	1998	29.8	21.2	$P < 0.001$
Phosphorus				
Total	1997	2580	3394	$P < 0.05$
Phytic		1621	2369	$P < 0.001$
Total	1998	2188	3284	$P < 0.001$
Phytic		1549	2726	$P < 0.001$

*Values for phytic phosphorus are based on one variety only and represent the phosphorus portion of the phytate molecule. Probability (*P*) values represent the organic versus conventional comparison.

Conventional plant breeding techniques as well as genetic engineering, and cultural techniques including organic farming and fertilizer technology, can be used as ways to help overcome micronutrient deficiencies within a food-based system. Cereals are an important part of any food-based plan to reduce micronutrient deficiencies as they form the basis for many diets and can target even the poorest and the least educated people.

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