Breeding for Improved Micronutrient Bioavailability and Gut Health

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Edible portions of staple food crops contain certain constituents (antinutrients) that can inhibit the absorption and/or utilization (i.e., bioavailability) of divalent and polyvalent trace element cations (e.g., Fe^{3+}, Zn^{2+}, and Cu^{2+}) from these foods and from other dietary components in a meal. These foods can also contain compounds that enhance or promote ("promoters") the bioavailability of essential trace elements even when antinutrients are present in a meal. Phytic acid is the most studied antinutrient. It can bind to these cations along with other dietary components because of its large negative charge, making the cations insoluble and unavailable for absorption by mucosal cells in the gut. Levels of these antinutrients and promoters in plant foods can differ depending on both genetic and environmental factors. Current plant molecular, biological, and genetic modifications, combined with plant breeding 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.

Some promoter compounds are normal plant metabolites and fewer genes control their levels in plants compared to the numerous genes required to regulate (via homeostasis mechanisms) the absorption, translocation, and deposition of iron, zinc, and other essential trace minerals in edible portions of staple food crops. Only small changes in their accumulation in edible plant products may be required to have significant effects on the bioavailability of micronutrients. Thus, breeding for increased levels of these promoters should be relatively simple compared to breeding for higher concentrations of essential trace minerals in staple seeds and grains, which involve numerous genes and their interactions with the environment. Below are discussions of the most promising promoter compounds found in plants.

Prebiotics: Staple food crops can contain prebiotics (i.e., food substances that simulate the growth of beneficial microbiota (probiotics) in the human gut). The most studied of these prebiotics are the non-digestible carbohydrates such as inulin (a fructooligosaccharide). Prebiotics have been shown to have positive effects on enhancing the bioavailability of some mineral nutrients (e.g., Fe, Zn, Ca, and Mg) in plant foods. The effects of human gut microbiota and their effects on human nutrition and health are just beginning to be recognized but not understood with any clarity. Undoubtedly, the effect of intestinal microbiota on our ability to use food, nutrients, and phytochemicals is immense.

The human intestine alone contains more microbiota than the eukaryotic cells of the entire body (i.e., at least 10 trillion intestinal microbial cells compared to about 1 trillion body cells). Metabolic activity of gut microbiota is equivalent to that of the body's vital organs. Microbial mass can account for 60% of the dry weight of feces. Studies have shown that microbial interactions with human cells are essential to normal mammalian physiology including metabolic activity and immune homeostasis. Gut microbiota provide energy from undigested food substrates, train the immune system, prevent growth of pathogens, transform certain nutrients and beneficial phytochemicals into usable substrates, synthesize certain vitamins, defend against certain diseases, stimulate cell growth, prevent some allergies, improve mineral absorption (e.g., iron and calcium), and produce anti-inflammatory effects. Most importantly, beneficial microbiota improve gut health in general, reduce gut inflammation, and improve the ability of people to use all nutrients in a meal more efficiently.

Changing gut microbiota populations to increase the numbers of probiotic bacteria through dietary means by providing prebiotics in staple food crops appears to have enhancing effects on iron, zinc, and other essential trace element bioavailability. Providing enhanced levels of prebiotics may overcome the negative effects of antinutrients on essential trace metal bioavailability because many bacteria in the gut can degrade antinutrients, such as phytates and polyphenols, releasing their bound metals and allowing absorption by enterocytes lining the intestine. Probiotic systemic effects on inducing the genes controlling the absorption of iron and other essential trace elements from the intestine can enhance the bioavailability of these essential trace elements to humans. Of equal and possibly more importance is the role of prebiotics in improving gut health and the intestine's ability to absorb and use numerous nutrients, regulate the immune system, and protect against invasion by pathogenic organisms. Thus, increasing the levels of prebiotics in staple food crops could be an extremely important strategy to enhance the nutrition and health of malnourished people worldwide.

Inulin and other non-digestible carbohydrates are common constituents of cereal grains and legume seeds. The biosynthetic pathways and genes associated with their accumulation in food crops have been explored. It is now possible to manipulate genes in staple food crops to accumulate significant amounts of some prebiotics (e.g., inulin) in their edible tissues. More research is needed to determine what types and amounts of prebiotics are required to enhance the bioavailability of iron, zinc, and potentially other micronutrients in staple food crops. This type of research should be expanded. Breeders should be informed and begin to enhance prebiotics in target crops to levels that would have health impacts.

Nicotianamine: Nicotianamine is a non-protein amino acid biosynthesized by all higher plants. It is the only known low molecular weight compound in plants that forms stable complexes with ferrous-iron (Fe^{2+}). It is required for the cellular, intercellular, and long-distance transport of iron throughout the plant. Several studies have shown that increasing nicotianamine levels in plants through molecular transformations results in greatly increased iron concentrations in seeds. Further, the iron accumulated in the seed as the Fe(II)-nicotianamine complex appears to be highly bioavailable. Therefore, nicotianamine appears to be an ideal promoter of iron bioavailability, and efforts should be started to find ways to increase its levels in seeds and grains of target crops in the HarvestPlus biofortification program.

Phytoferritin: All aerobic organisms store excess iron in a 450 kDa protein of 24 subunits–ferritin (i.e., phytoferritin in plants). This protein stores up to 4,500 ferric-iron atoms in its core. It accumulates in various cell plastids including chloroplasts. Excess plant iron is stored in phytoferritin. The iron stored in ferritin is bioavailable and does not interact with antinutrients present in a meal. Ferritin iron is transported into gut mucosal cells *in toto* by binding to gut membrane sites and absorbed via endocytosis. Phytoferritin is an ideal promoter for inclusion in staple food crop biofortification programs.

References

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