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Research review paper

Nutritional enhancement of rice for human health: The contribution of biotechnology

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ABSTRACT

Micronutrient malnutrition is widespread, especially in poor populations across the globe where daily caloric intake is confined mainly to staple cereals. Rice, which is a staple food for over half of the world's population, is low in bioavailable micronutrients required for the daily diet. Improvements of the plant-based diets are therefore critical and of high economic value in order to achieve a healthy nutrition of a large segment of the human population. Rice grain biofortification has emerged as a strategic priority for alleviation of micronutrient malnutrition. Nutritional enhancement of crops through conventional breeding is often limited by the low genetic variability for required dietary micronutrient levels. In this case, biotechnology strategies offer effective and efficient perspectives. In this review, we discuss genetic engineering approaches that have been successful in the nutritional enhancement of rice endosperm. These advancements will make substantial contributions to crop improvement and human nutrition. Their practical application, however, also demands visionary changes in regulatory policies and a broader consumer acceptance.

Contents

1. Micronutrient malnutrition worldwide

Micronutrient malnutrition is widespread especially in poor populations across the globe, reducing productivity of adults and leading to premature death in severe cases, particularly among women and children. Around 49 nutrients are essential to meet the metabolic needs of humans and deficiencies of various minerals and vitamins together are often addressed as 'Hidden Hunger', which is considered one of the most serious global challenges faced by mankind (Hirschi, 2009; White and Broadley, 2009). Iron deficiency anemia, vitamin A deficiency and iodine deficiency are recognized as three most common forms of micronutrient malnutrition, followed by other micronutrients including zinc, folate, calcium, proteins and other vitamins. Iron deficiency anemia affects around 2 billion people in both developed and

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developing countries (WHO, 2011). Main consequences of iron deficiency include mental retardation, decreased immune function and increased mortality of mother and child at birth (Puig et al., 2007). The severity of the problem for pregnant women is illustrated by the fact that around 200,000 deaths associated with childbirth each year can be attributed to this deficiency (Seymour, 1996). The daily recommended iron intake for human ranges between 8 and 18 mg/day depending upon age and gender, with recommended 30 mg/day for pregnant women (IOM Report, 2011). However, a large number of people in the world do not have the privilege of enriching their diets to allow this recommended intake.

Vitamin-A deficiency is equally important as it can lead to night blindness, xerophthalmia, and to total blindness if remains untreated. Even prior to blindness, vitamin A-deficient children are at a 23% higher risk of death as a result of measles, diarrhea, or malaria (UNICEF, 2009). Adequate supply of vitamin A is important during normal growth and repair of different body tissues and particularly has a vital role in visual system functioning. According to WHO (2009) and UNICEF (2009), vitamin A deficiency is a clinical problem in 45 countries and a sub-clinical problem in 122 countries, with around 190 million pre-school age children and 19 million pregnant women on the globe suffering from it. In some countries of sub-Saharan Africa and South East Asia the incidence is even higher, affecting around 40% of pre-school age children (UNICEF, 2010). Iodine deficiency is often associated with low production of thyroid hormone (hypothyroidism), which plays essential role in normal functioning of the human body. This deficiency can lead to brain damage, and if severe during pregnancy, it can cause stillbirth, spontaneous abortion and other congenital abnormalities (WHO, 2011). Likewise, other micronutrients play vital roles in normal body functioning, and lack of these components in the human diet has severe consequences.

2. Strategies to tackle micronutrient malnutrition

Micronutrient malnutrition can be avoided by dietary diversification, mineral supplementation and food fortification. However, such strategies have not always been successful, mostly for economic or social reasons and/or because of technical difficulties related to the choice of compounds (Frossard et al., 2000; Mayer et al., 2008). For instance, iodine or vitamin C can easily be added to dietary salt whereas addition of folic acid is difficult because of its high water solubility. Iron is one of the most difficult minerals for food fortification, because iron compounds such as $FeSO_4$ that are most soluble and have high bioavailability are unpalatable and often provoke unacceptable color and taste. Less soluble compounds such as elemental iron, are poorly absorbed by the human body (Hurrell and Egli, 2010). Recently, Hilty et al. (2010) used scalable flame aerosol technology to produce nanosized Fe and Fe/Zn compounds. Based on a rat feeding experiment, these compounds were as bioavailable as $FeSO_4$ but caused less color change in reactive food matrices than conventional iron compounds used for biofortification. In case of vitamin A, medical supplementation could notably reduce ocular forms of vitamin A-deficiency in many countries (Mayer et al., 2008). Although these vitamin A capsules (which cost around one USD/capsule) have the potential to significantly reduce vitamin A deficiencies, the implementation of this strategy relies a lot on the economic situation of countries (Mayer et al., 2008).

Meanwhile, research has also focused on molecules that promote the bioavailability of micronutrients (e.g., ascorbate and cysteine) and on reducing the activity of antinutrient compounds such as phytate and polyphenolics (Hurrell and Egli, 2010). Other food ingredients such as non-digestible carbohydrates, often termed prebiotics, were found to promote mineral absorption in animal models and in humans (Bouis and Welch, 2010; Hurrell and Egli, 2010; Yeung et al., 2005). Fructans (i.e. the fructo-oligosaccharides), including inulin, have received increasing attention recently (Roberfroid, 2005). They improve systemic absorption and utilization of micronutrients through promotion of beneficial microbiota in the hind gut (Abrams et al., 2005; Dethlefsen et al., 2007), with the potential added benefit that bacteria metabolize antinutrients such as phytate and polyphenols.

The majority of people suffering from micronutrient malnutrition often do not have access to supplementation strategies or possibilities of diversifying their diets. In the long term, therefore, biofortification strategies must include delivery of sufficient micronutrients through locally grown crops that have been optimized for their micronutrient content. Biofortification is feasible for different food crops and complements public health interventions, in addition to being an economical and sustainable solution. Research in crop biofortification is particularly focused on populations that otherwise cannot afford a nutritionally balanced diet in the foreseeable future. Since its official launch in 2004, the HarvestPlus Challenge program is supporting biofortification of staple food crops, including rice, maize, wheat, cassava, pearl millet, beans and sweet potato, primarily for iron, zinc and vitamin A (http://www.harvestplus.org/).

3. Significance of nutritional improvement of rice endosperm

Together with wheat and maize, rice is one of the most important food crops for humans and the main staple food for half of the world population. It provides around 21% of per capita energy and 15% of protein to global human populations (IRRI, http://irri.org/about-rice/rice-facts/rice-basics). Around 3 billion people, mostly in Asia, depend on rice for 35–59% of their caloric intake (Meng et al., 2005) and in many developing countries the dietary contribution of rice is substantially higher. For example, in Cambodia, Myanmar, Bangladesh and Vietnam, rice provides over 70% of dietary energy (Kennedy et al., 2003). This contribution of rice is a success of breeders who over thousands of years made rice productive, high yielding, and an affordable calorie source. However, progress towards improving the micronutrient content of rice has been limited, partially because it was the not the focus of rice breeding until recently.

Starch accounts for approximately 90% of total dry matter in rice seeds, followed by a fraction of storage proteins. Furthermore, rice grains are polished since the oil-rich aleurone layer turns the seed rancid upon storage and therefore makes rice unsuitable for consumption. The essential micronutrients which are almost exclusively stored in the husk, aleurone and embryo of rice, are removed during this process. Consequently, polished rice grains contain only small amount of key micronutrients or lack them entirely (Kennedy et al., 2003; Lucca et al., 2006). Importantly, many rice consumers are among the world's poorest whose diet is largely restricted to rice because it is filling and the most accessible and affordable food. Considering the above facts and the severity of widespread micronutrient malnutrition, improving rice grain (specifically endosperm) nutritional quality would have a significant impact on global human health. This calls for new, high-yielding and high-quality rice varieties containing higher levels of bioavailable vitamins, minerals and essential amino acids for nutrition.

4. Biofortification through plant breeding

Fortification by agronomic practices, e.g. soil fertilization with trace elements, is very difficult for developing countries and technically not feasible in case of complex molecules such as vitamins. Fertilization strategies targeted at improvement of mineral content in cereals grains were partially successful, e.g. in the case of zinc in wheat (Cakmak, 2008; Cakmak et al., 2010) while iron appears to be difficult in this regard. Breeding crop plants for increased levels of promoter substances, such as ascorbate and cysteine to enhance bioavailability of micronutrients, or by reducing antinutrient content (e.g., phytic acid) in their seeds has also been a focus during the last ten years. Mutants with low seed phytic acid content are now available for different staple crops, including rice, wheat, barley and