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Golden Rice: Genetically Modified to Reduce Vitamin A Deficiency, Benefit or Hazard?

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Introduction

During the past decade, there has been growing public interest in Genetically Modified (GM) foods, otherwise known as Genetically Engineered, Bioengineered, Transgenic Food or Genetically Modified Organisms, etcetera. As foretold by the many synonyms for GM foods, this is a field in food technology that is new, developing, and growing thus its nomenclature is inconsistent. In “natural” food stores, labels such as “NO GMOs” are appearing on food products. Genetically Modified Organism, what does that mean? There is no international definition for GMO. It can be loosely defined as any biological unit genetically modified by molecular biological techniques (1).

Plant genetic engineering was first demonstrated in 1983 when three different research groups independently showed that T-DNA vectors could transfer bacterial antibiotic resistance genes into plant cells (2). Subsequently, the first GM crops were introduced in the early 1990s. Molecular genetic techniques are more precise and controlled compared to traditional plant crossbreeding (Table 1). Molecular biology techniques allow for transfer of a verified number of specific genes into a transgenic product. With plant breeding, an unknown hundreds of genes that can be transferred from the parent to the progeny plants. Molecular biology allows sequencing and selection of the specific genes that are transferred. In crossbreeding, the genes are not known. Since there is a large scale genomic change in traditional breeding, there can be considerable changes in protein expression in the daughter plants compared to the parent plants (1). Genetic engineering allows transferring of gene interspecies; therefore, there is a higher capability for producing greater diversity with genetic engineering (1). Genetic engineering is efficient because precise genes are targeted and transferred; while crossbreeding takes repeated trial and error to produce the desired phenotype.

Table 1. Contrasting plant genetic engineering and traditional crossbreeding
(Adapted from Lack *et al*.)

Genetic Engineering	**Plant Crossbreeding**
Transfer of single gene	Transfer of hundreds of genes
Gene sequence known	Genes are not known
Small change in protein expression	Large changes in protein expression
Between species	Within species

Currently, some common GM food crops include soybean, corn, cotton, canola, potatoes, and tomatoes. Worldwide, more than one half of soybean crops and one third of corn crops are genetically modified (3). More than 40 GM food crops are approved for human or animal consumption by the US Department of Agriculture (USDA), the Environmental Protection Agency (EPA), and the Food and Drug Administration (FDA) (3).

Initially, GM plants were designed to benefit the producers. Bioengineering was created plants with resistance to herbicides, increased productivity and yields, resistance to high salinity of the soil. Over time, new plant developments have been made to benefit the consumer. Fruits have been developed to be more esthetically appealing such as seedless or sweeter taste. Research has been developing food as a vehicle for administering vaccines, such as Hepatitis B surface antigen expressed in potato tubers. Various crops are being developed to have higher nutritional value such as increasing levels of vitamins and minerals or elevating starch levels in potatoes so they absorb less fat when frying (4).

Public awareness and opinion of GM foods and biotechnology is variable and controversial. A 2001 survey showed that only 44% have “heard a ‘great deal’ or ‘some’ information regarding genetically modified food” (5). When asked what percentage of food found in a typical grocery store contains GM products, 14% of the respondents answered correctly: more than 50% of the food contains GM products. 62% answered no when asked if they had ever eaten GM food products (5). The lack of knowledge about GM foods had caused some skepticism and concern. A simple search for GM food on an internet search engine will bring up hundreds of websites protesting the production and sales of GM foods or demanding for labeling of GM food. While awareness of GM foods has been growing over the past decade, knowledge about GM foods is still low.

This paper will focus on the use of genetic engineering to increasing the nutritional value of edible plants, specifically describing a GM crop, Golden Rice, developed to increase dietary vitamin A. Secondly, the benefits and hazards of Golden Rice and other GM foods will be discussed.

Elevating vitamin A content by plant genetic engineering

Vitamin A (retinol) is an essential vitamin used in the retina to create pigment; therefore, it promotes good day and night vision. Vitamin A deficiency can cause visual impairment which can ultimately lead to blindness. It can also cause keratinization of the mucous membranes and soft tissue such as the lungs, GI and urinary tracts (6). Vitamin A deficiency is a problem in developing countries. Plants synthesize provitamin A carotenoids, such as β-carotene, which are converted to retinol in the human body. Natural sources of β-carotene include green leafy vegetables, yellow vegetables, and broccoli. However, when these vegetables are cooked or processed, their nutritional levels decline. Formed vitamin A is found as retinol in meats, milk, cheese, and butter. High levels (5 times RDA, 800-1000 RE) of vitamin A is toxic and can lead to coma or respiratory failure (6). However, it requires even higher levels of intake of β-carotene to be toxic to the body because the provitamin has to be converted to vitamin A. The conversion of β-carotene to vitamin A is not fast enough to cause toxicity. β-carotene is not toxic and can be stored by body (7). Therefore, researchers decided to use β-carotene as a means to increase dietary vitamin A.

Plant genetic engineering has been developed in rice, canola seed, and tomato to increase the levels of provitamin A cartenoids in the end food product. Golden rice has been developed which has 1.6 μg of β-carotene / g of dry rice (8). Shewmaker *et al.*developed canola seeds that had a 50 fold increase in cartenoids, consisting of mainly alpha and β-carotene (9). Transgenic tomato fruit (*crtI*) had a two fold increase in carteniods for a total of 5 mg of β-carotene or 800 retinol equivalents per fruit; therefore, one ripe *crtI* tomato fruit contained 45% of the RDA, while the control had 23% of the RDA for retinol (10). Golden rice has the most potential to have an impact on vitamin A deficiency globally because rice is a staple food in many populations.

Designing Golden Rice

Rice (*Oryza sativa*) is a global food staple. It is eaten often and in high amounts. Rice is usually processed to remove the husk and natural oil to leave the rice endosperm (rice grain) for long term storage and use. The oil-rich aleurone layer is removed so that the rice will not become rancid in storage (8). The rice endosperm is the edible part. While rice is a staple food for many populations, essential nutrient content is low. Therefore, it is a good candidate for ectopic production of β-carotene.

Rice endosperm does not naturally produce β-carotene; instead, it produces geranylgeranyl diphosphate (GGPP) which is an early precursor of β-carotene. Therefore it was necessary to use recombinant genetic techniques, not conventional breeding, to develop a rice endosperm that would produce β-carotene. To convert geranylgeranyl diphosphate to β-carotene, four additional plant enzymes were needed: phytoene synthase, phytoene desaturase, β-carotene desaturase, and lycopene β-cyclase. These enzymes were identified and their genes were isolated from various plants and bacterium. In 2000, Ye *et al.*put all this information together. The phytoene desaturase and β-carotene desaturase were circumvented by using a bacterial enzyme, carotene desaturase, that gave the combined result. The entire β-carotene biosynthesis pathway (three genes on three vectors) were transformed into rice endosperm using Agrobacterium. The result were yellow endosperms and gained the name Golden Rice. The yellow color was from the β-carotene formed in the endosperm (8). By 2002, Beyer *et al*. had refined the technique and were able to transform the β-carotene biosynthesis pathway by either single- or co-transformations of cDNA constructs. They used 2 genes from daffodil *Narcissus psuedonarcissus* (phytoene synthase and lycopene β-cyclase) and 1 gene from a bacterium *Erwinia uredovora* (carotene desaturase) (11).

The resulting Golden Rice yielded 1.6 – 2.0 μg β-carotene/g of dry rice. With a conversion factor of 6 μg of β-carotene to 1 μg of retinol, 200 g/day of rice would yield 70 μg /day of retinol which is not enough to fulfill the recommended daily allowance of retinol (1000-800 RE) (12). Since this crop is still relatively new, further research can improve the system and increase the levels of β-carotene produced in the rice. There have also been considerations for crossing Golden Rice with a rice producing high iron because β-carotene helps increase the bioavailability of iron (11). At this point, Golden Rice is a good resource for a supplementary source of β-carotene and subsequently, vitamin A.

Benefits: Golden Rice as a vitamin A supplement

For the general population, Golden Rice can be beneficial because it serves as a source of supplementary vitamin A and β-carotene. High intake of specific vitamins and minerals, such as carotenoids, vitamin A and β-carotene, have been linked with reducing risk of coronary artery disease, specific cancers, and macular degeneration (10). β-carotene is an antioxidant; therefore, it can help the protect the body from destructive free-radical reactions (13).

Malnutrition is a global problem. As of 1995, 800 million people in the world have diets are inadequate in macronutrients (carbohydrates, lipid, and protein) and micronutrients (minerals and vitamins) (14). The major deficiencies include vitamin A, iron, iodine, and vitamin E. Specifically, vitamin A deficiency causes blindness, premature death, and xerophthalmia (thickening on conjunctiva) (10). Even people in the industrialized nations suffer from vitamin and mineral deficiencies due to poor diets (14). Therefore, a food staple such as rice, which is widely consumed globally, can serve as a means to address the vitamin A deficiency. Once the Golden Rice has been enhanced and developed, it can be cultivated, grown, and widely dispersed to eliminate vitamin A Deficiency.

Hazards: Concerns for Genetically Modified foods

Despite the potential of plant genetic engineering to increase nutritional value and other benefits, GM foods continue to be a controversial topic in the public arena. Concerns include increased toxicity, decreased nutritional value, gene transfer, and allergencity of the GM food. Some think exogenous genes can insert in a way that silences an endogenous gene that would can cause a decreased nutritional value of the progeny plant. Conversely, the gene can interrupt a promoter region causing a gene to be over active and cause increased toxicity in the plant. A study suggest that these situations are rare. It demonstrated that plant toxins and antinutrients are similar in GM plants and their parent plants (15). There is also concern that genes from the GM crops can transfer in to the soil or other plants and that genes can transfer into human cells while a person is digesting GM foods. However, there is no concrete scientific evidence that this occurs. (16, 17). Allergencity of GM foods is a valid and real concern for GM foods. Allergencity is not easily predictable. A gene extracted from one source may not be allergenic; however, in the transgenic product the novel gene can cross react with other proteins or be over expressed and cause an allergic response in the consumer (1). Since allergens cannot be reliably predicted by physio-chemical characteristics or level of expression, GM foods should be rigorously tested before approval for mass production and sale of the product. Overall, there is not much research showing evidence that GM foods are hazardous to consumers; however, a systematic protocol should be developed by the existing food regulation organizations (FDA, USDA, EPA) to evaluate the safety of new GM food products.

Plant genetic engineering is a modern twist to traditional plant crossbreeding that provides precision and specificity. They both have a common goal: producing bigger, resilient, tastier crops with higher nutritional value. As genetic engineering continues to progress, a standardized evaluation of the safety of these GM foods needs to be developed and mandated. Furthermore, the general population should be educated about GM foods to dispel the myths and increase knowledge. Long-term studies need to be conducted concerning the potential hazards and impact of GM crops on human health and the environment. While there are concerns about the safety of GM foods, the potential they have for improving health and nutrition currently allows for the benefits to outweigh the hazards.

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