**Golden Rice: A Sustainable Solution to Combat Vitamin A Deficiency and Global Malnutrition**

**Abstract:** In order to combat food insecurity which disproportionately affects vulnerable children in developing countries, food modification was identified as a necessary solution. Researchers leveraged genetic engineering to infuse rice with the pro-vitamin A pathway, yielding Golden Rice, a nutrient-enhanced variety with a higher percentage of β-carotene. By adopting Golden Rice, healthcare costs can be substantially reduced, making it a cost-efficient solution. The focus has now turned to establishing efficient pathways to get Golden Rice into the hands of farmers, an unprecedented approach in public sector research, made possible by global research partnerships and collaborations. Scientists are currently conducting additional studies to boost the nutritional profile of Golden Rice even further.

**Keywords:** Vitamin A deficiency, Golden rice, β-carotene, Genetic engineering, Agriculture

**Introduction:** Rice is one of the most important staple food consumed by more than 3 billion people of world’s population in at least 33 developing countries. Globally, malnutrition is a serious problem causing millions of death, under-development in children, and poor health of adult men and women (Datta and Bouis, 2000). Several strategies have been adopted to produce rice enhanced in nutrients with iron and provitamin A. Genetic engineering of metabolic pathway for β-carotene biosynthesis in endo-sperm was demonstrated in japonica type model rice cultivar, and the transgenic rice produced 1.6 μg/g total carotenoids (Ye *et al.,* 2000). To combat micronutrient malnutrition globally, various approaches are being explored, including the nutritional enrichment of rice and other cereals through fortification, traditional breeding, and genetic engineering. The development and improvement of Golden *indica* rice was emphasized as 90% of world’s population consume *indica* rice.

**History:**

Geranylgeranyl-PP

Phytoene synthase

Phytoene +2 pyrophosphate

crt1

Zeta-carotene

crt1

Lycopene

Lycopene cyclase

beta-carotene

alpha-carotene

Research for development of golden rice began as a Rockefeller Foundation initiative in 1982. Peter Bramley found in the 1990s that lycopene may be produced from phytoene in genetically modified tomatoes (GM tomatoes) using a single phytoene desaturase gene (bacterial *CrtI*), instead of introducing several carotene desaturases, which are generally employed by higher plants. Golden rice's endogenous cyclase then converts lycopene to beta-carotene. Reference 10 After an eight-year effort led by Peter Beyer of the University of Freiburg and Ingo Potrykus of the Swiss Federal Institute of Technology, the scientific specifics of the rice were first published in 2000. The Louisiana State University Agricultural Center carried out the first field trials of golden rice varieties in 2004. More trials were carried out in Bangladesh (2015), Taiwan, and the Philippines. Feeding studies may be carried out thanks to the precise nutritional value measurement made possible by field testing. Field-grown golden rice yields four to five times more beta-carotene than golden rice cultivated in a greenhouse, according to preliminary findings from experiments conducted in the field.

 In 2018, Canada and the United States approved golden rice, with Health Canada and the US Food and Drug Administration (FDA) declaring it safe for consumption. However, in April 2023, the nation's Supreme Court issued an order for the agriculture department to cease commercializing golden rice in response to a petition filed by MASIPAG, a group of farmers and scientists who asserted that the food is hazardous to the environment and public health.

 On 17 April 2024, the Court of Appeals in the Philippines issued a cease-and-desist order on the commercial propagation of Golden rice regarding it's health and environmental impact.

**Benefits of Golden rice:**

* Golden rice contains β-carotene that can assist in addressing vitamin A deficiency (VAD) which prevents blindness and reduce the risk of illness like measles, malaria and diarrhea.
* Up to 50% of the estimated average daily need for vitamin A can be met by consuming golden rice.
* A strong immune system depends on vitamin A, which is present in golden rice.
* Golden rice is an affordable alternative because it should cost the same as regular rice.
* Golden Rice has the same taste as regular rice.
* Golden Rice has been engineered to be more resilient and more resistant to disease and have higher yields.

**Designing of Golden Rice:** Consumption of dietary carotenoids offers various health benefits, such as reducing the risk of cancer and eye (Sadhu and Kole, 2024). In order to preserve the rice endosperm (rice grain) for long-term usage and storage, rice is often treated to remove the husk and natural oil. Preventing the rice from being rancid while being stored, the oil-rich aleurone layer is removed. Rice endosperm is the edible part. Rice endosperm does not naturally produce β-carotene as well as does not contain other micronutriens like Fe. Instead of producing β-carotene, it produces geranylgeranyl diphosphate (GGPP) which is an early precursor of β-carotene. Therefore it was necessary to develop golden rice that is rich in β-carotene and Fe.

* **Introduction of β-carotene into the rice endosperm:** The production of intermediate phytoene from geranylgeranyl diphosphate (GGPP) in the endosperm of rice grains is dependent on phytoene synthase for the synthesis of β-carotene. Three further plant enzyme processes are required for the synthesis of β-carotene from phytoene: phytoene desaturase, ζ-carotene desaturase, and lycopene β-cyclase. A first step towards the production of β-carotene in staple crops has been reported in rice with the constitutive and endosperm-specific expression of a recombinant daffodil phytoene synthase cDNA (Burkhardt *et al*., 1997). Transgenic plants exhibited a significant rate of sterility due to the transgene induced by the constitutive promoter CaMV 35S. To obtain the complete provitamin A biosyntheticpathway only in rice endosperm, we have introduced the genes encoding the three enzymes, necessary to synthesize β-carotene form GGPP, into Japonica rice variety (Ye et al. 2000). Carotenoid production was shown by the distinct yellow color displayed by mature seeds derived from altered lines. The buildup of β-carotene in the rice endosperm was the cause of the color, as shown by high performance liquid chromatography analysis, indicating that this enzyme was either constitutively expressed in the rice endosperm or stimulated by the lycopene generated, this product was even found in seeds that did not express lycopene β-cyclase. The fact that "golden rice" was a Japonica variety, which is not consumed in the regions with the highest prevalence of provitamin A insufficiency and that it only had modest levels of β-carotene surprised early critics of this transgenic biofortification. To overcome this problem *indica* rice lines are biofortified with Vitamin A. To conform with regulatory constrains and because of major public concerns, *indica* varieties IR64 and MTL250 were obtained (Hoa *et al., 2003*) avoiding the antibiotic selection system, using a positive selection strategy (Lucca *et al*., 2001b). Despite the yellow colour observed, the polished indica rice seeds contained lower level ofβ-carotene compared with the previous Japonica rice variety (Ye *et al*., 2000). Recently, new golden rice lines have been developed that contain extremely high amount of β-carotene (Paine *et al.,* 2005). The gene encoding phytoene synthase i.e. one of the two genes utilized to create the initial golden rice lines, seems to be the rate-limiting step for carotenoid production in the transgenic rice seeds. Using psy cDNAs from other plant sources that are very high in carotenoids in a comprehensive examination suggested that using maize's phytoene synthase (psy) rather than daffodil's was likely the best course of action. This psy was combined with the E. uredovora carotene desaturase, which was driven by an endosperm-specific promoter to create transgenic rice seeds that had a provitamin A concentration that was almost 23 times greater than that of the original Japonica golden rice variety.

Isopentenyl-diphosphate (IPP)

Geranylgeranyl diphosphate

Vitamin A pathway is complete and functional

Daffodil gene

Phytoene synthase

Phytoene

Single bacterial gene, performs both functions

Phytoene desaturase

β-carotene desaturase

Lycopene

Daffodil gene

Lycopene-beta-cyclase

Golden Rice

β-carotene

(Vitamin A precursor)

**Fig:** Pathway of introduction of β-carotene in rice endosperm

* **Biofortification of rice seed with Iron:** The strategy to boost iron accumulation in the seeds is by amplifying the body's natural iron reserves. Ferrutin is used in the form of iron storage by both plants and animals during development. Plant ferritin and when combined, they may hold up to 4000 iron atoms in the ferritin complex's central cavity. Recently, ferritin is considered as a iron source that indicates the enhancement of seed ferritin by biotechnology or conventional breeding shows promise as a long-term remedy for the worldwide dietary iron deficit. In rice, the same ferritin expression, driven by a constitutive promoter, led to an increase in iron content of the vegetative parts but not in the seeds (Drakakaki *et al*., 2000). the endosperm-specific expression of soybean ferritin in rice seeds with maximum three-fold increase in one of the transformants (Goto *et al*., 1999). Lucca (Lucca *et al*., 2001a) reported expression of the French bean ferritin under control of the glutelin promoter in the endosperm of Japonica rice and showed an increase of iron content up to two-fold. The overexpression of the soybean ferritin gene driven by the endosperm-specific glutelin promoter in indica rice grains lead to an increase of both iron and zinc concentration in brown grain as well as, for the first time, in the polished grain (Vasconcelos *et al*. 2003). Recent research on rice endosperm revealed a remarkably strong expression of soybean ferritin induced by the rice glutelin promoter, with transgenic protein levels up to 13 times greater than previously reported. Unforfunately the highest iron content found in the new lines' seeds was only around 30% more than that of the previous transformants and roughly three times higher than that of the non-transformed control seeds. Even on iron rich media, the plants exhibited chlorosis after blooming, and the mean iron content in the leaves of high ferritin-expressing lines dropped to less than half of the non-transformed plants and concluded that iron buildup in the hyper-expression ferritin rice seeds may be restricted by Fe absorption and transport in addition to the expression level of exogenous ferritin.

**Present status:** ThePhilippines approved Golden Rice for commercial propagation in July 2021, becoming the first country to produce it. The Philippines has launched a pilot-scale deployment of Golden Rice, spearheaded by DA-PhilRice, with the initial seed distribution taking place in 2022. The Bangladesh Rice Research Institute submitted an application for biosafety approval of Golden Rice in 2017, and the crop remains under regulatory review in the country. IRRI is working in partnership with national research institutions to develop Golden Rice varieties adapted to the specific needs of smallholder farmers in various countries. In order to guarantee the efficacy and safety of Golden Rice, IRRI is also evaluating its nutrition and safety.

**Support:** Golden Rice has received support from various organizations and individuals including: International Rice Research Institute (IRRI), Food and Agriculture Organization (FAO), World Health Organization (WHO), Bill and Melinda Gates Foundation, Rockefeller Foundation, World Bank, Asian Development Bank, Philippine government, Bangladesh Rice Research Institute, Nobel laureates (107 Nobel laureates signed a letter supporting Golden Rice in 2016). These organizations and individuals support Golden Rice as a potential solution to address vitamin A deficiency (VAD) which is a significant public health problem in many developing countries.

Some of the reasons for their support include:

* Potential to improve nutrition and health outcomes
* Ability to address VAD in a sustainable and cost-effective way
* Compatibility with existing farming practices
* Potential to improve crop yields and disease resistance
* Alignment with the United Nations' Sustainable Development Goals (SDGs)

**Conclusion:** Golden rice is genetically engineered to produce beta-carotene, a precursor of vitamin A, in its grains. This breakthrough leverages advanced genetic engineering techniques to address a critical nutritional deficiency. By increasing vitamin A intake, golden rice has the potential to significantly reduce the incidence of VAD, which can lead to blindness, weakened immune systems, and increased mortality rates, especially among children and pregnant women and also fortified with iron, making it a valuable tool in combating iron deficiency and anemia. Golden rice is now at the third stage of agricultural development which means that the three earlier stages—research, lab testing, and field testing have been finished, and it is currently being utilized in large-scale farming. As a cost-effective and sustainable solution, golden rice can improve the nutritional status of vulnerable populations and support smallholder farmers by enhancing the value of their crops. The development and deployment of golden rice have been supported by a wide range of stakeholders, including scientific communities, international organizations, governments, and NGOs. This collective effort underscores the importance of collaboration in addressing global health challenges. Despite its potential, golden rice faces challenges such as public skepticism towards GMOs, regulatory hurdles, and the need for effective distribution and adoption strategies. Continued research, education, and advocacy are essential to overcome these barriers.

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