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RESEARCH ARTICLE

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

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ABSTRACT

Food modification has been recognized as an essential solution to combat food insecurity, particularly among vulnerable children in developing countries. Researchers used 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 foods consumed by more than 3 billion people worldwide (Zafar and Jianlong, 2023). Globally, malnutrition is a serious problem causing millions of deaths, under-development in children, and poor health of adult men and women (Datta and Bouis, 2000; Deepika *et al.,* 2023). Several strategies have been adopted to produce rice enhanced in nutrients with iron and provitamin A. Genetic engineering of the metabolic pathway for β-carotene biosynthesis in endosperm was demonstrated in japonica type model rice cultivar, and the transgenic rice produced 1.6 μg/g total carotenoids (Ye *et al.,* 2000). Various approaches are being explored to combat micronutrient malnutrition globally, including the nutritional enrichment of rice and other cereals through fortification, traditional breeding, and genetic engineering. The development and improvement of Golden indica rice were emphasized, as 90% of the world's population consumes indica rice.

Research for the development of golden rice began as an initiative by Rockefeller Foundation 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. 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 conducted the first field trials of golden rice varieties in 2004. More trials were conducted in Bangladesh, Taiwan, and the Philippines.

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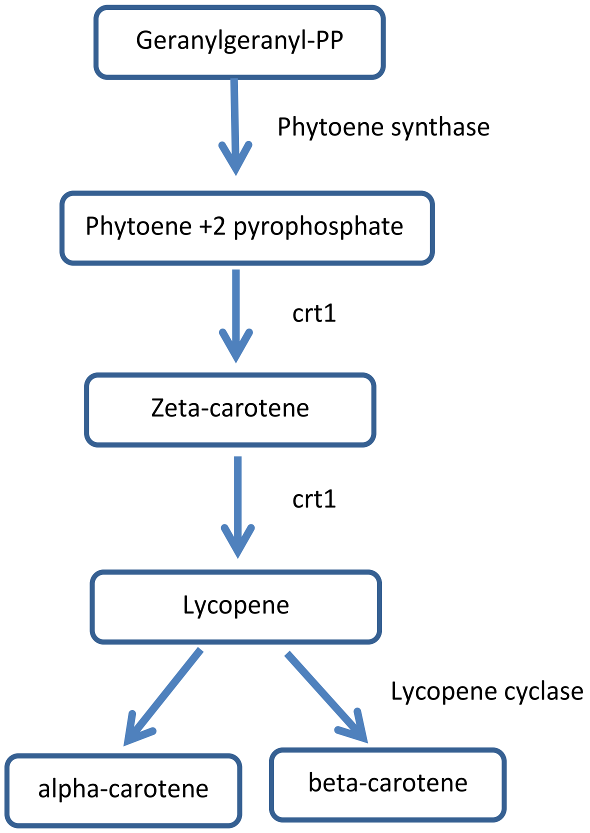
History:



Feeding studies may be carried out thanks to the precise nutritional value measurement made possible by field testing. According to preliminary findings from experiments conducted in the field, field-grown golden rice yields four to five times more beta-carotene than golden rice cultivated in a greenhouse.

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 ordered 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 golden rice commercial propagation regarding its 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 reduces the risk of illnesses 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 to disease and has 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). To preserve the rice endosperm (rice grain) for long-term usage and storage, rice is often treated to remove the husk and natural oil. To prevent 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 micronutrients 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 rich in β-carotene and Fe.

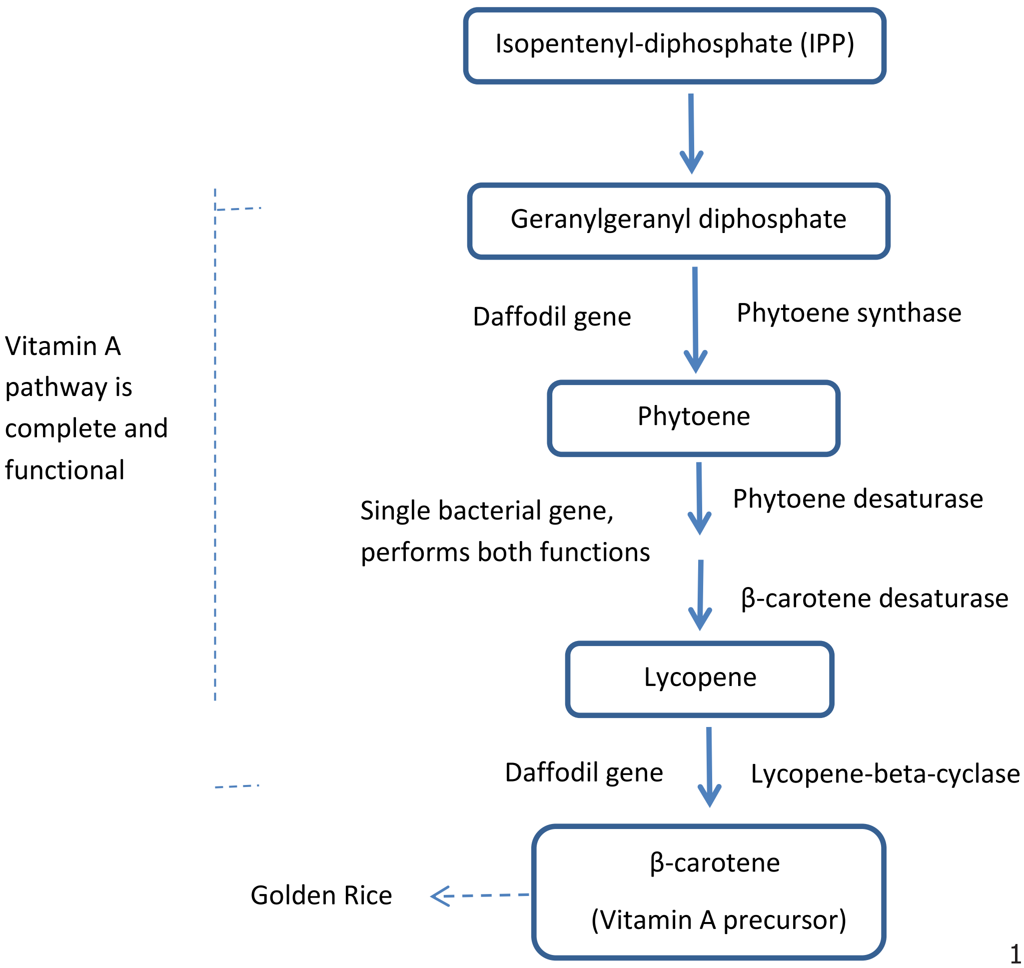
Introduction of β-carotene into the rice endosperm:

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 biosynthetic pathway only in rice endosperm, 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 colour, 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 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 significant problem, indica rice lines are biofortified with Vitamin A. To conform with regulatory constraints and because of significant 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 colour observed, and the polished indica rice seeds contained lower levels of β-carotene compared with the previous Japonica rice variety (Ye *et al*., 2000). Recently, new golden rice lines have been developed that contain extremely high amounts 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. In a comprehensive examination, psy cDNAs from other plant sources that are very high in carotenoids suggested that using maize's phytoene synthase (psy) rather than daffodil 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.

Biofortification of rice seed with Iron:

The strategy to boost iron accumulation in the seeds is amplifying the body's natural iron reserves. Ferritin is used in the form of iron storage by both

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



plants and animals during development. Plant ferritin, and, when combined, may hold up to 4000 iron atoms in the ferritin complex's central cavity. Recently, ferritin has been considered an iron source that indicates the enhancement of seed ferritin by biotechnology or conventional breeding, which 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 increased iron content of the vegetative parts but not in the seeds (Drakakaki *et al*., 2000) endosperm-specific expression of soybean ferritin in rice seeds with a 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 leads 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. Unfortunately, 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 might be restricted by Fe absorption and transport in addition to the expression level of exogenous ferritin.

Present status:

The Philippines 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 applied for biosafety approval of Golden Rice in 2017, and the crop remains under regulatory review in the country. IRRI is working with national research institutions to develop Golden Rice varieties adapted to the specific needs of smallholder farmers in various countries. 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 the International Rice Research Institute (IRRI), the 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. It is 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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