Golden illusion:

The broken promises of "golden" rice

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Summary

"Golden" rice is a genetically engineered (GE, also called genetically modified, GM) rice variety developed by the biotech industry to produce pro-vitamin A (beta-carotene). Proponents portray golden rice as a technical, quick-fix solution to Vitamin A deficiency (VAD), a health problem in many developing countries. However, not only is golden rice an ineffective tool to combat VAD it is also environmentally irresponsible, poses risks to human health, and compromises food security.

Golden rice has been in development for over 20 years, yet no commercial applications have resulted – largely because of the complexity of the genetic engineering. Exactly how the beta-carotene is made in the plant is not well understood, and the complexity of the genetic engineering increases the potential for unexpected and unpredictable effects, which could affect food safety. Yet assessing food safety is problematic for regulators because the concept of substantial equivalence is not applicable to golden rice.

There are many technical questions surrounding the beta-carotene in golden rice: exactly what is produced, how stable it is, and exactly what happens when it is processed in the human body. While the food safety of golden rice is in doubt, what *is* known is that GE rice will undoubtedly contaminate the non-GE rice supply, particularly traditional varieties and landraces. GE contamination of food supply poses risks to health. By encouraging a diet based on one staple rather than an increase in access to the many vitamin-rich vegetables, golden rice could – if introduced on a large scale – exacerbate malnutrition and ultimately undermine food security.

The tens of millions of dollars spent on this project would have been better spent on VAD solutions that work. Golden rice is simply the wrong approach and a waste of money. Golden rice diverts significant resources away from dealing with the real underlying causes of VAD and malnutrition, which are mainly poverty and lack of access to a more diverse diet. Indeed, it is a risky distraction from solutions that are already helping to tackle VAD and malnutrition more effectively without subjecting the population to unknown health risks.

Dangerous glitter: the risks of golden rice

Feeding an illusion

So-called golden rice has been under development since 1990 (Potrykus 2000). From the outset, the project appeared to be designed more towards helping the biotech industry overcome the widespread consumer rejection of GE crops, than to help overcome malnutrition. The first prototype (GR1) was unveiled in 2000 (Ye et al. 2000), but this was much criticised as it contained so little beta-carotene. In 2001, Greenpeace pointed out that, in addition to environmental and human health concerns of golden rice, the low concentrations of beta-carotene present meant that people would need to consume vast quantities of rice (over 12 times the normal daily intake of rice) in order to obtain the recommended dietary allowance of vitamin A (Greenpeace 2001).

Then, in 2005, Syngenta announced golden rice 2 (GR2; Paine et al. 2005), this time containing more beta-carotene than GR1. But despite the millions of dollars and over 20 years spent on the research and development, golden rice remains a research project, with no applications for commercialisation anywhere in the world. This is largely because the complex nature of plant biochemistry means that attempting to genetically engineer a whole new biochemical pathway (i.e. to produce beta-carotene) is fraught with difficulties. Genetically engineered golden rice is simply the wrong tool to tackle VAD.

Although it is difficult to estimate exactly how much money has been spent on golden rice to date, it is clear that it runs to tens of millions of dollars, and includes substantial investment by the Bill and Melinda Gates Foundation (Greenpeace 2010).

Money spent on golden rice is money that would have been a significant and welcome contribution to VAD solutions that use proven and reliable methods.

Rice at risk: Contamination of conventional rice will occur

The environmental risks inherent in GE organisms apply to golden rice without exception. Next to nothing is known about how this GE rice interacts with the environment – for instance, its effect on the beneficial insects that prey on rice pests. More importantly, rice is a staple food in many parts of the world, and contamination of the food supply with this GE rice is a real risk.

Rice is widely cultivated throughout many parts of the world, particularly Asia. Seed saving is common. This means that if any seed gets mixed up, or cross-pollination causes contamination, it will be difficult to eradicate. Rice is known to cross-pollinate (outcross), and wild and weedy relatives grow in close proximity to rice cultivation (Lu et al. 2003; Chen et al. 2004). Thus, the spread of genes to landraces and wild varieties of rice is likely to happen over time. This could lead to genetic contamination of wild populations as well as cultivated seed supply. Although there is no commercial growing of GE rice anywhere in the world, there have now been at least two incidents of rice contamination that have caused problems for export: one from China in 2005 (Europa Press Release 2008), one from the US in 2006 (Nature Biotechnology 2006). It is self-evident that GE rice cannot be controlled.

Releasing GE rice in Asia could irreversibly affect traditional rice varieties, landraces and wild relatives of rice, decreasing our ability to use these valuable genetic resources in the future. For example, if a hazardous unexpected effect arises with the GE rice, e.g. increased toxicity or susceptibility to disease, there could be no withdrawal of the gene because of contamination. It is conceivable that this could undermine the food security of a region if the problem became widespread.

The potential for unexpected effects with GE golden rice

Plant chemistry is complex, making even the simplest of genetic alterations likely to produce unexpected effects. The genetic engineering constructs used in golden rice (both GR1 and GR2) are more complex than many current GE crops (e.g. Roundup Ready soya and insect resistant (*Bt*) maize). GE Roundup Ready soya and GE *Bt* maize generally contain one or possibly two genes with very few additional elements. Their function is relatively simple: to produce one protein. By contrast, the synthesis of a whole new biochemical pathway is being attempted in golden rice, with more complex genetic constructs. Even in these comparatively simple GE crops, extra fragments of the inserts and re-arrangements or deletions of the plant's own DNA are known to occur (Windels et al. 2001; Hernández et al. 2003). There are concerns that these irregularities may affect or interfere with the plant's own metabolism, for example, by creating unintended novel protein, or altering or interfering with the production of an existing plant protein. These concerns are magnified with the complex genetic engineering attempted in golden rice, and there is an increased likelihood of unexpected and unpredictable effects.

Attempting to introduce a new biochemical pathway has a high probability of altering another pathway. The genetic engineering of a biochemical pathway can result in unintended changes in plant composition.

"*[Plant metabolic] pathways pull components from various genetic tool kits; some of those components evolve independently and others do not. A push in one place can produce unexpected responses in other pathways. And metabolic pathways multiply with modifications, tweaks, and twinges every step of the way."* (Hines & Zahn 2012)

Unexpected effects have already been observed in golden rice. GR1 was engineered with two genetic constructs: one (*psy* + *crt1*) to make lycopene (tomato red) and another (*lcy*) to convert lycopene to beta-carotene (yellow) (Ye et al. 2000). However, the developers discovered "to our surprise" (Beyer et al. 2002), that those without one of the genes (*lcy*) were yellow when they should have remained a red colour. This was because there was an unexpected pathway in rice that converted lycopene to beta-carotene. Thus, the insert to convert lycopene to beta-carotene was superfluous. Five years later, it was found that intrinsic rice genes cause the conversion of lycopene to beta-carotene (Schaub et al. 2005). Other unexpected effects include changes to levels of closely related compounds, particularly lutein and zeaxanthin (Ye et al. 2000; Schaub et al. 2005).

Other compounds may also have changed in the rice: they could be higher or lower. New compounds could be produced. The case of golden rice is a typical example of how little is actually known about the complexity of plant physiology – it would not be a surprise if additional unexpected changes in the plant occurred, posing new risks to the environment or human health.

Evaluating the importance of any unexpected changes found in golden rice for food and environmental safety would be highly important. However, it is virtually impossible to look for unexpected effects – by definition, one cannot know what these effects might be, or where to look for them!

Risks to human health

Beta-carotene occurs naturally in many plants. It is a reasonably complex pathway, with two different types of carotene (alpha and beta), and also different isomers (with the same chemical make-up but different structure) (Cazzonelli 2011). Technical questions arise over which isomers are present, and whether they will be effective. Are there any health implications if different isomers are present to those that occur naturally? The precise pathway utilised by the inserted genetic constructs and the rice itself to create beta-carotene golden rice is poorly understood (see www.goldenrice.org), yet might be vitally important for human health.

Large doses of beta-carotene can have negative health effects, including in conjunction with cigarette smoking (see, e.g. Eroglu et al. 2012). The processing of beta-carotene to vitamin A also creates related compounds that can negatively affect health at high concentrations (Schubert 2008). Researchers found that these compounds from the processing of beta-carotene to vitamin A can block important signalling in cells (Eroglu et al. 2012). Thus, the exact type of beta-carotene, and the way it is processed in the human body, is vitally important. But exactly how beta-carotene from golden rice would be processed in the human body, and how the products compare to natural beta-carotene in plants, is not yet known.

"Our analyses of both beta-carotene-containing animal diets and fruits containing beta-carotene suggest that any dietary source of beta-carotene also contains beta-apocarotenoids. It may also be useful to consider these findings in attempts to alleviate vitamin A deficiency in humans through the biofortification of crops with high levels of beta-carotene." Eroglu et al. (2012)

Any food safety assessment of golden rice would be extremely complex. Most regulatory systems rely on the concept of substantial equivalence, where the plant is considered equal to its non-GE counterpart except for the protein produced by the introduced genes. However, because golden rice attempts to introduce a whole new biochemical pathway, the concept of substantial equivalence is not applicable. If golden rice ever reached the stage where the developers were to apply for commercialisation, regulators would have to find whole new ways of assessing the food safety of golden rice (Glenn 2008; ILSI 2008; Schubert 2008).

The food safety of any GE rice is of vital importance because rice can make up a large part of people's diet in Asia and other parts of the world, yet it would be very difficult to give any assurances regarding the food safety of golden rice.

Compromising food security

Questions remain concerning the effectiveness of golden rice. Does the beta-carotene degrade during storage or cooking? Would it be bioavailable (available for uptake and conversion to vitamin A in the human body) to people with VAD? The developers and researchers claim that the beta-carotene is efficiently converted to vitamin A in the body, and that it can make a substantial contribution to vitamin A intake (Tang et al. 2009; Tang et al. 2012). However, the first results have been questioned as the volunteers in the study were not vitamin A-deficient and, if they were deficient, it is likely their diet would also lack the necessary fat for bioconversion (Krawinkel 2009). The same criticism also applies to the more recent results:

"One of the arguments used for advertising Golden Rice is that the people at risk of vitamin A deficiency have such poor diets that other sources of beta-carotene and vitamin A are not accessible to them. Because diet definitely has an effect on the bioavailability of beta-carotene from any beta-carotene-containing food, the choice for a study diet that included meat, oil, and nuts, which does not represent a poor diet, is of concern. Therefore, the results of the study do not much help us in preventing vitamin A deficiency in populations at risk." (Krawinkel 2009 commenting on the study by Tang et al. 2009)

In addition, the researchers conducting the trials have been criticised for using human subjects, especially children, in an experimental study (Tuffs Daily 2009; Greenpeace 2012).

Alongside the technical issues of how beta-carotene would be metabolised in the human body, there are concerns that golden rice could undermine food security, because it encourages a diet based on one staple rather than an increase in access to the many vitamin-rich vegetables. So, if introduced on a large scale, golden rice can exacerbate malnutrition and ultimately undermine food security.

Golden rice is neither needed nor necessary

In the past decade, great progress has been made against VAD and other malnutrition problems. Well-proven solutions to fight VAD, multi-nutritional deficiencies and malnutrition, are known, available and cost-effective. For example, VAD is currently being successfully tackled by a combination of supplementation and home gardening in Bangladesh, whereas 20 years ago it was considered one of the worst public health problems (for a review, see Greenpeace 2010). Despite such successes, VAD remains a serious health problem in many countries; not because there is a lack of tools for combating the deficiency, but rather due to political instability, a lack of funds, or a lack of political will to combat the underlying causes.

VAD often occurs in conjunction with other micronutrient deficiencies. Genetic engineering approaches to these nutrient deficiencies are bound to fail because they don't address the root cause of these problems. Effective short and medium-term interventions are already being employed, such as fortification of food with vitamins and minerals, food additives and supplementation. Dietary diversification addresses multiple deficiencies, and in the case of home gardens empowers people to diversify their own diet. By looking at the root causes of the problem, a range of projects such as home gardens and diversifying farms can eradicate not only VAD but also tackle all other nutrients and malnutrition in the same instance. Sustainable solutions to VAD and other micronutrient deficiencies are proven and in use. The real need is to ensure that these solutions are rolled out to the people who need them.

Biofortification can be an effective mid-term intervention for micronutrient deficiencies. It does not require genetic engineering. Whereas genetic engineering approaches to bio-fortification have attracted much publicity in recent years, it has remained largely unnoticed by the general public that conventional breeding and Marker Assisted Selection (MAS) represent a viable alternative to genetic modification strategies for biofortification. MAS is a modern breeding technique that complements traditional breeding and makes it more efficient (for a review, see Greenpeace 2009). It uses our knowledge of how genes and genomes operate, but does not result in a GE plant. HarvestPlus, for example – an interdisciplinary alliance of institutions and scientists working to breed bio-fortified crops – devotes 85% of its resources to conventional breeding, because of regulatory and political restrictions on the use of genetic engineering approaches, and because significant progress can be made through conventional breeding (Nestel et al. 2006). MAS has already achieved success enriching beta-carotene in maize enriched with beta-carotene (Harjes et al. 2008), which is already being used in Zambia to help tackle VAD (Harvestplus 2010).

Greenpeace advocates the long-term solution of supporting people to diversify their diets with food grown in a system of ecological farming (a particularly appropriate technology requiring minimal resource/input investment), as well as acknowledging the intermediate steps of supplementation and fortification. A key to micronutrition is a healthy, balanced diet (IAASTD 2008), requiring access to a variety of foods.

Conclusions

- **After over 20 years and millions of dollars, 'golden' rice remains an illusion. It is simply a research project with good public relations**
- **GE rice will contaminate (via outcrossing and seed mixtures) traditional rice varieties, landraces, wild and weedy rice relatives, raising cultural, agronomic, environmental concerns and potentially affecting food security**
- **The specific pathway of beta-carotene synthesis in the plant is not well understood and the complexity of the genetic engineering increases the potential for unexpected and unpredictable effects.**
- **The human food safety of golden rice is unknown. There are concerns regarding unexpected changes in plant biochemistry, and technical questions over exactly what would be produced when the human body processes the beta-carotene present in golden rice. Golden rice cannot be considered substantially equivalent, meaning it cannot be assessed under existing regulations in most countries.**
- **GE golden rice is not a solution for VAD, no matter how much beta-carotene is in it. It is simply the wrong approach. Over the past 20 years, the world has been tackling VAD using safer and more effective techniques.**
- **If required, biofortification does not require genetic engineering. Non-GE biofortified crops are already in farmers' fields and on people's plates.**
- **Spending even more time and money on golden rice development is not only environmentally irresponsible, it is also a disservice to humanity.**

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