Overview of Evidence and Recommendations for Effective Large-Scale Rice Fortification

Saskia de Pee
World Food Programme, Rome, Italy
Friedman School of Nutrition Science and Policy, Boston, USA

Cecilia Fabrizio, Jennifer Rosenzweig
World Food Programme Regional Bureau for Asia

Key Messages

- Multiple efficacy and effectiveness studies have established the impact of fortified rice on micronutrient status.
- To prepare for the introduction of fortified rice, countries should conduct a landscape analysis to assess feasibility and consumer acceptability. Given the existing evidence base, it is not necessary to conduct additional efficacy trials prior to the introduction of rice fortification.
- Based on available evidence of efficacy, stability and needs, the following micronutrients are recommended for rice fortification: iron, zinc, and vitamins A, B_1 (thiamin), B_3 (niacin) B_6 (pyridoxine), B_9 (folic acid) and B_{12} (cobalamin).
- Rice fortification programs should use technology and micronutrient fortificant forms that produce fortified rice that is acceptable to consumers, retains micronutrients during storage and preparation, and releases them for absorption by the body.
- When introducing fortified rice, countries should monitor implementation. This includes appropriate fortification (i.e., of fortified kernels and their blending), storage and distribution, and monitoring of acceptance and consumption.

Introduction

In populations where rice is a major staple food, fortification of rice with micronutrients has the potential to increase micronutrient intake. Decades-long experience with fortification of other staple foods and condiments has proven that large-scale fortification is efficacious. This article discusses country-level considerations for rice fortification and reviews the global evidence base for the efficacy and effectiveness of rice fortification.

Country-level considerations for food fortification

Identifying suitable micronutrients for fortification

An analysis of which micronutrient deficiencies are likely to exist and are of public health significance will help determine which micronutrients should be used to fortify rice, and in what form. The comprehensive publication by the World Health Organization (WHO) and the Food and Agricultural Organization of the United Nations (FAO), "Guidelines on Food Fortification with Micronutrients" assists countries in the design and implementation of appropriate food fortification programs and is particularly helpful for low- and middle-income countries.[1] The WHO/FAO publication provides guidance on the selection of food vehicles, and which micronutrients to add, in what chemical form, and in which quantities. More specific rice fortification guidelines are in development.

"An analysis of which micronutrient deficiencies are likely to exist will help determine which micronutrients should be used to fortify rice"

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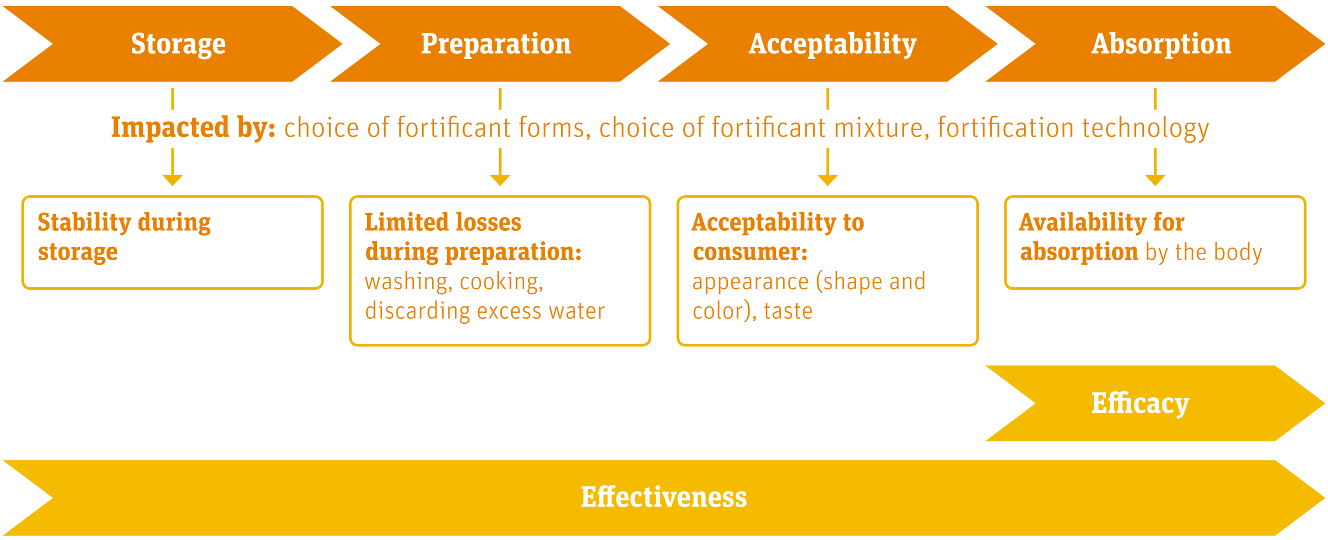
A father feeding his young child, Bolivia 2012

FIGURE 1: Factors that determine the efficacy and effectiveness of rice fortification



Requirements for rice fortification to be effective

For a rice fortification program to be effective, the following conditions need to be met:

a) The micronutrients used to fortify the rice should remain stable during storage, i.e., losses over time are limited.
b) The micronutrients should be retained after preparation (washing, cooking, discarding excess water).
c) The fortified rice should be acceptable to the consumer in appearance (shape and color), taste and smell.
d) The micronutrients remaining post-cooking should be available for absorption by the body (see **Figure 1**).

These requirements are affected by the fortificants' chemical forms and formulation, the fortification technology, and any possible interaction between micronutrients, or the rice matrix. Finally, the fortified rice needs to be consumed regularly and in the expected quantities by the desired population groups in order to make a good contribution to micronutrient intake.

Global evidence for rice fortification

The following is a review of two types of studies conducted on micronutrient fortification of rice that address the conditions illustrated in **Figure 1**. One type of study examines the *efficacy* of key micronutrients used in rice fortification. These carefully controlled studies assessed whether consumption of a given amount of rice, fortified with micronutrients in a specific concentration, using specific fortificant forms and fortification technology, resulted in the micronutrients being absorbed and utilized by the body. In *effectiveness* studies, people in specific population groups were provided with fortified rice under less controlled circumstances. The studies assessed whether these groups – who prepared and consumed the fortified rice in their homes – showed a reduction in the signs of micronutrient deficiencies or changes in micronutrient status. Under these studies, impact on the micronutrient status of participants was also dependent on storage, preparation, acceptance, and unsupervised consumption of the fortified rice.

Efficacy studies of fortified rice

Since early 2000, thirteen efficacy studies have been published that assessed the impact of fortified rice on micronutrient status.[2–14] All studies used fortified kernels that were produced using extrusion technology. Each study was conducted in a controlled environment, and aimed to compare impact on micronutrient status among individuals who received fortified rice, versus individuals who received non-fortified rice and/or micronutrients in supplement form. In nine of the studies, the rice was fortified only with iron, in one study only with vitamin A,[14] and in three studies a combination of micronutrients was used, i.e., iron, zinc and vitamin A in the studies by Pinkaew et al,[11,12] and iron, zinc, vitamins A, B_1, B_6 and B_{12} and folic acid in the study by Thankachan et al.[13] The studies were conducted in low- and middle-income countries, including the Philippines, India, Nepal, Thailand, Mexico and Brazil. Study populations included children aged 6–23 months, preschool and school-age children, women of reproductive age, and anemic individuals.

Iron results

All 12 efficacy studies on iron-fortified rice used ferric pyrophosphate (FePP) as the iron form. One study also included a group that received ferrous sulfate.[10] Although FePP is not the most bioavailable iron fortificant, it has so far been the only type of

TABLE 1: Studies on iron-fortified rice

Reference	Country	Study group	Dosage	Findings
Angeles-Agdeppa I, Capanzana MV, Barba CV et al[2]	Philippines	6–9 y old anemic children	10 mg/d (2 groups: FePP and ferrous sulfate)	Hb improved, anemia declined, no change of serum ferritin
Beinner MA, Velasquez-Meléndez G, Pessoa MC et al[3]	Brazil	6–24 mo old anemic children	23.4 mg/d	Hb improved, anemia declined, serum ferritin increased, iron status improved
Hotz C, Porcayo M, Onofre G et al[4]	Mexico	18–49 y old women (non-pregnant, non-lactating)	20 mg/d	Hb increase non-sign. (p=0.069), plasma ferritin, transferrin receptor, and iron stores improved
Nogueira Arcanjo FP, Santos PR, Leite J et al[5]	Brazil	10–23 mo old children	56.4 mg/meal, one meal/wk	Hb improved, anemia declined
Nogueira Arcanjo FP, Santos PR, Segall S[6]	Brazil	2–5 y old children	56.4 mg/meal, one meal/wk	Hb remained the same, whereas it declined in control group
Nogueira Arcanjo FP, Santos PR, Arcanjo C[7]	Brazil	10–23 mo old children	56.4 mg/meal, one meal/wk	Hb improved, anemia declined
Moretti D, Zimmermann MB, Muthayya S et al[8]	India	6–13 y old schoolchildren	13 mg/d	Body iron stores improved (all other Hb and iron status parameters, no change)
Radhika MS, Nair KM, Kumar RH et al[9]	India	5–11 y old schoolchildren	19 mg/d	Hb and anemia no change, serum ferritin increased, iron deficiency reduced
Zimmermann M, Muthayya S, Moretti D et al[10]	India	5–9 y old schoolchildren	10 mg/d	Hb no change, transferrin receptor no change, serum ferritin increased, iron deficiency declined
Pinkaew S, Winichagoon P, Hurrell RF et al[11]	Thailand	4–12 y old schoolchildren	12.3 mg/d	Hb and serum ferritin, no change, iron deficiency declined
Thankachan P, Rah JH, Thomas T et al[13]	India	6–12 y old schoolchildren	6.25 mg/d and 12.5 mg/d	Hb and iron status indicators, no change

iron identified that does not affect the color and taste of rice. Research has very recently been conducted that successfully increased the bioavailability of this type of iron.[14] The amount of fortified rice that was provided in the studies ranged from 50 g/week to 140 g/day and was often provided as one meal per day. The blending ratios of the fortified rice ranged from 0.5 to 2.5%, and the iron content of the fortified rice meal ranged from 6 to 56 mg. The studies did not report on the color of the fortified kernels or the acceptability of the fortified rice, but as feeding took place under controlled conditions, all participants were apparently willing to consume the rice. Eleven of the 12 studies with rice fortified with iron assessed impact on hemoglobin concentration or anemia. None of the studies found a negative impact, while five found an improvement. Six of the eight studies that assessed iron status found an improvement. In total, 10 of the 11 studies found a positive impact on either hemoglobin concentration or iron status, or on both (see **Table 1**). The authors of the one study that found no impact on hemoglobin concentration or iron status reported that they discovered post-study that the participants had actually received iron supplements until a few months before the study started.[13]

These results provide strong evidence that the fortification with iron was effective. The fact that a greater proportion of studies found an impact on iron status as compared to the proportion that found an impact on hemoglobin concentration may be due to homeostatic control (i.e., there is limited room for improvement of hemoglobin concentration among non-anemic individuals) and due to the fact that iron deficiency causes only approximately 50% of anemia. As other nutritional and non-nutritional causes also affect anemia, there are limits on the impact of iron on hemoglobin concentration.

When considering fortification of rice with iron at scale, cost and consumer acceptability are key. Blending ratio impacts cost. Color and taste, which depend on choice and level of iron fortificant, can affect consumer acceptance. These aspects were less important in the efficacy studies. With the current recommended fortificant form of micronized ferric pyrophosphate in order not to have a colored fortified kernel, the concentration of iron cannot exceed 7 g/kg. When fortified kernels are blended with normal rice at 1%, which is a commonly used ratio, the iron content of the fortified rice will be 7 mg/100 g. Most of the efficacy studies blended at a higher ratio, and some also had a higher concentration of iron in the fortified kernels. The high iron concentration in the fortified rice, and the fact that most studies provided all the iron in one meal per day, resulted in high iron content in comparison to that of

TABLE 2: Studies on vitamin A fortified rice

Reference	Country	Study group	Dosage	Findings
Pinkaew S, Wegmuller R, Wasantwisut E et al[12]	Thailand	8–12 y old children	3,000 µg RE/d	BL* serum retinol 1.21 µmol/L – total body retinol increased – serum retinol unchanged
Pinkaew S, Winichagoon P, Hurrel RF et al[11]	Thailand	4–12 y old children	2,500 µg RE/d	BL serum retinol 1.01 µmol/L – No significant increase
Thankachan P, Rah JH, Thomas T et al[13]	India	6–12 y old children	500 µg RE/d	BL serum retinol 2.1–2.6 µmol/L – No change
Haskell MJ, Pandey P, Graham JM et al[15]	Nepal	Night-blind pregnant women	850 µg RE/d	Serum retinol increased in all groups, most in liver & high-dose capsule groups

*BL: baseline

iron absorption inhibitors. This may have had a further positive impact on iron absorption in the studies.

Vitamin A results

Four studies included rice fortified with vitamin A, three of which were also fortified with other micronutrients. The one study that fortified rice only with vitamin A was conducted among night-blind pregnant women in Nepal and provided study groups with different sources and levels of vitamin A.[15] This study reported an improvement of vitamin A status in all groups, with the greatest improvement in the two groups that received vitamin A from either a high-dose capsule or liver. The other three studies were conducted among schoolchildren with an average baseline serum retinol concentration considered indicative of adequate, or close to adequate, vitamin A status [11–13] (see **Table 2**). Their serum retinol concentration did not increase further. However, the one study that also measured total body retinol reported an improvement.[12] This evidence shows that vitamin A can effectively be added to rice. However, it is important to consider whether rice is the most appropriate vehicle. For example, where cooking oil is already adequately fortified with vitamin A, it is not also necessary to fortify rice with vitamin A.

Results with other micronutrients

The impact of fortification of rice with zinc, folic acid, vitamins B_1 (thiamin) and B_{12} on micronutrient status has also been assessed. Thankachan et al[13] studied rice fortified with iron, zinc, vitamins A, B_1, B_6 and B_{12} and folic acid. In a study by Pinkaew et al,[11] impact on zinc status by rice fortified with iron, vitamin A and zinc was assessed. Thankachan et al found an improvement of vitamin B_{12} status and a decrease of homocysteine levels.[13] This indicated that both vitamin B_{12} and folic acid were well absorbed and utilized. They found no change of indicators of thiamin or zinc status. Thiamin status was already sufficient. The absence of impact of zinc fortification on serum zinc concentration, which has also been reported by other studies,[16] may be due to the fact that only a small fraction of the body's zinc pool appears in serum. This makes it insensitive to modest changes of status. The study by Pinkaew and colleagues reported a decline of zinc deficiency in both the intervention and the control groups. The improvement of serum zinc was greater in the fortified rice group compared with the unfortified rice group.[11]

Effectiveness studies – impact of rice fortification under programmatic circumstances

Four studies analyzed the effectiveness of rice fortification under less controlled, more programmatic, circumstances.[17–20] The first study, conducted in the Philippines in 1947–49, used coated rice fortified with thiamin, niacin and iron. Results showed a substantial reduction of beriberi, a well-known consequence of thiamin deficiency, as well as a lower incidence of infant deaths in the areas that received fortified rice.[20] No biochemical indicators of micronutrient status were assessed at that time. A second effectiveness study in the Philippines in 2008 provided rice fortified with iron at approximately 3–4 mg/100 g. This study found higher hemoglobin concentrations among children after the program than before, and a decline in anemia prevalence. No changes were found among mothers.[18] A study conducted in Thailand between 1971 and 1975 distributed fortified rice among different age groups of children. No significant differences were found in anthropometry, hemoglobin and hematocrit between children of the villages that received the fortified rice and those that received non-fortified rice. According to the authors, caloric insufficiency was widespread and may have affected the results.[19] More recently, after observing declines in neural tube defects (NTD) after the introduction of flour fortification with folic acid, Costa Rica also began fortifying rice and milk with folic acid. Studies conducted in 2011 demonstrated further NTD declines.[17]

Recommended micronutrients for rice fortification

The above reviewed evidence from efficacy and effectiveness studies supports the fortification of rice with iron, vitamin A, folic acid, vitamin B_{12} and thiamin. Zinc is also recommended, although one study found an impact on zinc status while the other one did not. These mixed findings are consistent with findings from studies on zinc fortification of other foods and may partly be due to the fact that zinc status is difficult to assess accurately.[16] For niacin and vitamin B_6, data of impact on micronutrient status have not yet been collected, but adding these is recommended as well, because polished rice is a poor source of these essential micronutrients,[21] bioavailable forms of these nutrients exist, and adding them to rice together with the other micronutrients does not markedly increase the costs of fortified rice.

> "The above evidence supports the fortification of rice with iron, vitamin A, folic acid, vitamin B_{12} and thiamin, and the addition of zinc, niacin and vitamin B_6 is also recommended"

Research and development

Research is under way to identify more bioavailable forms of iron, which is important for safeguarding the impact on iron status under normal circumstances (see iron section above) while maintaining good consumer acceptability. Research is ongoing to compare micronutrient retention and absorption of fortified rice produced with rinse-resistant coating versus extrusion technology.

What to assess when introducing rice fortification at scale

Figure 1 shows essential components for effective rice fortification. First is the choice of the appropriate fortification technology, and identification of required micronutrients. The selected fortificants must be in efficacious forms and required amounts, and stable. Required evidence and information for this step is presented in this article, in the article on technology by Montgomery et al (see p. 159), and in the paper on standards by de Pee and Fabrizio (see p. 165). After technology and types of levels of fortificants have been chosen, it is very important to assess production feasibility (initially, just for blending, later also fortified kernel production), and consumer acceptability. Then the following should be put in place:

- **Quality assurance, quality control and monitoring**
  Manufacturers should conduct their own quality assurance and quality control. Separately, independent monitoring should determine whether the rice is fortified as expected, i.e., the fortified kernels have the required composition and are blended at the required ratio and staying within a given range of variation. In addition, stability testing needs to be conducted under prevailing storage, preparation and cooking conditions to assure content remains adequate.
- **Monitoring of coverage, acceptability and consumption levels**
  These aspects need to be monitored, and adjusted where necessary. The contribution of fortified rice to micronutrient intake depends on whether consumers obtain, accept and consume it in required quantities.
- **Monitoring of micronutrient intake, morbidity and micronutrient status**
  Since rice fortification is one component of a broader strategy to address micronutrient deficiencies, monitoring should assess whether the combination of strategies is improving the health and nutritional status of different target groups in the population and/or whether additional measures may be required. Monitoring should be conducted over time, including assessment before and after implementation of the program has started at scale.

> "Countries considering rice fortification do not need to conduct additional efficacy studies"

Conclusion

Multiple studies have established that with the appropriate levels of micronutrients and fortificant forms, and with effective technology, fortified rice is an effective intervention to improve micronutrient status. Countries considering rice fortification as an intervention to address micronutrient deficiencies do not need to conduct additional efficacy studies. Rather, countries should apply their resources to assess their own public health needs for micronutrient fortification and ensure close monitoring of implementation. The recommended micronutrients for rice fortification are iron, zinc, folic acid, niacin and vitamins A, B_1 (thiamin), B_6 and B_{12}, although if vitamin A is added to vegetable oil, it may not need to be added to rice. These recommendations are based on efficacy data, and the public health significance of the deficiencies of these micronutrients. In addition consideration is given to the feasibility of adding specific fortificants while maintaining consumer acceptability and stability during storage. Countries should therefore focus on appropriate fortification (i.e., fortified kernels and their blending), storage and distribution, and monitoring acceptance and consumption (adequate quantities and by different subgroups).

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