

# Biofortified Crops Can Alleviate Micronutrient Deficiencies: Review of Evidence from Randomized Feeding Trials

Ronoh AK<sup>1\*</sup>, Were GM<sup>1</sup> and Mueni MM<sup>2</sup>

<sup>1</sup>Department of Family and Consumer Science, University of Eldoret, Kenya

<sup>2</sup>Department of Health Sciences, Kisii University, Kenya

\*Corresponding author: Ronoh AK, Department of Family and Consumer Science, University of Eldoret, Kenya, Tel: +254-774249552; E-mail: ronoamos00@gmail.com

Received date: March 17, 2017; Accepted date: April 03, 2017; Published date: April 10, 2017

Copyright: © 2017 Ronoh AK, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

## Abstract

Micronutrient deficiencies are still common in developing countries. Biofortification of staple crops is one of the food based strategies that has been introduced to alleviate this. The purpose of this review is to document randomized feeding trials on efficacy of biofortified crops in alleviation of micronutrient deficiencies of Vitamin A, Zinc and Iron among humans. NCBI abstracts, BioMed Central, Wiley Online Libraries and two other databases were searched to identify effective studies. The search identified 45 studies and 17 met the inclusion criteria. Thirteen of the seventeen studies showed that biofortification of commonly consumed staples improved the micronutrient status of the study subjects. Two studies showed that biofortified foods had a significant bioavailability as compared to conventional food crops. Evidence of biofortified crops combating micronutrient deficiencies is positive. Policies should be made to support cross-sectorial implementation of biofortification in areas such as research, agriculture and biotechnology, and so that the intervention can be scaled up to cover most of the micronutrient deficient population.

**Keywords:** Micronutrient; Vitamins; Serum; Isotope

## Introduction

The prevalence of micronutrient deficiencies (MND) or “hidden hunger” is still high in developing countries particularly Sub-Saharan Africa and South East Asia [1]. These deficiencies are caused by lack of vital vitamins and minerals. The three critical micronutrients that have been recognized to be lacking in the diets of these populations in developing countries are Vitamin A, Zinc and Iron [2]. WHO [3] documents that iron deficiency anaemia (IDA) is the most prevalent micronutrient condition globally, where 50% of anaemia cases are caused by iron deficiency. It is estimated that 65.5% of pre-school children suffer from anaemia and 45.7% and 48.2% of women of reproductive age suffer from IDA respectively, which is the highest prevalence in the world [3]. Vitamin A deficiency (VAD) affects 190 million children under the age of 5 [4].

The implications of the deficiencies of these nutrients are far reaching particularly on children and women of reproductive age because of their increased nutrient requirements for growth and pregnancy and lactation respectively [5]. Anaemic pregnant women have higher risk of pre-term delivery, and therefore one of the major contributors of maternal deaths in the developing world [6]. IDA in children causes growth retardation, slowed learning and behavioural development resulting in reduced psychomotor and cognitive abilities [7]. VAD can lead to slowed growth, weakened immunity and xerophthalmia leading to blindness in children [8]. Zinc deficiency is a major cause of stunting among children and these children run a risk of compromised cognitive development [9].

The use of food-based strategies to reduce the prevalence of hidden hunger has been recognized [2]. Diet diversification is the ideal

solution to hidden hunger; however, poverty and rising food prices make it harder to achieve this [2]. The main method that has been used to reduce the prevalence of MND is provision of supplements such as iron tablets and vitamin A pills and fortified foods. Even though these methods have achieved great success, they are quite expensive and require proper market infrastructure and effective health channels of delivery, which are rarely found in many regions of the world and rural areas where most poor people live. Biofortification is a novel and an additional strategy introduced to help people meet their daily micronutrient requirements [10].

Biofortification is a process of improving the nutritional content of staple crops by breeding varieties that have a high content of the three limiting micronutrients (Vitamin A, Iron, Zinc) or their precursors than conventional ones [11]. This strategy provides a comparatively cost-effective, long term and sustainable way of delivering more nutrients. The approach not only seeks to reduce the prevalence of micronutrient deficiencies but also provides a means of improving the nutritional status of people. As compared to supplementation and fortification, biofortification provides a feasible means of reaching malnourished population who are mostly found in the rural areas and who have a limited access to commercially marketed fortified foods and supplements which mainly targets urban populations that consume processed foods [10,12].

In order to make biofortification a success, one of the issues that should be addressed is whether the extra nutrients bred into the food staples will be bioavailable and be absorbed at levels sufficient to have an impact on the micronutrient status of human beings. This review therefore sought to document evidence on the efficacy of biofortified food crops to alleviate Iron, Vitamin A and zinc deficiency.

## Methods

### Search strategy and selection criteria

English-language literature was systematically searched to identify human studies examining the effect of biofortified crops on the nutrient status of human under experimental conditions. The search was conducted by the using the following bibliographic databases from the year 2000 to the year 2016: NCBI abstracts, BioMed Central, Wiley Online Libraries, Medline, Google Scholar and Harvest Plus repository. Following a trail of cited papers, snowball technique was used where one selected study led to relevant heading or topic. The search was further supplemented by used of published papers where the study design met the inclusion criteria. Only accessible studies were included in this review [13].

The search terms used were: “Randomized controlled trials”, “biofortification”, “beta carotene”, “high iron beans”, “vitamin A improved cassava”, “efficacy trials”, “bioavailability”, “OSFP” “Plant breeding” “zinc”.

## Results

The search yielded 45 articles, after exclusion based on the above-named criteria, 17 articles were eligible to be included in the review. The studies are presented in Tables 1-3.

### Study characteristics

The ages of the study subjects differed among studies ranging between 22 months to 45 years old. The study subjects included young children (22-35 months); school going children [14-16], and adults, both male and females. The intervention periods, form in which the food was fed, and the feeding intervals for each of the studies differed. The sample sizes also differed. However, some articles, mostly the ones that were only accessible in abstracts-only did not give the details on the age, gender, sample size and the duration of the feeding trial. The micronutrient status of the subjects at the baseline differed. Some were deficient [14,17,18] while others were healthy [19].

Authors, Country	Population description	Methodology/ Intervention	Main results and Conclusion
Haas et al. [13] Philippines	Filipina religious sisters 69 high iron (HI) 69 control (C), Non-anemic (Hb> 12 g/dl at baseline)	Feeding trial for 9 months on high iron-biofortified beans	Increase in serum ferritin, Increase in total body iron
Cercamon di et al. [14] Western Maharashtra, India	Secondary school children-males and females; HI 99 C 98; Low ferritin (20 µg/l at baseline)	Feeding on pearl millet flat bread twice a day (midday and evening) for 4 months	A significant improvement in serum ferritin, total body iron in iron deficient adolescent boys and girls.  The prevalence of IDA was reduced significantly in the HI group; children who were iron deficient at baseline significantly improved their iron status by 64%.  The trial resulted in reduction in IDA by the 6th month
Hallberg and Hulthen, [15] Mexico	Mexican primary school children-males and females HI 269 C 166  Low morbidity, low inflammatory schools	Feeding trial on biofortified black beans for 105 days	Acute phase protein and serum ferritin did not improve significantly because of high levels of infections in this population
Petri et al. [16] Rwanda	Iron depleted university women HI 166 C 118  Low ferritin (<15 µg/l at baseline)	Biofortified black beans; feeding trial for 4.5 months	Significant increase in haemoglobin and total body iron after consumption of biofortified beans for 4.5 months
Haas et al. [17] Mexico	Religious sisters 18-45 years; HI 92 C 100	High iron biofortified rice, 9 months feeding trial	Modest increase in serum ferritin, total body iron  No significant increase in haemoglobin  Greater response in non-anemic subjects for ferritin and body iron
Finkelstein et al. [18] Serole Pathar, India	Male and female adolescents HI 122 C 124  Low ferritin (15 µg/l) haemoglobin (12 g/dl) at baseline	Iron biofortified pearl millet snack as Bhakri at midday and evening	The experimental group significantly improved their iron status at the 4th month  Those children who were iron deficient at start and ate iron rich pearl millet (Fe-PM) were 1.64 times likely to have resolved IDA  The effects of Fe-PM on IDA were greater among children who were deficient at the baseline
Haas [17] Mexican school children	Male and female children,	Biofortified against conventional black beans for 110 days	Children in High iron beans group had a greater reduction in transferrin receptor from baseline to end compared to the control group
Kodkany et al. [20] Karnataka, India	40 Children aged 22-35 months	Three test meals providing 84 ± 17 g dry pearl millet flour were fed for 2 d for iron between 0900 and 1600 h.  The quantities of iron were measured using stable isotope	Increase in the amount of iron absorbed in the diet of these children  Quantities of iron absorbed from iron biofortified pearl millet fed to children aged 2 years as the major food staple is

		extrinsic labeling techniques and analyses of duplicate diets	more than adequate to meet the physiological requirements of these nutrients
Ceremoni et al. [21] Bengal	20 Binese Women (17-35 years) marginal iron stores (Plasma ferritin 25 µg/l)	Consumption of biofortified millet Iron absorption was measured as erythrocyte incorporation of stable iron isotope	Consumption of iron biofortified millet would double the amount of iron absorbed. Iron biofortified millet should be highly effective in combating ID in millet consuming populations
Donangelo et al. [22] United States of America	23 women of different races At entry into the study, all women had haemoglobin concentrations >110 g/L and plasma ferritin concentrations <25 µg/L	The subjects were randomly divided into two groups; Group 1 (n=12) received a meal of typical common beans (CB), Group 2 received a test meal of high iron/Zinc beans (HFEZnB) Iron status was determined using extrinsic labeling	Total iron absorbed from the test meal was very low for both bean varieties (0.03-0.04 mg).

**Table 1:** Results from Iron biofortification studies.

**Methods of nutrient analyses**

In the studies on iron biofortified crops the biochemical tests that were done to test improvement in the iron status were: Inflammation (measured by C-reactive protein and α-1-acid glycoprotein concentrations) [14,15], total body iron [13-18,21,22], haemoglobin

concentration [16], serum ferritin concentration [13-17], acute phase proteins [18] and serum transferrin receptor concentration [19]. The baseline cut-offs for each of the parameter differed among the studies (Table 2).

Authors, Country	Population description	Methodology/ intervention	Main results and conclusion
Van Jaarsveld et al. [23] South Africa	Children 5-10 years Treatment group n=50; Control n=90	Experimental group; Mashed OSP (1032 retinol equivalent/day as β-carotene) Control group; Equal amount of white fleshed Sweet Potato devoid of βcarotene for 53 days	Greater improvement in VA livers stores in the treatment group than the control group Significant increase in the normal VA status in experimental children. Consumption of OSP improves the VA status and plays a significant role in developing countries as a viable food-based strategy for combating VA deficiency in children
La Frano et al. [24] America	10 healthy well-nourished adult American women	Subjects consumed three different types of porridges separated by 2 weeks of wash out. Each of the treatment meals contained 100 g of cassava Treatment 1: Biofortified cassava (2 mg β-carotene) porridge with added oil (15 ml peanut butter or rapeseed oil (20 g total fat) Treatment 2: Biofortified cassava porridge without added oil (6 g total fat) Treatment 3: Unfortified cassava porridge with 0.3 g retinyl palmitate reference dose and added oil (20 g total fat)	The AUC for retinylpalmitate increased after the biofortified cassava meals were fed Biofortified cassava increased the β-carotene and retinyl plamitate. It was concluded that biofortified cassava is a viable intervention for preventing VAD
Gannon et al. [25] Zambia	140 rural Zambian children	Treatments; White maize with placebo oil (VA-), orange maize with placebo (Orange), White maize with Vitamin A in oil (400 µg RE) and 214 µ daily (VA+) Assessment of VA was done using paired [13] C-retinol isotope dilution test that was used to measure TBRs before and after 90 days of intervention	In total, 133 children completed the trial and were analyzed for TBRs (n=44 or 45/group). Change in TBR residuals were not normally distributed (P , 0.0001); median changes (95% CI) were as follows: VA2, 13 (219, 44) mmol; orange, 84 (21, 146) mmol; and VA+, 98 (24, 171) mmol. Nonparametric analysis showed no statistical difference between VA+ and orange; both were higher than VA2. Median calculated liver reserves at baseline were 1.04 mmol/g liver, with 59%.1 mmol/g, the subtoxicity cut off; none were 0.1 mmol/g, the deficiency cut off. Serum retinol did not change in response to intervention (P=0.16) but was reduced with elevated C-reactive protein (P=0.0029) and a-1-acid glycoprotein (P=0.0023) at baseline.

			$\beta$ -Carotene from maize was efficacious when consumed as a staple food in this population and could avoid the potential for hypervitaminosis A that was observed with the use of preformed VA from supplementation and fortification
Li et al. [26] United States of America	Six healthy women objective was to quantify the vitamin A equivalence of the $\beta$ -carotene in $\beta$ -carotene-biofortified maize based on consumption of a single serving of maize porridge	Each consumed three 250-g portions of maize porridge as follows: 1) $\beta$ -carotene-biofortified maize porridge containing 527 $\mu$ g (0.98 $\mu$ mol) total $\beta$ -carotene, 2) white maize porridge with a $\beta$ -carotene reference dose containing 595 $\mu$ g (1.11 $\mu$ mol) added $\beta$ -carotene, and 3) white maize porridge with a vitamin A reference dose containing 286 $\mu$ g retinol activity equivalent (1.00 $\mu$ mol) added retinylpalmitate. Each portion contained 8.0 g added sunflower oil. The porridges were consumed in random order separated by $\geq 2$ wk. Blood samples were collected over 9 h. Retinylpalmitate was analyzed in plasma triacylglycerol-rich lipoprotein (TRL) fractions by HPLC with coulometric array electrochemical detection.	On average, $6.48 \pm 3.51$ $\mu$ g (mean $\pm$ SD) of the $\beta$ -carotene in $\beta$ -carotene-biofortified maize porridge and $2.34 \pm 1.61$ $\mu$ g of the $\beta$ -carotene in the reference dose were each equivalent to 1 $\mu$ g retinol. $\beta$ -Carotene in biofortified maize has good bioavailability as a plant source of vitamin A.
Haskell et al. [27] Bangladesh	Bangladeshi men (n=14/group) 60 d of daily supplementation with 750 microg retinol equivalents (RE) of either cooked, puréed sweet potatoes; cooked, puréed Indian spinach (Basella alba); or synthetic sources of vitamin A or beta-carotene on total-body vitamin A stores in Bangladeshi men.	Total-body vitamin A stores in=14/group) were estimated by using the deuterated-retinol-dilution technique before and after 60 d of supplementation with either 0 microg RE/d (white vegetables) or 750 microg RE/d as sweet potatoes, Indian spinach, retinylpalmitate, or beta-carotene (RE=1 microg retinol or 6 microg beta-carotene) in addition to a low-vitamin A diet providing approximately 200 microg RE/d. Mean changes in vitamin A stores in the vegetable and beta-carotene groups were compared with the mean change in the retinylpalmitate group to estimate the relative equivalency of these vitamin A sources.	Vitamin A equivalency factors (beta-carotene: retinol, wt:wt) were estimated at approximately 13:1 for sweet potato, approximately 10:1 for Indian spinach, and approximately 6:1 for synthetic beta-carotene Daily consumption of cooked, puréed green leafy vegetables or sweet potatoes has a positive effect on vitamin A stores in populations at risk of vitamin A deficiency
Jamil et al. [28] Bangladesh	Bangladeshi Women (n=30/group) with low initial vitamin A status	Daily consumption of orange-fleshed sweet potatoes (OFSP), with or without added fat, received one of the following for 6 d/wk over 10 wk: 1) 0 $\mu$ g retinol activity equivalents (RAE)/d as boiled white-fleshed sweet potatoes (WFSP) and a corn oil capsule, 2) 600 $\mu$ g RAE/d as boiled OFSP and a corn oil capsule, 3) fried OFSP and a corn oil capsule, or 4) boiled WFSP and a retinylpalmitate capsule in addition to their home diets. Plasma concentrations of retinol and $\beta$ -carotene and total body VA pool size were assessed before and after the 60-d intervention.	Daily consumption of OFSP did not result in a net gain of total body reserves of vitamin A over negative controls, but did contribute to higher circulating serum $\beta$ -carotene concentrations Despite an increase in plasma $\beta$ -carotene concentration, the impact of OFSP on VA status appears to be limited in Bangladeshi women residing in a resource-poor community.
Gannon and Tanumihardjo [29]	3- to 5-year old children	70 days feeding trial Using the stable $^{13}\text{C}$ -signature of maize, the change in natural abundance of $^{13}\text{C}$ in serum retinol was shifted eating orange maize	This shows that the $\beta$ -carotene is bioavailable from the maize and contributing to the vitamin A pool of these children
Tanumihardjo [30]	5- to 7-year old children	90 days of feeding orange maize $^{13}\text{C}_2$ -retinol isotope dilution test was used to measure the total body pool of	Improvement in the vitamin A status of the children It was concluded that the total body pool of vitamin A before and after the intervention in the same community produced promising results in combating VAD in children

		vitamin A before and after the intervention	
--	--	---	--

**Table 2:** Results from Vitamin A biofortification studies.

Studies on Vitamin A biofortification studies the parameters used were: Vitamin A liver stores [23], retinyl palmitate [24,26], total body reserves of VA [25,27,28,30], serum retinol [29]. The methods of analyses used were: 13-C paired retinol isotope dilution test [25,29,30], and HPLC [26].

Zinc biofortification studies used total daily zinc intake [31], dual isotope technique [30], stable isotope extrinsic labelling technique [30], and dual isotope tracer ratio technique [32].

### Biofortified staple crops

The biofortified crops that were used in the studies were; Vitamin A (Orange) maize [25,26,29], vitamin A (yellow) cassava [24], Vitamin A (Orange) sweet potatoes [23,27,28], high iron beans [13,15,16,19,22], iron pearl millet [14,18,21], Zinc wheat [32], High iron rice [17], high zinc maize [31], High zinc millet [21] and high zinc beans [22].

Authors, Country	Population description	Methodology/ Intervention	Main results and conclusion
Chomba et al. [31] Zambia	60 rural Zambian children with a mean age of 29 months	Subjects were randomly assigned to receive 1 of 3 maize types (control, biofortified, or fortified) all of which were readily consumed (>100 g on 1 d).  Total daily zinc intake (from maize and low-zinc relish) was determined from duplicate diet collections.  Multiplication by fractional absorption of zinc, measured by a dual isotope ratio technique, determined the total daily zinc absorption on the day the test meals were given.	The mean total daily zinc intake (milligrams per day) from the biofortified maize was higher than for the control maize.  Intake of zinc from the fortified maize did not differ from the biofortified maize. Fractional absorption of zinc from control maize did not differ from the biofortified maize.  Total daily absorption of zinc (milligrams per day) from the biofortified maize was higher than for the control maize but did not differ from the fortified maize  Results indicated that feeding biofortified maize can meet zinc requirements and provide an effective dietary alternative to regular maize for this vulnerable population
Kodkany et al. [21] Karnataka, India	40 children aged 2 y in Karnataka, India (n = 21 test; 19 controls)	Three test meals providing 84 ± 17 g dry pearl millet flour were fed on a single day for zinc between 0900 and 1600 h.  The quantities of zinc absorbed were measured with established stable isotope extrinsic labeling techniques and analyses of duplicate diets.	There was an increase in the amount of zinc absorbed in the diet of these children, the test group having the highest amount  Quantities of zinc absorbed from iron biofortified pearl millet fed to children aged 2 years as the major food staple is more than adequate to meet the physiological requirements of these nutrients
Rosado et al. [32] Mexico	27 adult women with habitual diet high in phytates; Non pregnant or lactating  18-42 years	The women consumed 300 g of 95 or 80% extracted wheat of tortillas for 2 consecutive days using either biofortified (41 mg Zn/g) or control (24 mgZn/g) wheat.  Samples were labeled with Zn isotopes and fractional absorption of Zn determined by dual isotope tracer ratio technique	Zn intake from the biofortified wheat was 5.7 mg/day (72%) higher at 75% extraction (p<0.001) and 2.7 mg/day (68%) higher at 80% extraction compared with the corresponding control wheat (p=0.007)  There were potential increases in Zn absorption achieved from biofortification of wheat with zinc.
Donangelo et al. [23] United States of America	23 women of ages 20-28 of mixed races	The subjects were randomly divided into two groups; Group 1 (n=12) received a meal of typical common beans (CB), Group 2 received a test meal of high iron/Zinc beans (HFEZnB)	Feeding the high zinc bean containing almost twice the concentration of the Common bean (CB) resulted in 40% more total zinc absorbed by the women.

**Table 3:** Results from Zinc bio-fortification studies.

### Effect of biofortified food crops on micronutrient status

Studies [13-15,17,18] revealed that the subjects' ferritin and total iron increased significantly after feeding intervention with high iron biofortified crops. There was notable increase in the total body iron for subjects who were deficient at the baseline. One study [15] showed that there was no significant improvement in the hemoglobin levels due to high levels of infection in the children. One study [16] showed significant improvement in the hemoglobin levels, whereas study [17] did not show any improvement in the hemoglobin levels. Studies

[20,21] showed that there was an increase in the amount of iron absorbed from the diet of the subjects. Furthermore study [20] showed that the amount of iron absorbed from the diet of the children aged 2 years is more than adequate to meet the physiological requirements of these children for iron needs. Study [22] reported that the total iron absorbed from the test meal of high iron/ high zinc bean varieties (HFEZnB) was very low (0.03-0.04 mg).

In vitamin A biofortified crops, studies [23,30] showed a significant improvement in the Vitamin A liver stores in the treatment groups as

compared to the controls. Furthermore it showed a significant increase in the normal vitamin A status. Study [24] reported an increase in the retinyl palmitate. Study [25] reported that there was no significant change in the serum retinol after consumption of yellow maize due to elevated C-reactive proteins and 1-acid glycoproteins. The study conclude that consumption of  $\beta$ -carotene rich maize was efficacious when consumed as a staple crop as it could avoid the potential for hypervitaminosis A as compared to other micronutrient intervention strategies such as supplementation and fortification. Studies [26,29] reported that the vitamin A from bio-fortified maize has good bioavailability as a plant source of Vitamin A.

Studies [21,22,31,32] showed that intake of staple food biofortified with zinc increases the amount of zinc absorbed in the diets of the subjects, which could translate to improved zinc status in the zinc deficient populations.

Studies were included in the review based on the following criteria:

**Study design:** Only randomized feeding trial studies were included. All efficiency studies were excluded.

### Data extraction

The abstract and the full text of each of the studies were reviewed. A data extraction sheet was developed including the interpretation of the methodologies and results. The extracted information included the following: Characteristics of the subjects (sex, age, nationality), methodology (study design, participants, setting, variables, methods of measuring the micronutrient status, intervention time, intervention fortified food staple).

### Discussion

Most [13,14,16-21] of the studies on iron biofortified crops showed significant improvement of the iron status of the study subjects based on the parameters used to evaluate the nutritional. Studies [2,6] showed that there was a significant improvement in the iron status of the subjects who were deficient at the baseline. The percentage of iron absorption from the diet generally increases with decrease in the iron stores [6]. In as much as the concentration of the iron differed in the staple crops that were used and that the feeding time periods were different, there was significant improvement in the iron status level of the subjects [33]. This shows that breeding of high iron staple crops such as pearl millet and common beans can help alleviate the prevalence of IDA which is commonly caused by inadequate intake of iron rich foods, particularly in populations from developing countries. According to Hunt [34] iron biofortification of selected crops has been documented to be efficacious when feeding trials followed specific guidelines to ensure a) adequate iron concentration difference exists between high-iron and control foods used in the study, b) subjects were iron deficient at baseline, c) sufficient consumption of the staple food was documented, d) adequate time elapsed to see a response, and e) appropriate biomarkers of iron status were used. Therefore, these guidelines should be taken into consideration to ensure that validity and consistency of the study results.

Study [21] showed that the total iron absorbed from the test meal was very low (0.03-0.04 mg) for both bean varieties used in the feeding trial. This could be attributed to low iron bioavailability in the test meal, and this could be probably because of high pyrate/zinc molar ratios in both bean varieties. Reduction in the Phytate levels in the beans might have increased the bioavailability of iron in the beans

[35]. Furthermore, the low bioavailability could be due to the fact that the subjects were fed on a bean only diet and the absorption would be higher if the subjects ate a complete diet [36]. This therefore demonstrates a challenge in the efficacy trials of iron biofortified crops as the study concluded that consumption of high-iron bean variety may not improve the iron status when consumed alone. This shows that other factors that can influence demonstration of efficacy include low iron bioavailability in the staple food due to inhibitors of absorption in the diet, other non-staple food sources of iron in the diet [34]. Therefore, there is need to develop varieties with high iron and low to moderate contents of phytic acid.

Study [15] did not show any significant improvement in the iron status of the children because of high rates of infections and inflammation. This presents a challenge in the demonstration of efficacy of micronutrient interventions, biofortification included, and therefore there is need to understand the role played by infection in micronutrient status [37]. According to Ramsay [38] intestinal parasitic infections such as heavy infection of helminthes are an important determinant of iron status. Primarily these organisms cause gastrointestinal bleeding resulting in the loss of blood, lowered hemoglobin levels, and therefore resulting in anemia. Moreover, some of these organisms cause poor absorption of micronutrients by damaging the mucosal surface of gut. This study therefore proves that the proposed target levels for iron content of biofortified foods may not be adequate to have a significant effect on the iron status of the infected persons and therefore this challenge should be addressed. Most of the studies concluded that consumption of biofortified staple crops improved the iron status of the subjects, and therefore considering the global prevalence of IDA and the billions of people who consume rice, iron-biofortified staples such as beans, pearl millet and rice could make an impact, especially among groups who do not consume significant amounts of animal-source foods (ASF).

Consumption of vitamin A biofortified crops significantly improved the VA liver stores of the subjects [23] and increased  $\beta$ -carotene circulating in the blood [24,28,30]. Studies [26,29] reported that vitamin A from biofortified maize had a higher bioavailability as a plant source of vitamin A, as evidenced by the increased VA pool of the children. These studies concluded that biofortified staples used can play significant role developing countries as a viable food-based strategy for combating increasing VAD among vulnerable populations such as young children. This is a promising strategy to combating VAD among rural, poor communities who may not have access to VA supplements and VA fortified foods. This will help to reduce the prevalence of night blindness, and improve the immunity of the children translating to reduced morbidity and mortality. Furthermore, evidence from study [25] shows that consumption of VA biofortified staples is one of the effective ways to reduce the potential of hypervitaminosis A which commonly results from the use of supplements and fortified foods. This is a proof that Vitamin A biofortified staples are effective in the delivery of the nutrients as chances of toxicity are avoided. This is significant to developing countries where the prevalence of VAD is high as consumption of VA rich fruits and vegetables is low, and their diet is lacking in diversity.

Consumption of Zinc biofortified foods resulted in the amount of zinc absorbed in the diets of the subjects [31-33]. Study [31] showed that zinc absorbed from fortified food did not differ significantly from that observed from zinc biofortified crops. This shows that biofortification can be a cheaper alternative for delivering zinc to the most vulnerable population such as children under the age of 5 years.

The amount of zinc absorbed from biofortified pearl millet as the major food staple was more than adequate to meet the physiological requirements of the study subjects (children aged 2 years). The experimental bioconversion factors are encouraging. This shows that selective breeding of high zinc crops may improve the zinc status of the populations which usually consume these foods. This could be a sustainable step in combating the high prevalence of zinc deficiency in developing countries, which results in stunted growth in children, lowered immunity and increased susceptibility to infections.

## Conclusion

This review concludes that efficacy trials of biofortified crops have shown a significant improvement in the micronutrient status of the subjects. Therefore, it can be recommended that the biofortification efforts be scaled up in developing countries; however, there is need to document much evidence to support the effectiveness of this nutrition intervention method. Policies should be put in place to support collaboration and cross-sectorial implementation of biofortification in areas such research, agriculture and biotechnology, and so that the intervention can be scaled up to cover most of the micronutrient deficient population.

## References

1. WHO (2014) Iron Deficiency Anemia.
2. Virk P, Bouis H (2015) What are nutritionally enhanced crops, and why does the world need them?
3. WHO (2008) Worldwide prevalence of anaemia 1993-2005: WHO Global Database on Anemia.
4. WHO (2009) Global prevalence of vitamin A deficiency in populations at risk 1995-2005: WHO global database on vitamin A deficiency. Geneva.
5. Hill DI, Webb P, Harvey P, Hunt JM, Dalmiya N, et al. (2005) Micronutrient deficiencies and gender: social and economic costs. *Am J Clin Nutr* 81: 1198S-1205S.
6. Clark SF (2008) Iron deficiency anemia. *Nutrition in Clinical Practice* 23: 128-141.
7. Choi HJ, Lee HJ, Jang HB, Park JY, Kang JH, et al. (2011) Effects of maternal education on diet, anemia, and iron deficiency in Korean school-aged children. *BMC Public Health* 11: 870-878.
8. Somner A, West KP (1996) Vitamin A deficiency: health, survival and vision. Oxford University Press, New York.
9. Wessells KR, Brown KH (2012) Estimating the global deficiency results based on zinc availability in national food supplies and the prevalence of stunting. *PLoS One*, 7e50568.
10. Bouis H, Low J, McEwan M, Tanumihardjo S (2013) Biofortification: Evidence and lessons learned linking agriculture and nutrition. FAO/WHO publication.
11. Saltzman A, Birol E, Bouis H, Boy E, Moura F, et al. (2013) Biofortification: progress toward a more nourishing future. *Global Food Security* 2: 9-17.
12. Bouis HE, Hotz C, McClafferty B, Meenkashi JV, Pfeiffer WH (2011) Biofortification: A new tool to reduce micronutrient malnutrition. *Food and Nutrition Bulletin* 32 (supplement 1) 31S-40S.
13. Haas JD, Beard LL, Murray-Kolb LE, del Mundo AM, Felix A, et al. (2005) Iron-biofortified rice improves the iron stores of non-anemic Filipino women. *J Nutr* 135: 2823-2830.
14. Cercamondi C, Egli I, Mitchikpe E, Tossou F, Zeder C, et al. (2013) Total iron absorption by young women from iron-biofortified pearl millet composite meals is double that from regular millet meals but less than that from post-harvest iron-fortified millet meals. *Journal of Nutrition* 113: 176-826.
15. Hallberg L, Hulthen L (2000) Prediction of dietary iron absorption: an algorithm for calculating absorption and bioavailability of dietary iron. *Am J Clin Nutr* 71: 1147-1160.
16. Petry N, Egli I, Gahutu JB, Tugirimana PL, Boy E, et al. (2012) Stable isotope studies in Rwandese women indicate that the common bean has limited potential as a vehicle for iron biofortification. *J Nutr* 142: 492-497.
17. Haas JD, Beard JL, Murray-Kolb LE, del Mundo AM, Felix A, et al. (2005) Iron-biofortified rice improves the iron stores of non-anemic Filipino women. *J Nutr* 135: 2823-2830.
18. Finkelstein JL, Mehta S, Udipi SA, Ghugre PS, Luna SV, et al. (2015) A randomized trial of Iron-biofortified pearl millet in school children in India. *J Nutr* pp: 1-6.
19. Haas JD, Villalpando S, Beebe S, Glahn R, Shamah T, et al. (2011) The effect of consuming biofortified beans on the iron status of Mexican school children. *The FASEB J* 25.
20. Kodkany BS, Bellard RM, Mahantshetti NS, Westcott JE, Krebs NF, et al. (2013) Biofortification of Pearl Millet with Iron and Zinc in a Randomized Controlled Trial Increases Absorption of These Minerals Above Physiologic Requirements in Young Children. *J Nutr* 143: 1489-1493.
21. Cercamondi C, Egli I, Mitchikpe E, Tossou F, Zeder C, et al. (2013) Total iron absorption by young women from iron-biofortified pearl millet composite meals is double that from regular millet but less than those from post-harvest iron-fortified meals. *J Nutr* 113: 176-826.
22. Donangelo CM, Woodhouse LR, King SM, Toffolo G, Shames DM, et al. (2003) Iron and zinc absorption from two bean (*Phaseolus vulgaris* L.) genotypes in young women. *J Agri Food Chem* 51: 5137-5143.
23. van Jaarsveld PJ, Faber M, Tanumihardjo SA, Nestel P, Lombard CJ, et al. (2005) Beta-carotene-rich orange-fleshed sweet potato improves the vitamin A status of primary school children assessed with the modified-relative-dose-response test. *Am J Clin Nutr* 81: 1080-1807.
24. La Frano MR, Woodhouse L, Burri B (2012) Vitamin A equivalence of carotenoids from high-carotenoid cassava in healthy well-nourished volunteers. Western Human Nutrition Research Center at UC Davis, Davis, California, USA.
25. Gannon B, Kaliwile C, Arscott A, Schuselzle S, Chileshe, et al. (2014) Biofortified orange maize is as efficacious as Vitamin A supplement in Zambian children even in the presence of high liver reserves of Vitamin A: a community-based, randomized placebo controlled trial. *Am J Clin Nutr* 100: 1541-1550.
26. Nugroho A, Rocheford T, White WS (2010) Vitamin A equivalence of the  $\beta$ -carotene in  $\beta$ -carotene-biofortified maize porridge consumed by women. *Am J of Clin Nutr* 92: 1105-1112.
27. Haskell MJ, Jamil KM, Hassan F, Peerson JM, Hossain MI, et al. (2004) Daily consumption of Indian spinach (*Basella alba*) or sweet potatoes has a positive effect on total-body vitamin A stores in Bangladeshi men. *Am J Clin Nutr* 80: 705-174.
28. Jamil KM, Brown KH, Jamil M, Peerson JM, Keenan AH, et al. (2012) Daily consumption of orange-fleshed sweet potato for 60 days increased plasma  $\beta$ -carotene concentration but did not increase total body vitamin A pool size in Bangladeshi women. *J Nutr* 142: 1896-1902.
29. Gannon BM, Tanumihardjo JL (2013) Linking agriculture to nutrition-the harvest is near and how do we measure impact? *FASEB J* 27: 638-725.
30. Chomba E, Westcott CM, Westcott JE, Mpabalwani EM, Krebs NF, et al. (2015) Zinc absorption from biofortified maize meets the requirements of young rural Zambian children. *J Nutr* 145: 514-519.
31. Rosado JL, Hambidge KM, Miller L, Garcia O, Westcott J, et al. (2009) The Quantity of Zinc Absorbed from Wheat in Adult Women is Enhanced by Biofortification. *Journal of Nutrition* 139: 1920-1925.
32. Petry N, Egli I, Gahutu JB, Tugirimana PL, Boy E, et al. (2012) Stable isotope studies in Rwandese women indicate that the common bean has potential as a vehicle for iron biofortification. *J Nutr* 142: 492-497.
33. Beck KL, Conlon CA, Kruger R, Coad J (2014) Dietary determinants of and possible solutions to iron deficiency for young women living in industrialized Countries: A review. *Nutrients* 6: 3747-3776.

- 
34. Hunt JR (2001) How important is dietary iron bioavailability? *American Journal of Clinical Nutrition* 73: 3.
  35. Hotz C, McClafferty B (2007) From harvest to health: challenges for developing biofortified staple foods and determining their impact on micronutrient status. *Food and Nutrition Bulletin* 28: 271-279.
  36. Stoltzfus RJ, Chwaya HM, Tielsch JM, Schulze KJ, Albonico M, et al. (1997) Epidemiology of iron deficiency anemia in Zanzibari schoolchildren: The importance of hookworms. *Am J Clin Nutr* 65: 153-159.
  37. Bhargava A, Jukes M, Lambo J, Kihamia CM, Lorri W, et al. (2003) Anthelmintic treatment improves the hemoglobin and serum ferritin concentrations of Tanzanian schoolchildren. *Food Nutr Bull* 24: 332-342.
  38. Ramsay LC, Charles CV (2015) Review of iron supplementation and fortification. Chapter 8 in *Topics of Public Health*. INTECH 176-198.