Vitamin A reduces the inhibition of iron absorption by phytates and polyphenols

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Abstract

In searching for an explanation for the rapid response to iron-fortification programmes, we focused on the interaction of vitamin A and inhibitors of iron absorption from a basal breakfast containing bread from either pre-cooked maize flour or wheat flour plus cheese and margarine. These breads were labeled with either ^{59}Fe or ^{55}Fe. These experiments demonstrated that vitamin A prevented the inhibiting effect of polyphenols and phytates on iron absorption. It was also demonstrated that vitamin A had the same effect on iron absorption as phytase.

Introduction

The project for fortification of pre-cooked maize flour and white wheat flour with iron and vitamins (vitamin A, thiamine, riboflavin, and niacin) on a national scale was initiated in Venezuela in 1993 (table 1).

One year after the fortification was begun, a survey was conducted on schoolchildren of both sexes 7, 11, and 15 years of age, living in Caracas under low socio-economic conditions. Comparison between a survey conducted in 1992, before the fortification programme was begun, and a 1994 survey of children of the same age and socio-economic stratum showed that the prevalence of iron deficiency had been significantly reduced from 37% to 16% and the prevalence of anaemia from 19% to 10%. This was confirmed by the iron reserve values, as measured by the serum ferritin concentration of all subjects tested, which increased from a median of 15 μg/L in 1992 to a median of 21 μg/L in 1994 [1].

Such results were impressive and provocative, since iron fortification usually takes a considerably longer time to produce favourable results [2]. These results motivated the authors to begin iron absorption studies to determine if the changes could be explained by characteristics of the fortified flours.

TABLE 1. Enrichment of food vehicles in Venezuela

Nutrient	Pre-cooked maize flour	White wheat flour
Vitamin A (IU/kg)	9,500	–
Thiamine (mg/kg)	3.1	1.5
Riboflavin (mg/kg)	2.5	2.0
Niacin (mg/kg)	51.1	20.0
Iron[a] (mg/kg)	50.0	20.0

a. Ferrous fumarate.

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Materials and methods

The first study was performed with a basal breakfast composed of bread made from either pre-cooked maize flour or wheat flour tagged with either ^{59}Fe or ^{55}Fe, plus 50 g of cheese and 10 g of margarine (table 2). In the first iron absorption test, the subjects received only the basal breakfast. In the other tests, they received the basal breakfast with various concentrations of coffee. The basal breakfast alone was administered on the first day after an overnight fast. The second meal was given on the afternoon of the same day.

The administration of food labelled with ^{59}Fe or ^{55}Fe in the morning after an overnight fast and on the afternoon of the same day was based on experiments previously published. Four-hour intervals between meals are sufficient for iron absorption studies [3]. Blood was drawn 15 days later to determine the haematological profile and measure the radioactivity. Blood was drawn again on the 30th day to measure the ^{59}Fe or ^{55}Fe and the ferritin concentration. Methods of measurement of radioactivity and haematological variables have been published previously [1, 4].

TABLE 2. Iron absorption in children 7 to 15 years of age given a basal breakfast with coffee[a]

Subjects and sex	Haemoglobin (g/dl)	Serum transferrin saturation (%)	Serum ferritin concentration (μg/L)	Iron absorption (%) from breakfast consisting of[b]:				
				A	B	C	D	E
Basal breakfast of maize bread, cheese, and margarine								
4M, 3F	11.9 ± 0.2	20 ± 0.5	17 ± 1	5.1 ± 1.4	7.7 ± 1.4	8.2 ± 1.4	7.8 ± 1.3	
1M, 9F	14.3 ± 0.4	27 ± 1	26 ± 1	4.4 ± 1.3	5.3 ± 1.3	4.6 ± 1.5		3.1 ± 1.5
Average of above 2 groups	13.3 ± 0.4	24 ± 2	22 ± 1	4.7 ± 1.3	6.1 ± 1.5	5.8 ± 1.5		
Basal breakfast of white wheat bread, cheese, and margarine								
2M, 8F	12.9 ± 0.8	29 ± 1	28 ± 2	6.8 ± 1.2	1.2 ± 1.4[c]	0.4 ± 1.4[c]		0.7 ± 1.2[c]

a. The basal breakfast consisted of bread made from either pre-cooked maize flour or commercial white wheat flour fortified with ferrous fumarate, plus 50 g cheese and 10 g margarine. Values are means ± SEM.
b. A, Basal breakfast alone; B, basal breakfast + 2 g American coffee; C, basal breakfast + 4 g espresso coffee; D, basal breakfast + 4 g cappuccino coffee; E, basal breakfast + 4 g espresso coffee.
c. Significantly different from absorption from breakfast A ($p < .05$).

In the first experiment, the bread was prepared from enriched, pre-cooked maize flour. The percentage of iron absorbed was practically the same when the breakfast was given alone and when it was given with various concentrations of coffee. When the breakfast was prepared from wheat flour, the percentage of iron absorbed decreased from 6% when the breakfast was given alone to less than 1% when it was given various concentrations of coffee (table 2).

The only vitamin present in pre-cooked maize flour and not in wheat flour was vitamin A. This difference encouraged the authors to perform further studies using pre-cooked maize flour fortified only with 5 mg of iron (as ferrous fumarate) per 100 g of flour.

In the next experiment, the basal breakfast was given alone in test A, with 1,000 IU of vitamin A in test B, and with 1,000 IU of vitamin A and 8 g of coffee in test C (table 3). Finally, the basal breakfast was given with coffee only in test D.

Results

The percentages of iron absorbed in tests A and C were not significantly different, indicating that vitamin A prevented the inhibitory effect of the polyphenols contained in coffee. This effect was not evident in test D, in which the breakfast was administered with coffee only. Iron absorption from the breakfast given alone (test A) was then compared with iron absorption from the breakfast enriched with 1,000 IU of vitamin A (test B)(table 3). The percentage of iron absorbed in test B was almost twice that absorbed in test A. All flours contain phytate, which is another inhibitor of iron absorption. In this experiment, vitamin A prevented the binding of phytate to iron.

The next experiment was designed to find out if the effect of phytase was similar to the effect of vitamin A on iron absorption. Table 4 compares iron absorption from the breakfast prepared with 50 g of pre-cooked maize flour (test A) with iron absorption from the same breakfast enriched with 1,000 IU of vitamin A (test B), and with iron absorption from the same breakfast in which the flour was mixed with 304 U of phytase, which reduced the phytate content of the flour from 150 to 40 mg/100 g. In this experiment, iron absorption in tests B and C was more than three times that in test A, when the breakfast was given alone, thus demonstrating that vitamin A has the same effect as phytase on the absorption of iron from cereals.

The incorporation of 1,000 IU of vitamin A in the basal breakfast made from commercial wheat flour was ineffective, because 50% of the vitamin A was denatured by the effect of yeast in the dough. Moreover, after baking it was further reduced to about 100 IU. This can be compensated for by dissolving 1,000 IU of vitamin A in water and drinking it slowly while eating the breakfast, or by incorporating 2,000 IU of vitamin A in the basal breakfast made with wheat flour.

Discussion

The same effects of vitamin A—to increase nonhaem iron absorption and to prevent the inhibitory effect of phytates and polyphenols—have also been demonstrated with β-carotene [5]. Vitamin A is an essential nutrient for vision, bone growth, cellular differentiation, and the integrity of the body's immune system [4]. It has been suggested that it is also essential for erythropoiesis [6–10].

This unexpected behaviour of vitamin A in reducing

TABLE 3. Iron absorption from a basal breakfast enriched with vitamin A and/or served with coffee[a]

Subjects and sex	Haemoglobin (g/dl)	Serum transferrin saturation (%)	Serum ferritin concentration (μg/L)	Iron absorption (%) from breakfast consisting of[b]:			
				A	B	C	D
1M, 17F	12.5 ± 0.2	25 ± 1	13 ± 1	5.8 ± 1.1		8.5 ± 1.2	2.0 ± 1.2[c]
4M, 8F	14.6 ± 0.3	28 ± 2	52 ± 1	2.7 ± 1.1	5.1 ± 1.1[d]		

a. The basal breakfast consisted of bread made from pre-cooked maize flour fortified with ferrous fumarate, plus 50 g cheese and 10 g margarine. Values are means ± SEM.
b. A, Basal breakfast alone; B, basal breakfast + 1,000 IU vitamin A; C, basal breakfast + 1,000 IU vitamin A + 8 g espresso coffee; D, basal breakfast + 8 g espresso coffee.
c. Significantly different from absorption from breakfast C ($p < .05$).
d. Significantly different from absorption from breakfast A ($p < .05$).

TABLE 4. Iron absorption from a basal breakfast with added vitamin A or phytase[a]

Subjects and sex	Haemoglobin (g/dl)	Serum transferrin saturation (%)	Serum ferritin concentration (μg/L)	Iron absorption (%) from breakfast consisting of[b]:		
				A	B	C
4M, 9F	12.3 ± 0.4	26 ± 2	19 ± 1	3.6 ± 1.1	10.6 ± 1.1[c]	15.4 ± 1.1[c]

a. The basal breakfast consisted of bread made from 50 g pre-cooked maize flour with 2.5 g ferrous fumarate added, plus 50 g cheese and 10 g margarine. Values are means ± SEM.
b. A, Basal breakfast alone; B, basal breakfast + 1,000 IU vitamin A; C, basal breakfast + 304 U phytase.
c. Significantly different from absorption from breakfast A ($p < .05$).

the inhibition of iron absorption by phytates and polyphenols is apparently a newly discovered property of vitamin A. The results suggest that vitamin A binds iron during the digestive process and forms a complex that acts as a chelating agent, thus blocking the effect of hydroxyl radicals present in phytates and polyphenols [4].

Present and future food fortification programmes should consider adding vitamin A to the enrichment mix for the control of iron deficiency.

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