PROPERTIES OF VITAMINS USED IN CEREAL FORTIFICATION (Section 7 in MI Fortification Handbook)

Vitamins are essential organic compounds that the body requires to maintain life and which it cannot synthesize itself, meaning they have to be in the food supply. Vitamins are either water-soluble (vitamin C and all the B vitamins) or fat soluble (vitamins A, D, E and K).

Folic acid

Folic acid has been included in cereal fortification programs for only the last ten years, but has proven so successful that now it is considered a leading reason to fortify cereal staples, even in developed countries with few overt micronutrient deficiency problems. The initial reason to include folic acid was to prevent the neural tube birth defects (NTD) of *spina bifida* and *anencephaly*. These can occur if the mother has insufficient stores of folic acid during the first few weeks of pregnancy. Folic acid supplements taken prior to pregnancy will help prevent this but many women are not aware they are early on in pregnancy when it is needed or they simply fail to take supplements.

It is nearly impossible to get adequate intakes of folate from natural sources, particularly so since the natural folates have only 60% of the vitamin activity of synthetic folic acid. The level of folates in cereals is low, even in whole grain products. The surest way to get folic acid to the whole population is to add it to a food staple, with wheat flour and maize meal being the preferred vehicles, particularly if it can be included with an existing or planned fortification program. A standard recommendation in the prevention of NTDs is to have women consume 0.4 mg/day of synthetic folic acid, not including natural folate sources, and this is only achievable with mass fortification of a cereal staple such as flour.

Folic acid fortification of flour has proven to be highly effective. Studies have shown a three-fold increase in serum folic acid after cereals were fortified in North America with 1.5 ppm folic acid (Lawrence 1999) and a 19% decrease in NTDs (Honein 2001). Canadian studies showed similar results in reducing serum folate insufficiency (Ray, Vermeulen 2002) and a 50% reduction in NTDs (Persad 2002) (Ray, Meier 2002) .

There is growing evidence that folic acid fortification will reduce the incidence of elevated homocysteine levels (Jacques 1999), considered a major factor in cardiovascular disease and strokes. A study in Chile showed that the national folic acid fortification program reduced serum homocysteine levels in the elderly (Hirsch 2002). While this could lead to a reduction in the incidence of heart disease and strokes, the extent to which it can do this has yet to be established. With the benefits of folic acid fortification now firmly established, over thirty countries are now adding to flour, as listed in Table 5.2. An expert panel convened by the Micronutrient Initiative recommended a 2.4 ppm folic acid addition level to all flours.

There has been concern that high folic acid levels could mask neurological problems in people with low intakes of vitamin B_{12}, and this has led to reluctance to fortify with folic acid in some countries. This is more of a worry in developed countries where people may get multiple sources of folic acid from supplements and other fortified foods. It may be possible then for some people to exceed the upper safety limit of folic acid of 1mg/day, which is based on this vitamin B_{12} interaction. An obvious solution to this is to add vitamin B_{12} along with folic acid.

Folic acid has a light yellow color, which does not carry over to the flour or cereal food because it is added at such low levels, typically from 1.5 to 2.4 ppm. There is some loss of the vitamin on exposure to light and during cooking and baking, but not as much as originally supposed. Yeast leavened breads will be actually higher in folic acid than what is contributed by the fortified flour since yeast has a significant level of folate activity. The biggest loss of folate will occur in cookies and pasta, but this is probably no more than 20%. Folic acid is difficult to analyze, so levels reported in fortified flour and baked products can have considerable assay error.

Riboflavin (Vitamin B_2)

Cereals are not very good sources of riboflavin, so people dependent on wheat, rice or white refined maize are likely to be deficient in this vitamin. This can result in a variety of skin and mucous membrane problems, that, while not life threatening can be very unpleasant. Riboflavin deficiency has been implicated with elevated serum homocysteine levels along with some of the other B vitamins (Jacques 2001).

There can be a large loss of the vitamin when the food is exposed to sunlight or UV light. Its bright yellow color, while desirable in some cereal foods, like pasta and yellow corn meal, may cause problems in products where whiteness is preferred, such as rice and white corn meal. Riboflavin has been part of most cereal fortification programs. Its cost is higher than folic acid and thiamin, but not excessive. There is good reason to include riboflavin in most cereal fortification programs.

Thiamin (Vitamin B_1)

Thiamin has been included in cereal fortification programs since their inception in the 1940s. The levels in wheat and maize are not particularly low, even in the refined products, but the level of the vitamin that makes it through to the final food product that is actually consumed is much reduced due to its poor stability, particularly under alkaline (high pH) conditions. The thiamin level in white rice is quite low, causing more of a problem with thiamin deficiency (beriberi) in rice eating populations. There is also concern about thiamin deficiency causing Wernicke-Korsakoff syndrome (WKS) in alcoholics (Yellowlees 1986). Australia and New Zealand started fortifying bread flour with thiamin for this reason. It has led to a significant reduction in the prevalence of WKS in these countries (Harper 1998).

Thiamin can be added as either thiamin mononitrate or thiamin hydrochloride. The mononitrate form is preferred because it is considered more stable. Both are white powders and add no color to the flour. There are no known functional problems in adding thiamin to flour and the cost of thiamin fortification is not very high.

Vitamin B_{12}

Cereals contain no vitamin B_{12}. It is present only in animal products. Deficiencies occur mainly in the elderly. The main justification for adding vitamin B_{12} is so that high levels of folic acid can be added without risk of masking B_{12} deficiencies (Ray 2000) but it is also implicated along with some other B vitamins in reducing serum homocysteine levels (Bower 1995). Currently only one country, Israel, has included vitamin B12 in their cereal fortification program but there have been increasing calls that it be included (Quinlivan 2002).

Vitamin B12 (cyanocobalamin) is a complex molecule and difficult to produce. Its cost is very high but the fortification cost is reasonable since it is needed in such small amounts. It is a dark red compound, typically sold in a 1% dilution to make it easier to handle. It is relatively stable, but its stability in baking has not been tested. It is one of the most difficult vitamins to analyze for in foods, with a microbiological procedure being the preferred method. There have been no reports of its addition adversely affecting the color or baking properties of wheat flour.

Pyridoxine (Vitamin B_6)

There is some suggestion that pyridoxine, along with folic acid and vitamin B_{12}, can help lower homocysteine levels and thereby reduce the incidence of heart disease and stroke (Duell 1997; Jacques 2001; Kelly 2003). While whole grains are good sources of this vitamin, refined wheat flour and maize meal are not. But because it is found in a variety of foods, overt B_6 deficiency is uncommon.

Pyridoxine hydrochloride is a white powder and is not known to cause any problems when added to cereals. Its cost of fortification is similar to that of riboflavin. There is some loss of pyridoxine on exposure to UV light. Currently, only South Africa includes vitamin B6 in their cereal fortification program.

Niacin (Vitamin B_5)

Niacin is low in refined flours, and much of the niacin in whole maize, while fairly high, is unavailable since it is in a bound form. The bound niacin is released and made available in the nixtamalation process of making tortillas, but other types of maize staples will be low in available niacin. This helped cause a high incidence of pellagra in the Southeastern United States, where maize was the main food staple, resulting in thousands of deaths each year. It was for this reason that niacin was included in the original cereal fortification program, which proved very successful in preventing pellagra. There is good reason to include it with any maize eating population, particularly those that do not use a nixtamalation process, such as sub-Sahara Africa and South America. However, it is relatively expensive and could be added at a lower rate to wheat flour, or even excluded from flour fortification programs in wheat consuming populations.

One reason for excluding Niacin is tryptophan, an amino acid in proteins that acts as a niacin precursor. 60 mg of tryptophan = 1 mg of niacin = 1 Niacin Equivalent or NE. The RDA for niacin is now given in NE units. When tryptophan content is considered even refined wheat flour becomes a fairly good source of niacin but maize meal is still inadequate, as shown in Tables 3.8 and 3.9.

Niacin comes in two chemical forms: niacinamide and nicotinic acid. The latter is normally referred to as niacin so as not to be confused with nicotine, a totally different compound. Niacinamide is slightly more expensive but it has the advantage of not be a vasodilator as is nicotinic acid, which results in a flushing and skin reddening reaction in those handling the fortification premix. Both are white powders and have no detrimental effects on taste or flour functionality. Niacin is very stable and has no problem with cooking or baking losses.

Vitamin A

Deficiencies of vitamin A are considered a serious health problem in many parts of the world. It affects visual function leading to night blindness and xerophthalmia. WHO estimates about 3 million pre-school children show ocular signs of vitamin A deficiency and that 254 million preschool children throughout the world are subclinically deficient.

Cereals contain no natural vitamin A and very low levels of beta-carotene, a vitamin A precursor. They are, however, potential vehicles for vitamin A fortification in deficient populations. Flour and maize meal are not usually fortified with vitamin A in developed countries, where margarine is often fortified, and vitamin A deficiency is not a problem. The U.S. Title II (Food for Peace) Food Program provides wheat flour and maize meal fortified with vitamin.

Vitamin A has been added to precooked maize flour in Venezuela since 1993. At the fortification level of 2.7 mg/kg and an intake of 80 g flour/day, it supplies about 40% of the recommended intake of the vitamin (Chavez 1997). South Africa adds it to flour (1.6 mg/kg) and maize meal (1.9 mg/kg). Nigeria started requiring the addition of vitamin A to flour at a very high level of 9 mg/kg in 2002. In the Philippines, wheat flour was fortified with 4.5 mg/kg so that the level in the bread was 2.2 ug/g. This supplied about 33% of the Filipino RDA for the vitamin for school children, and increased their liver stores of retinol significantly by the end of a 30-week efficacy trial (Solon 2000).

Several forms of vitamin A are available for food fortification. These include retinyl acetate, retinyl palmitate, and provitamin A (β-carotene). β-carotene has an intense orange color that makes it unsuitable as a fortificant for many foods, but it is used to give an orange-yellow color to margarines and beverages. The retinyl esters are available in an oil-soluble form (for fortification of oils and fats), spray-dried (for flours and powdered milk) and as water-dispersable beadlets (for fortification of sugar and other water-soluble foods). A special coated, protected form of retinyl palmitate, often generically referred to as *SD250*, is the recommended form of vitamin A for flour fortification because it is considered to be the most stable in this application. This product contains encapsulates and antioxidants that differ between manufacturers, making it impractical to specify its exact composition. Alternatively, the USDA specifies that the product used in PL480 (Food for Peace) commodities retain at least 80% of its activity under defined storage conditions. The stability of vitamin A in these commodities was found to be surprisingly good, with over 95% retained after nine months (Ranum, 1999). There were additional losses during milling and baking, so that about 80% of the vitamin A added is actually consumed. Lower retentions, even down to 50%, can occur for non-bread baked products and maize meal.

It would be feasible to add vitamin A to any kind of flour or maize meal, including the high extraction or whole wheat (atta) flours prevalent in some countries. The primary constraint is the cost (see Table 7.1). Inclusion of vitamin A can double or triple the cost of a cereal fortification program. Vegetable oil may be better carrier because the form of vitamin A that can be used in oil is cheaper and the stability is somewhat better. However, in many countries, wheat flour or maize meal may be the only processed food consumed widely enough to deliver vitamin A to at-risk populations through food fortification.

Vitamin D

Vitamin D is an important regulator of calcium metabolism and can help prevent rickets in breast-fed infants and osteomalacia in the elderly. People who are exposed to sunlight will not need much vitamin D, but adult deficiencies have been shown to exist in northern latitudes, with a higher prevalence in older subjects (Yan 2000). Low levels of exposure to UV light in urban settings, clothing practices and air quality can lead to an increased need for dietary vitamin D.

Milk, including dry and evaporated milk, is the preferred vehicle to fortify with vitamin D. It was included as optional in the early cereal fortification programs in the U.S., but it was never practiced and has since been removed. No country currently adds vitamin D to cereal staples, but it has been proposed for Mongolia. It is often added to complementary foods targeted for children, such as CSB, and to margarine.

Vitamin D is a fat-soluble compound. Either vitamin D2 (also called cholecalciferol or ergocalciferol) or D3 (cholecalciferol or 7-dehydrocholesterol) can be added to foods, and have a similar biological activity, but the D3 form is preferred for cereals. One International Unit (IU) of vitamin D is equivalent to 0.025 ug of the vitamin. Both forms are very sensitive to oxygen, moist air and minerals. Dry stabilized vitamin D is available, and contains an antioxidant (usually tocopherol) that protects potency for much longer, even in the presence of minerals. The form commonly used in cereals contains 100,000 IU or 2.5 mg of D3 per gram.

Vitamin C

Ascorbic acid or vitamin C provides a number of important nutritional benefits (Bendich 1995), but the one considered most desirable for cereal products is its ability to enhance the absorption several fold of both native and added iron.

Ascorbic acid is routinely added to bread flour around the world at levels from 15 to 100 ppm to improve the flour's bread baking properties. Enzymes in the flour quickly convert it to dehydroascobic acid, which acts as an oxidative improving agent during fermentation giving a larger loaf volume and a lighter crumb. Unfortunately, further oxidation during and after baking destroys any remaining vitamin C activity. Foods prepared from maize meal retain more added vitamin C than with bread. About half of the ascorbic added to CSB, which is mainly maize meal, was retained when it was prepared as a paste (ugali or pap), commonly used in Africa (Ranum 1998). The ascorbic acid added to CSB is lightly coated with ethyl cellulose (4%), but this has little benefit in preventing loss during cooking. Greater cooking stability is possible with more heavily coated products.

Unfortunately, the cost of adding the levels of ascorbic acid necessary to improve iron absorption may be prohibitive. It could be cheaper to use iron EDTA. This is an area that needs more research and development before it can be effectively applied to cereal fortification.

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Table 7.1 Micronutrient fortification levels and costs

Nutrient	Chemical Compound	Levels Added			Cost**
		As nutrient ppm	As compound gram/MT	As % of RDA per 100g	US$ per MT of fortified flour
Iron*	Elemental Reduced Iron	50	52	14% women	0.12
	Electrolytic Reduced Iron	50	51	31% men	0.16 –0.36
	Ferrous Sulfate	25	78	25% children	0.14
	Ferrous Fumarate	25	78		0.31
	Sodium Iron EDTA	15	111		0.96
Zinc	Zinc Oxide	15 – 25	19 - 31	15% - 25%	0.04 – 0.07
Calcium	Calcium Sulfate	1 – 2 g/kg	4400 – 8700	10% - 20%	0.57 – 1.14
	Calcium Carbonate		2500 – 5000		0.55 – 1.10
Selenium	Sodium Selenate	0.1 – 0.2	0.2 – 0.5	18% - 36%	0.01
Iodine	Calcium Iodate	0.2 – 0.4	0.3 – 0.7	13% - 27%	0.01
Folate	Folic acid	1.5 – 2.2	1.7 – 2.5	38% - 55%	0.06 – 0.08
Vitamin B1	Thiamin Mononitrate	2 – 5	2 – 5	17% - 42%	0.04 – 0.10
Vitamin B2	Riboflavin	2 – 4	2 – 4	15% - 31%	0.07 – 0.14
Niacin	Niacin (Nicotinic Acid)	20 – 50	20 – 50	13% - 33%	0.15 – 0.37
	Niacinamide				0.16 – 0.39
Vitamin B6	Pyridoxine Hydrochloride	3.2	3.8	25%	0.16
Vitamin B12	Cyanocobalamine, 1%	0.01	1.0	42%	0.17
Vitamin A	250SD Palmitate	5 – 10 IU/g		17% - 33%	0.78 – 1.54
Vitamin D	Vitamin D3, 100 SD	0.4 IU/g		20%	0.08
Vitamin C	Ascorbic Acid	15 – 50		(2% - 7%)	0.06 – 0.22

* Iron levels based on adding twice as much elemental reduced iron as ferrous salts in order to adjust for their having half the bioavailability.
** Cost estimate does not include shipping or duties.