Fortification of industrialized foods with vitamins

Fortificação de alimentos industrializados com vitaminas

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A B S T R A C T

Vitamins are essential to life. Inadequate eating habits, high caloric intake and metabolic defects lead to micronutrient deficiencies, affecting more than two billion people worldwide. The increasing intake of industrialized foods, combined with low vitamin stability has led to the common practice of adding these nutrients to processed foods. This review discusses the terminology, availability, intake and risk of hypervitaminosis, due to the intake and nutritional importance of foods fortified with vitamins. The addition of nutrients should occur in foods that are effectively consumed by the target population and must meet the real needs of a significant segment of the population. In Brazil, a total of 166 products available in supermarkets are vitamin-enriched. A 10-year study involving children and adolescents in Germany showed that 90% of those surveyed used at least one fortified food. During this 10-year period, 472 fortified products were consumed. The enrichment of foods should be based on the needs of each country and, if possible, regional needs. For instance, in order to increase its intake, Vitamin D is added to foods in Denmark during the winter, mainly for the elderly. However, in Brazil, there is no evidence of the need to fortify food with this vitamin. A survey showed that of the 76 enriched dairy products, 37 contained vitamin D. Food-fortification is a very important strategy to solve nutritional deficiency problems, but it can also cause many health problems.

Indexing terms: food, fortified; food habits.

R E S U M O

Vitaminas são nutrientes essenciais à vida. Hábitos alimentares inadequados, alto consumo energético e falhas no metabolismo levam a deficiências de micronutrientes, que afetam mais de dois bilhões de pessoas mundialmente. O consumo, cada vez maior, de alimentos industrializados, somado à baixa estabilidade das vitaminas, têm induzido à prática de adição de nutrientes aos alimentos processados. Esta revisão discute terminologia, disponibilidade, ingestão e risco de hipervitaminose devida ao consumo desses produtos, e a importância nutricional dos de alimentos fortificados com vitaminas. A adição de nutrientes deve ocorrer em alimentos que, efetivamente, participem da dieta da população alvo e deve obedecer às necessidades reais de segmentos significativos da população. No Brasil, se encontra, disponível em supermercados, um total de 166 produtos enriquecidos com vitaminas. Um estudo de coorte de 10 anos, desenvolvido na Alemanha, com

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crianças e adolescentes, comprovou que 90% dos pesquisados utilizaram, pelo menos, um alimento fortificado. Ao longo do período estudado, observou-se o consumo de 472 diferentes produtos fortificados. O enriquecimento de alimentos, entretanto, deveria basear-se nas necessidade de cada país, e, se possível, nas necessidades regionais, que variam de região a região. Na Dinamarca, por exemplo, durante o inverno, e principalmente nos idosos, a vitamina D necessita ser adicionada aos alimentos, para que aumente o seu consumo. No Brasil, diferentemente, não há evidências de necessidade de fortificação de alimentos com essa vitamina. Apesar disso, uma investigação mostrou que, de 76 produtos lácteos enriquecidos, 37 continham vitamina D. A fortificação de alimentos é uma estratégia importante para resolver problemas de deficiência nutricional, porém também pode ocasionar muitos danos à saúde.

Termos de indexação: *vitaminas; alimentos fortificados; hábitos alimentares.*

INTRODUCTION

Vitamins are micronutrients essential to normal growth and health maintenance. They can act as coenzymes and are indispensable to various metabolic reactions in the organism. They are classified into two groups: fat-soluble vitamins: vitamin A (retinol) or carotenes, D, E (tocopherols) and K; and water-soluble vitamins: C (ascorbic acid), folic acid or folate, and the B complex vitamins: B_1 or thiamin, B_2 or riboflavin, B_3 or PP or niacin, B_5 or pantothenic acid, B_6 or pyridoxine, B_{12} or cobalamine, H or biotin[1]. Folate is a generic term for compounds presenting chemical structures and nutritional properties similar to folic acid, which is the synthetic form of the vitamin utilized for food fortification[2].

Vitamin deficiencies, due to insufficient intake or poor absorption, frequently induce diseases with characteristic symptoms. Of the liposoluble vitamins, deficiencies in vitamins A, D and K cause xerophthalmia, rickets in children and hemorrhagic diarrhea, respectively, with the first being more common, especially in developing countries. Vitamin E deficiency is rare[3]. Of the water-soluble vitamins, deficiencies in vitamins B_1, B_2, B_6, B_{12}, niacin, folate, pantothenic acid and biotin cause beriberi, angular estomatitis, neuritis, megaloblastic anemia, pellagra, defects in the formation of the neural tube, feet burning syndrome and hair loss, respectively[4].

Currently, more than 2 billion people suffer worldwide from micronutrient deficiencies[5]. In the USA, 10 to 20% of the population consumes less than 50% of the Recommended Daily Allowances (RDA) of folic acid and vitamins B_6, C and E[6]. Vitamin A deficiency (VAD) is a public health problem in over 70 countries. Two hundred and fifty million children are vitamin A deficient and every year, 3 million children develop xerophthalmia[1].

Deficiencies in vitamin A, iron and iodine contribute to deficiencies in vitamins C, B complex and zinc. Vitamin deficiencies are aggravated by man-produced polluents. Smoking and alcohol drinking also contribute to malnutrition[7].

The increasing intake of industrialized foods along with losses of vitamins naturally occurring in these foods during their processing and storage, have led to the practice of adding vitamins and minerals to processed foods so as to reduce nutritional deficiencies in the population.

According to Nilson & Piza[5], food fortification is the most efficient and viable solution, since it is available to the poor, pregnant women, young children and the population in general, whose needs could never be fully met by the social services. Food fortification is also available to the elderly, the sick and other groups that somehow do not maintain a balanced diet.

This review discusses the terminology, availability, intake, risk of hypervitaminosis due to intake, and the nutritional importance of foods fortified with vitamins.

Terminology, definitions and basic principles of nutrient addition to foods

Different terms have been used to characterize vitamin-added processed foods. These terms are: vitamin-added foods, enriched, fortified, reconstituted. There is disagreement in the literature as to the definitions of these terms[8-10].

According to the Codex Alimentarius, food with nutritional equivalence is food to which a minimum of 5% of the RDA was added to the portion, reconstituted food is that to which 10% to 30% of the RDA was added and fortified food is the responsibility of the authorities of each country[11].

According to the FDA (Food and Drug Administration), enriched, fortified and vitamin-added are similar terms that can be used alternatively to indicate the addition of one or more vitamins, minerals or proteins to the food[12].

In Brazil, enriched or fortified food is defined as food to which one or more nutrients are added, containing a maximum of 15% and 30% of the RDA in 100g or 100ml, in liquid and solid foods, respectively. Nutrient added food is food in which a maximum of 7.5 and 15% of the RDA was added to 100g or 100ml of solid or liquid food, respectively. Reconstituted food is food to which a nutrient is added to replace the quantity lost during processing and/ or storage[13]. Vitamin supplements are foods to which vitamins were added at a rate of 25% to 100% of the RDA, to the daily portions indicated by the manufacturer[14].

The Codex Alimentarius, which is part of the Food and Agriculture Organization / World Health Organization Food Standardization Program, has adapted the general principles for the addition of essential nutrients to foods (GLO9-1991) making the commercialization of fortified foods possible among countries[11]:

1) The essential nutrient should be present at a level that will not result in either an excessive or an insignificant intake of the added essential nutrient, considering amounts obtained from other sources in the diet;

2) The addition of an essential nutrient to a food should not result in an adverse effect on the metabolism of any other nutrient;

3) The essential nutrient should be sufficiently stable in the food under the customary conditions of packaging, storage, distribution and use;

4) The essential nutrient should be biologically available in the food;

5) The essential nutrient should not impart undesirable characteristics to the food and should not unduly shorten the shelf life;

6) Technological and processing facilities should be available to permit the addition of the essential nutrients in a satisfactory manner;

7) The addition of essential nutrients to foods should not be used to mislead or deceive the consumer as to the nutritional merit of the food;

8) The additional cost should be reasonable for the intended consumer;

9) Methods of measuring and controlling the levels of the added essential nutrients in foods should be available; and

10) When provision is made in food standards, regulations or guidelines for the addition of essential nutrients to foods, specific provisions should be included, identifying the essential nutrients to be considered or to be required and the levels at which they should be present in the food to achieve their intended purpose.

Food fortification is achieved by the addition of natural materials rich in vitamins or the addition of pure or mixed synthetic vitamins, denominated "premix"[9], whose use has the following advantages: addition of up to 13 vitamins as simple ingredients; higher vitamin stability, lower cost and easier quality control[8].

Availability of fortified foods

Most vitamins were discovered and artificially synthesized in the early 20th century. Later, their deficiency was found to cause diseases. There are several examples in recent history where alterations in the standard food intake of a country led to a diminished intake of vitamins, and consequently to epidemics of disease.

In Denmark, in 1910, the introduction and large-scale intake of margarine instead of butter, which is an important source of vitamin A, led to a high incidence of xerophthalmia, which lasted until 1917. During 1918 and 1919, xerophthalmia almost disappeared due to an increase in butter intake, which was subsidized by the government. Xerophthalmia reappeared in 1920, when butter subsidies were discontinued[5,15].

In the USA, in 1928, many deaths were reported due to diseases caused by a deficiency of the B complex vitamins. Approximately 7,000 people died due to pellagra. In the mid 1930s, the nutritional causes of this disease were reported. In 1938, bakers started to voluntarily enrich breads with yeast, a rich source of vitamins, since synthetic vitamins were expensive. This action led to a high reduction in the incidence of pellagra in 1939[4]. In 1944, fortification of wheat flour with vitamins A, B1 and B2 became mandatory in 22 states. From 1944 to 1947, beriberi was eliminated and infant mortality during the first year of life dropped from 102 to 61 for every 1000 live births[5].

In the Philippines, in 1947, more than 12% of the population was affected by beriberi, due to the substitution of brown rice, which is an important source of vitamin B_1, by polished rice. Since October 1948, polished rice has been fortified with vitamin B_1 and deaths due to beriberi reduced by 69%[5].

In the United Kingdom, food fortification has been carried out for 50 years[10]. Currently, food fortification is carried out in several countries, the main foods being margarine, milk and derivatives, cereal flours and sugar (Table 1). These are low-cost, widely consumed foods, and their sensory characteristics are not altered by fortification. Besides, the population consumes some, such as sugar, in relatively constant quantities.

In Germany, Sichert-Hellert et al.[23], applied questionnaires to consumers between 1987 and 1995, and reported the availability of 479 products fortified with vitamins and/ or minerals, especially drinks and baby foods (for children younger than 4 years of age). These products were fortified with one (38%) or more of the following nutrients: A, B_1, B_2, B_3, B_6, C, E, folate, iron, calcium, potassium, phosphorus and magnesium. No product was fortified with the 13 vitamins. Vitamin C was the most commonly used vitamin, followed by vitamins E, B_1, B_6 and B_3. Almost all the cereals were fortified with vitamins B_1, B_2, B_3, B_6 and folate. About 60% of the dairy products contained added vitamins B_1, B_2, B_6 and E.

The food industry has, in some cases, fortified foods voluntarily. However, in some countries this fails to occur due to a lack of consumer and government information on the prevalence of nutrient deficiencies and their impact on health. Without consumer demand, there is no motivation for the industry to voluntarily fortify food[5]. On the other hand, voluntary fortification could serve as a good marketing tool.

Hundreds of vitamin-fortified foods are available to the Brazilian consumer. In supermarkets in Belo Horizonte, 166 products from 44 industries are available[24], of which about 65% are enriched with at least one of the following vitamins: A, B_1, B_3, B_6 and C. Only 9.2 and 4.8% contained biotin and vitamin K, respectively (Table 2). None of the enriched foods surpassed the maximum RDA (Table 3), according to their labels.

Intake of fortified foods

In developing countries, there is a growing intake of industrialized foods as well as the supply of fortified food. Thus fortified food intake has become a routine. However, little quantitative information on the intake of these foods is available. In Guatemala, almost all sugar commercially available and consumed by 90% of the population, is fortified with vitamin A[25], which, combined with fortified margarine, supplies about 50% of the vitamin A consumed by children between 5 and 6 years of age[26]. In El Salvador fortified sugar is consumed by 55% of the population, and in Pakistan fortified butter is consumed by 80%[16].

Infants constitute a population at risk for vitamin D deficiency because of their relatively large vitamin D needs brought about by their high rate of skeletal growth. At birth, infants have acquired *in utero* vitamin D stores that must carry them through the first months of life[1].

Although human milk has low concentrations of vitamin D, only infants fed human milk and living in places with restricted

Table 1. Vitamins added to foods in different countries.

Food	Vitamin	Country
Sugar	A	South Africa, Costa Rica, El Salvador, Guatemala, Honduras, Nicaragua, Panama and Zambia
Rice	A	Philippines
	B_1 and B_3	Philippines
	B_1, B_2 and B_3	Thailand
Cereals and bread	B_1	Australia
Cereals	A, B_1, B_2 and B_3	Venezuela
Cereals, flour and bread	B_1, B_2, B_3, D and folic acid	USA
Ready to eat cereals	A , B_1, B_2, B_3, B_6, C and folate	USA
Flour and bread	B_1 and B_3	United Kingdom
Wheat flour	B_1, B_2, B_3 and folic acid	Bolivia, Canada, Colombia, Ecuador, Guatemala Saudi Arabia, Australia, Chile, Costa Rica, El Salvador, Honduras,
Wheat flour	B_1, B_2 and B_3	Malta, Nigeria, Panama and Dominican Republic
	B_1, B_2, B_3 and B_6	Sweden
	B_2, B_6, C and D	Turkey
Pre-cooked corn flour, wheat flour	A, B_1, B_2 and B_3	Venezuela
Milk	A and D	Argentina, USA, Philippines, Malaysia, Mexico
	A and D	United Kingdom
Margarine	A and D	German, Australia, Austria, Belize, Brazil, Canada, Chile, Colombia, Ecuador, USES, Greece, Netherlands, Honduras, Iceland, Indonesia, Malaysia, Mexico, Norway, Panama, Pakistan, Peru, United Kingdom, Singapore, Sweden, Turkey
	A	Denmark, El Salvador, Philippines, Guatemala, India, Portugal and Taiwan
	A, D and E	Morocco
Corn	B_2 and B_3	South Africa
Oils	A	Pakistan
Olestra	A, D, E and K	USA
Fruit juice	A, C and E	German
Fruit juice	C	United Kingdom

Source: 4, 5, 10, 11, 12, 15, 16, 17, 18, 19, 20, 21, 22.

Table 2. Number of foods fortified with vitamins available in Belo Horizonte, MG, 2001.

Foods	A	B_1	B_2	B_3 [1]	B_5 [2]	B_6	B_{12}	C	D	E	K	AF[3]	Biotin	Total
Juices	1	2	1	1	1	2	1	10	0	1	0	1	0	11
Cereals	29	64	63	62	22	60	37	37	9	16	0	35	3	66
Sweets	11	10	10	8	0	6	3	11	4	7	0	2	0	13
Dairy	68	34	28	39	24	40	30	46	37	45	8	30	13	76

[1] B_3: niacin; [2] B_5: pantotenic acid; [3] AF: folic acid.
Source: 24.

exposition to ultraviolet (UV) light for seasonal, latitudinal, cultural or social reasons, may have a problem. Infants born in the autumn months at extremes of latitude may be at risk because they spend the first 6 months of their life indoors and therefore have little opportunity to synthesize vitamin D in their skin during this period[1].

Infant formulas are supplemented with vitamin D at levels ranging from 40 international units (IUs) or 1mg / 418.4kJ to 100IU or 2.5mg/418.4kJ, providing approximately between 6mg and 15mg of vitamin D, respectively. These amounts of dietary vitamin D are sufficient to prevent rickets[1].

Healthy children between 6 and 9 months with an adequate diet do not need to consume fortified foods. During the weaning period, between 6 and 9 months, many parents feed their babies with fortified baby foods because they think that their children need this or simply because most of these industrialized products are fortified.

Alexy et al.[27] verified that, in Germany, 6 to 9 month old babies consumed increasing amounts of most vitamins, reaching from 150% to 400% of the RDA. During their second and third years of life, the children consumed reduced amounts of vitamins after adopting their family food habits. Sichert-Hellert et al.[16] reported that, between 1986 and 1996 in Germany, the "per capita" intake of fortified foods increased by 20% among 2 to 13 year old children, with the intake of cereals and drinks increasing 400% and 500%, respectively. The intake of vitamins derived from fortified products increased from 1987 to 1995. In 1995, the intake of vitamins B_1, B_2, B_3, B_6, C, E and folate from fortified foods increased by approximately 30% of the total intake of these vitamins[28]. Between 1986 and 2000, the intake of vitamins derived from fortified foods corresponded to 70% of the RDA for vitamin B_6; 40% of the RDA for vitamins B_1, B_2, B_3 and C and 20% of the RDA for vitamins A and folate. With the exception of E, of the total number of fortified foods, fortified drinks contributed to over 50% of the intake of micronutrients[29]. In Germany, between 1986 and 1996, over 90% of the children consumed at least one fortified food[23].

In Austria, in 1998, 42% of the adults consumed foods fortified with vitamins and or minerals, principally instant drinks, fruit juices and cereals[30].

In the USA, 59.9% of the women in their second trimester of pregnancy, consumed the

Table 3. Minimum and maximum amounts (% RDA)**1** of vitamins in enriched industrialized foods marketed in Belo Horizonte, MG, 2001.

Vitamins	Juices	Cereals		Sweets	Dairy	
	Adults**2**	Adults	Children**3**		Adults	Children
A	22.9	1.2 - 20.4	26.4 - 41.8	3.4 - 82.5	6.6 - 64	11.3 - 46.3
B_1	29.2 - 35	11.7 - 92.5	28 - 102.7	4.4 - 46.9	9.7 - 58.3	21 - 50
B_2	30.8	12 - 98.1	35 - 56	4.6 - 46.9	0.8 - 43.1	25.5 - 52.1
B_3	28.1	11.3 - 104.1	31.5 - 135.3	4.2 - 46.9	9.4 - 60	20.3 - 45
B_5	30	12 - 45	33 - 66.9	-	1.4 - 80	6.8 - 29.2
B_6	38.5 - 92.3	15.4 - 137.3	42 - 75	2.9 - 46.2	12.3 - 92.3	25.5 - 50
B_{12}	10.4	6.3 - 45	9.6 - 14	1.6 - 30	1.8 - 42	11.6 - 64
C	0.8 - 30 (40 - 155.6)**4**	15 - 45	29.3 - 52	3 - 46.9	2 - 76.7	10.9 - 38.7
D	-	25.5 - 45.5	84 - 133.7	15 - 30	6.1 - 120	13.5 - 72
E	25	11 - 45	24 - 86.2	3.8 - 102	8.1 - 71	7.1 - 57.1
K	-	-	-	-	8.25 - 17.3	10 - 133.3
Folic acid	12.5	3.7 - 45	7.4 - 11.7	15 - 30	2.7 - 42	7.3 - 40
Biotin	-	-	5.3 - 83.4	-	12.5 - 90.7	35.4 - 50

1 Present in the portion of food discriminated on the label; **2** RDA for adults over 13 years of age; **3** Children from 4 to 8 years of age; **4** Juices destined for children.
Source: 24.

recommended amount of folate, derived, mainly among white women, from fortified foods[31].

Agreement on nutrient intake was found between the nutrient database of the First National Health and Nutrition Examination Survey (NHANES I) (1975) and up-to-date (December 1998) nutrient databases, suggesting that food formulation, enrichment, and fortification practices have not changed substantially over time[32].

Risk of hypervitaminosis due to the intake of fortified foods

The frequent intake of enriched foods may lead to an accumulation of some nutrients, increasing acute or chronic intoxication leading to an essential nutrient imbalance[10,23] The maximum tolerable intake (UL), i. e., the maximum amount that can be ingested daily without causing risks or adverse effects to healthy individuals, has already been determined for most vitamins[34]. The UL / RDA ratio is extremely variable, depending on the vitamin, being 2 and 1250 for vitamins B_3 and B_{12}, respectively (Table 4).

Richardson[10] classifies the vitamins in the following four risk categories:

1) Low risk and no known adverse effects: Thiamin, Riboflavin, Vitamin B_{12}, Pantothenic acid, Biotin, Niacin, a-carotene and vitamin E;

2) Low risk and acceptable safety: Vitamin C, Vitamin B_6 and Folic acid;

3) Known risk and low safety: vitamins A (Retinol Equivalent) and D; and

4) Uncertain risk and low safety: vitamin K.

A wide range of vitamins and minerals can be added safely to foods at nutritionally important levels in the current diets of Europeans. Flynn et al.[36] identified three categories of micronutrients, which could be added safely to foods at levels (per serving, i. e. 100kcal)

1) greater than one European Commission Recommended Daily Intake (EC RDA): vitamin B_{12}, vitamin C, vitamin E, riboflavin, panthothenic acid, niacin and thiamine;

2) between 50% and 100% of the EC RDA: vitamin B_6, vitamin D, folic acid, biotin, copper, iodine and selenium;

3) between 10% and 40% of the EC RDA: iron, zinc, calcium, phosphorus and magnesium.

A fourth category consists of retinol, for which the high end intake levels are close to UL for some population subgroups in Europe, and thus it requires further consideration[37].

The high intake of a vitamin may mask the deficiency of another vitamin, a condition that can be diagnosed, similar to hypervitaminosis, via laboratory tests. The vitamin reference plasma levels are presented in Table 4.

Only a few reports have been published on hypervitaminosis due to an excessive intake of fortified foods. Between 1953 and 1955, a clinical

Table 4. RDA[1], tolerable upper intake levels (UL) and reference serum levels.

Vitamin	RDA	UL[2]	Serum levels[4]
A			
Retinol	600µg	3300µg	360 – 1200µg/l
Carotene	-	25mg[3]	48 – 200µg/dl
B_1	1.2mg	50mg[3]	5.3 – 7.9µg/dl
B_2	1.3mg	200mg[3]	3.7 – 13.7µg/dl
B_3	16mg	35mg (500mg[3])	
B_5	5mg	1000mg[3]	
B_6	1.3mg	100mg	
B_{12}	2.4µg	3000µg[3]	190 – 900pg/ml
C	120mg[5]	1000mg	0.2 – 2.0µg/l
D	5µg	50µg	
25(OH) D			14 – 41ng/ml (winter) 15 – 80ng/ml (summer)
1.25 $(OH)_2$ D			15 – 60pg/ml
E	10mg	800mg[3]	5.5 – 17.0mg/ml
K	80µg	20 000µg	
Biotin	30µg	2500µg[3]	
Folate	400µg	1000µg	
Serum			>3.5ng/ml
Eritrocitaric			180 – 600ng/ml

[1] Recommended dietary allowance[34]; [2] Tolerable upper intake level[34], [3] Richardson[10], [4] Wallach[35]; [5] Levine et al.[36].

survey in the United Kingdom found 204 cases of hypercalcaemia in infants, resulting from the excessive ingestion of vitamin D-fortified foods. This observation led to the cessation of the vitamin D fortification of milk[10], which had been initiated in 1923 to prevent rickets[5].

A serious problem is making errors in the vitamin doses used for fortification during food processing. In Massachusetts (USA), the concentration of vitamin D_3 in milk was found to be 70 to 600 times higher than the RDA (10µg/l)[38, 39]. In another study, it was found that 80% of the vitamin fortified milk samples presented a variation in vitamin content of 20% in relation to the amount printed on the label. One sample presented 914% more vitamin D than specified[40]. In Honduras, despite mandatory sugar fortification, vitamin A was not detected in 34% and 21% of the sugar consumed in rural and urban regions, respectively[41].

Mills[42,43] reported that in the United States, fortified cereals, consumed in large quantities by children, contained 200% or more folate than stated on the label.

The nutritional importance of fortified foods

Vitamin A

Vitamin A is a dietary compound, soluble in fat, essential for vision, growth, reproduction, cell proliferation and differentiation and integrity of the immune system. The vitamin A needs are supplied as pre-formed retinol (in the form of its ester), present in foods of animal origin, and as carotenoids (pro-vitamin A), present in foods of plant origin. In the blood, vitamin A is present in the form of retinol, while in the liver, human milk and other animal sources, it appears as retinyl ester, which is quickly hydrolyzed before analytical detection. The absorption of carotenoids and their conversion to vitamin A is less efficient than that of retinol[1].

WHO defines VAD as the tissue concentration of vitamin A low enough to cause adverse consequences, even without clinical evidence of xerophthalmia. VAD manifests itself in different tissues. In the eyes, the symptoms and signs, referred to as xerophthalmia, are more specific indicators of VAD. VAD can be fatal in children below six years of age and blindness is more prevalent in children below three. The plasmatic levels of retinol are associated with clinical and sub-clinical deficiencies of vitamin A. Serum retinol levels below 10µg/dl (severe deficiency) are associated with xerophthalmia; levels between 10 and 20µg/dl (moderate deficiency) are characteristic of sub-clinical deficiencies, which can also occur between 20 and 30µg/dl and occasionally above 30µg/dl[1]. Sub-clinical VAD levels are considered to be low, moderate and severe if the occurrence of plasmatic retinol levels below 10µg/dl is less than 10%, 10% to 20% or ≥20% respectively in a determined population. Table 5 lists the classification of some countries according to their VAD levels. According to Mora et al.[25], sub-clinical VAD is a public health problem when the prevalence of plasmatic retinol < 20µg/dl is higher than 10%.

The main causes of VAD are: deficient intake of foods rich in vitamin A, low utilization of absorbed vitamin A due to conditions that reduce absorption and increase vitamin A requirements, such as infections or during pregnancy. According

Table 5. Countries classified according to degree of sub-clinical vitamin A deficiency.

Severe[1]	Moderate[1]	Low[1]	No information
Brazil[2]	Bolivia	Argentina	Caribe
Dominican Republic	Colombia	Belize	Chile
El Salvador	Ecuador	Costa Rica	Cuba
Nicaragua	Guatemala[4]	Panama	Haiti
Peru	Honduras	Venezuela	Paraguay
Vietnam[3]	Mexico[1]		Uruguay

[1] Classified as low, moderate and severe if the prevalence of serum retinol below 10µg/dl is <10%, 10% to 20% or >20%, respectively; [2] Observed in Manaus in 22.0% of pre-school children[44]; [3] Observed in 47% children aged 6 to 24 months[45]; [4] Classified as severe Vitamin A Deficiency by Ramakrishnan & Martorell[46].
Source: 25, 41.

to Casanueva et al.[47], the reduction of serum retinol levels occurs principally in the last trimester of pregnancy.

Fetal reserves of vitamin A are low due to the selective barrier imposed by the placenta to this vitamin, causing low vitamin A reserves in the liver of the newly born, regardless of maternal intake[48]. After birth, the fetal reserves tend to rapidly increase depending on the food fed the newly born. The vitamin A concentration in breast milk is sufficient to meet the daily needs, provided ideal conditions of breast-feeding exist.

VAD is more prevalent in Southeast Asia, Africa and East Pacific, where plant sources contribute to 80% of Equivalent Retinol (ER). In contrast, in America, Europe and the Eastern Mediterranean, where the vitamin A supply ranges from 800 to 1000µg ER/day, one third comes from animal sources[1], although, according to Denke[49], in the USA, foods from animal sources represent 2/3 of the RDA of vitamin A. Amongst 4 to 8 year old children in the cities of São Paulo and Rio de Janeiro (Brazil) the intake of vitamin A varied from 189 to 2.128µg ER, corresponding to 65.1% and 34.9% of pre-formed vitamin A and carotenoids, respectively[50].

Short, medium and long-term measures must be implemented to control VAD. Short-term measures include medicinal supplementation (distribution of capsules) to all the population or to specific groups such as young children and women after childbirth[25]. According to Phillips et al.[51], capsule distribution offers the advantage of attracting the population to other community health services. Some countries adopt such policies for children, such as in Brazil[52], Micronesia[53] and Mexico[54]. In Mexico a three-month supplementation of 100,000 and 200,000 IU of vitamin A to children between 6 to 12 months and 12 to 36 months of age, respectively, promoted a moderate VAD reduction from 42% to 7% and the disappearance of severe VAD in 6.3% of the children[53].

Medium to long term VAD control measures include nutritional education programs aiming to improve the intake of other nutrients besides vitamin A[51] and encouraging home grown--vegetable gardens with plants rich in vitamin A and dietary diversification, adopted by Micronesia[53].

Medium to long term measures also include the increased intake of vitamin A in natural and fortified foods. According to Barba & Feliciano[55], the fortification of commonly consumed food items increased nutrient availability and consequently increased nutrient intake in the Philippines. The results of the 1998 Fifth National Nutrition Survey (NNS) of the Food and Nutrition Research Institute of the Department of Science and Technology revealed that micronutrient deficiencies of vitamin A still persist in the USA. Some advantages of food fortification are: lower cost, greater population coverage and no changes in food habits[51]. Presently, some countries fortify sugar with vitamin A (Table 1).

In Guatemala, vitamin A fortification of almost 100% of the sugar reduced VAD from 40% in 1966 to 14% in 1996[25] with the cost of the sugar fortified with vitamin A being 2% higher than that of non-fortified sugar[56]. To reach the RDA of vitamin A, the annual cost per high-risk person was 0.98, 1.68 to 1.86 and 3.10 to 4.16 dollars for fortification, capsule distribution and nutritional education programs, encouraging the planting of vegetable gardens, respectively. Sugar fortified with 5µg ER/g was assumed to have reached 90% of the population; 80% of the children from 6 to 12 and from 12 to 72 months of age had received capsules containing 100,000 and 200,000 IU, respectively, every 6 months, and 87% of the housewives had received seeds for and started home vegetable gardens[51]. According to Mora et al.[25], fortification costs are normally transferred to the consumer because it accounts for less than 2% of the final cost of non-fortified sugar. Government costs are limited to supervision and monitoring. According to Dary et al.[57], in Honduras and Guatemala, it would be possible to reduce the total costs of the fortification program by 17%, since 90% of the total cost is due to retinol and 10%-30% of the sugar consumed is used by industry, which does not need to use fortified sugar. In South Africa, the substitution of cooking oil in confectionary products by red palm oil containing 450ppm of carotenoids and 500ppm of vitamin E provides 4 times more retinol, as compared to products using common oil[58].

In the Philippines, the fortification of wheat bran with 490μg ER/100 is twice as efficient in reducing inadequate intakes of vitamin A/person/year at half the cost of vitamin A capsule distribution. A combination of fortification and capsule distribution would be more effective[59].

Sugar[60] or cookies[60,62] fortification led to an increase in vitamin A and plasmatic retinol levels in children, especially in those whose basal levels were below 20μg/dl[60, 61], reducing the percentage of children with inadequate liver vitamin A reserves[61,63]. The fortification of cookies with β-carotene at a level of 50% of the RDA was sufficient to maintain the concentration of plasmatic retinol on a daily basis, but not during long vacation periods, in primary school children[62].

Vitamin D

Vitamin D is essential to maintain normal blood levels of calcium and phosphorus, which are necessary for normal bone mineralization, muscle contraction and nerve conduction in all the body cells. Vitamin D can be synthesized by the skin from the precursor 7 - dehydrocholesterol, referred to as D_3 or cholecalciferol, by exposure to sunlight, or supplied preformed in the diet as D_2, or ergocalciferol, which is metabolized in the liver to 25-hydroxyvitamin D [25(OH) D or calcidiol] and subsequently in the kidneys to the active form 1.25-dihydroxyvitamin-D [1.25$(OH)_2$ D][1].

However, vitamin D synthesis is influenced by the latitude and season of the year, which both influence the quantity of UV radiation reaching the skin; aging, which reduces the efficiency of vitamin D synthesis; complete covering of the skin with clothes, preventing skin exposure to sunlight and the use of solar filters, which reduce skin damage by the sun, but also reduce vitamin D synthesis[1,39].

In regions located between the latitudes 42° N to 42° S, the most efficient way to acquire vitamin D is via endogenous synthesis in the skin by UV light exposure. Exposure of arm and face skin to sunlight for 30min supplies the daily amount of vitamin D the body needs[1,39]. In Brazil, located at a latitude below 24°S, the plasmatic levels of 25(OH) D and 1.25$(OH)_2$ D were normal in both healthy men and in epileptics using anticonvulsive drugs, which reduce these levels[64].

In Canada, located above the 42ºN latitude, the intensity of UV light from October to March is insufficient to stimulate the production of an adequate amount of vitamin D in the skin. The elderly (over 65 years old) presented plasmatic levels 25(OH) D lower in March (39.9nmol/l) than in October (44.9nmol/l). The prevalence of vitamin D deficiency [25(OH) D<25nmol/l) increased from 9% in October to 18% in March and the prevalence of hipovitaminosis D [25(OH) D<40nmol/l) from 38% to 60%[65].

The prevalence of hipovitaminosis D [25(OH) D<15ng/ml] was 42.4% among 15-49 year old Afro-American women and 4.2% among white women of the same age. Even when the Afro-American females consumed vitamin D supplements (5μg/day), 28.2% showed D hipovitaminosis[66]. Due to the high prevalence of D hipovitaminosis, Holick[67] recommends monitoring serum levels of 25(OH) D annually.

Food intake does not supply the recommended amount of vitamin D (5 and 10mg for children and adults, respectively) since only a few foods such as meats, milk, eggs and mainly fish (especially fatty fish containing 5 to 15μg), are rich in vitamin D sources. In Denmark, the intake of vitamin D ranged from 1.5 to 2.0μg/day and 2.5 to 4.0μg/day for children and adults, respectively[39].

Dietary changes increasing fish intake, increased sun exposure, dietary supplements and food fortification are some of the strategies used to increase the availability of vitamin D in Denmark[39]. In the USA, milk fortification increased the content of vitamin D_3 from 0.3 to 12µg/l and minimized the reduction in the levels of 25(OH) D due to seasonal variations. In volunteers who ingested fortified and non-fortified milk, the reduction in the concentration of 25(OH) D from March to October was from 77 to 62nmol/l and from 85 to 54nmol/l, respectively[68].

In Denmark, in order to increase the intake of vitamin D, only fortification at high doses, which could be toxic to certain population groups, would be effective for the elderly population, which has a low food intake[39].

An excessive intake of vitamin D causes an increase in the intestinal absorption of calcium and bone re-absorption. D hypervitaminosis can lead to hypercalciuria or hypercalcaemia or both. Hypercalciuria can lead to stone formation along the lower urinary tract. Hypercalcaemia, if prolonged, can cause calcification of soft tissues, renal and cardiac damage, and, in severe cases, death[38,39].

Folic acid

Folate plays an important role in the synthesis of nucleotides, cell division, gene expression[2], prevention of some types of cancer and Alzheimer's disease[69-71]. Folic acid fortification was associated with a 60% reduction in neuroblastoma, the most prevalent solid extracranial tumor in children younger than 5 years and the most commonly diagnosed malignant tumor in infancy, because it develops in the uterus[71].

Half the 2,500 annual occurrences of neural tube defects (NTD), such as spina bifida and anencephaly could be prevented if all women of a fertile age consumed 0.4mg/day of folate for a minimum of three months before conception and during pregnancy. However, in the USA, 50% of the pregnancies are unplanned[10,69,72] and in developing countries, this value is even higher.

Lack of awareness of the importance of folate was the most common reason given for choosing not to use folic acid supplements before pregnancy among 148 women (aged 18 to 45 years) in the Vancouver area of British Columbia, Canada in an interviewer-administered survey. Although 86% of the women met the 0.32mg/day for folate, only 26% met the recommendation (0.4mg/day) for women capable of becoming pregnant. Most (95%) of the women had heard of folate, but only 25% knew that it could prevent birth defects. One-fourth of the women had good or very good knowledge of folate-rich foods[71].

NTD develop rapidly during pregnancy (18 to 30 days after conception) and an adequate plasmatic concentration of folate (above 3.5 and 160ng/mg in the plasma and erythrocyte, respectively) is important during the preconception period. Folate concentration in the erythrocytes functions as a long term indirect indicator while folate plasmatic concentration is more sensitive to recent folate intakes[69,73]. Higher folate concentrations in the erythrocytes and in the plasma can be achieved by consuming supplements and naturally rich or fortified foods[43,69,74-77].

The intake of an adequate diet supplies the RDA (400µg)[77]. The folate intake amongst 201 pregnant women was 0.7 and 1.1mg/day for high and low income pregnant women, respectively, at the *Hospital Miguel Couto*, in *Rio de Janeiro*, Brazil[78]. However, according to Becker[72], Choumenkovitch et al.[76], Boushey et al.[77] and Angelis[79], folate RDA supplied only through the intake of non fortified foods is achieved by few. Adolescents between ten and 18 years of age in *Ouro Preto*, Brazil, consumed 262µg/day of folate[80]. In the USA, the intake of folate from non-fortified foods among 289 women was 320µg/day[77].

Sichert-Hellert et al.[29] verified that, in Germany, folate fortification would raise the low intake of non-fortified foods from 50% to 80% of the RDA.

In Canada, there has been a significant decline in the prevalence of folate, but not vitamin B_{12}, insufficiency amongst adults, of which 63.2% were female, since Canada introduced a mandatory folic acid food fortification program in November 1998[81]. There was also a decrease of more than 50% in the incidence of open NTDs[82].

In the USA, after 1998, fortification with 140μg of folic acid for each 100g of cereals became mandatory in order to increase the intake to 100μg/day, aiming to reduce NTD. However, since this represented only 20% of the RDA, Wald et al.[83] suggested a fortification of 240μg of folic acid/100g of cereals in the United Kingdom, besides the ingestion of 5mg of folic acid supplied to all women and not only to those who had had NTD pregnancies, as already occurs in Australia. However, Wright et al.[2] suggested further studies before recommending folic acid fortification in the United Kingdom. According to Mills[43] and Murphy et al.[84], the use of supplements containing folic acid is the safest and most effective way to prevent NTD.

Folate plays an important role in homocysteine metabolism[85]. Folate deficiency can cause moderate hyperhomocysteinemy (total homocysteine when fasting=12μM), increasing the risk of cardiovascular diseases and fractures[74, 85-89].

Besides NTD reduction, cereal fortification with folic acid would reduce the number of cardiac deaths. According to Tice et al.[87], cereal fortification that could furnish all cardiac patients with 1mg of folic acid and 0.5mg of vitamin B_{12}, would reduce the plasmatic levels of homocysteine by 32%, reducing the number of deaths by 310,000 over 10 years.

Fortification with 140μg of folic acid for each 100g of cereals was estimated, aiming at a maximum intake of 1g/day principally in those who consume large quantities of cereals[10,43,69]. This maximum folic acid limit was established because folic acid is known to mask anemia associated with vitamin B_{12} deficiency, which are associated with the dose and duration of treatment with folic acid[70]. The non-occurrence of megaloblastic anemia may confuse the diagnosis and irreversible neurological damages may occur due to B_{12} deficiency[10,43,70,72,90,91]. Ray et al.[92] and Quinlivan et al.[93] consider the possibility of adding vitamin B_{12} besides folic acid, in cereal fortification programs. Hirsch et al.[94] also suggest adding vitamin B_{12} to food, at least in foods for elderly people, given that vitamin B_{12} deficiency was shown to be more common than folate deficiency and that vitamin B_{12} levels were unchanged, while homocysteine levels showed a moderate lowering effect after flour fortification with folic acid.

To verify whether the folic acid fortification levels in cereals suggested by the FDA were effective, Neuhouser & Beresford[69] suggested: a) to monitor NTD levels; b) to estimate the absolute intake of total folate derived from natural foods, fortified food and supplements by the target population and c) to use nutritional biomarkers of folic acid levels. This last method provides objective measurements and is sensitive to alterations in folic acid intake, allowing for the monitoring of the levels of plasmatic folate, erythrocyte folate and total homocystein.

Synthetic l-5-methyltetrahydrofolate may be more appropriate than folic acid in fortification because it is unlikely to mask the hematological indicators of vitamin B_{12} deficiency. Synthetic l-5-methyltetrahydrofolate was more effective than folic acid in lowering total homocysteine in a 24-wk study with free-living healthy volunteers randomly receiving a daily supplement containing folic acid (100μg), synthetic l-5-methyltetrahydrofolate (113μg) or placebo[95].

Cho et al.[96] reported that the folate levels in baked products, cereal grains, and pasta doubled or tripled after the new regulation took effect. However even with increased fortification, most baked products and cereal grains still contain about one-fourth of the amount of folate (on a μg/100g basis) in breakfast cereals.

CONCLUSION

Vitamin deficiency is a problem in many countries, involving all age groups and leading to serious consequences, even death. Children and pregnant women suffer the most damage. The elderly are very affected by vitamin D deficiency in countries where sunlight is not sufficient to meet their daily needs.

In order to solve the problem of vitamin deficiency, short-term solutions are necessary such as vitamin supplementation. Medium and long-term strategies, such as nutritional education focused on food diversity are ideal to prevent deficiencies but must not be used alone to solve an existing deficiency, since such strategies may take decades to show effects.

Fortification offers a medium to long-term solution and is an excellent way to increase vitamin intake. However, awareness of the target population with respect to the importance of fortified products and better sources is also necessary. Food fortification ought to be a part of nutritional education.

Food fortification as part of a national or regional program has the objective of increasing the intake of one or more deficient nutrients in certain population groups or even the whole population. In this case, a careful study must be conducted to determine which nutrient should be furnished, its synthetic form, stability, cost, concentration and type of food to be fortified. Defining the food to be fortified and its cost is also important, for if it is not available to the target population, the program will not supply the desired result.

Fortification is optional for industries. Industries use labels to attract consumer attention and use fortification as a marketing tool. Consumers can be led to choose products based on their contents of added nutrients rather than on their nutritional quality, as a whole.

Food fortification worldwide must be based on national needs and, if possible, on regional needs, since each region has different necessities. Vitamin D should be added to foods to increase its intake in particular seasons and regions. However, in some countries, such as Brazil, there is no need for the addition of this vitamin although a recent study showed that almost 50% of the dairy products contained vitamin D in amounts ranging from 6.1 to 120% of the RDA in the portion recommended by the manufacturer.

As important as having adequate legislation is applying it properly. Food labeling can improve consumer awareness. Inadequate terms on labels regarding health benefits must also be revised.

Measures to provide quality control are necessary to guarantee food fortification in pre-established concentrations. Great variation was found in the concentration of vitamins as pre-established on the labels. Losses during storage or importation of foods from countries where fortification is not mandatory, may lead to a violation of consumer rights.

It is important to remember that even without fortification, an adequate diet furnishes all the nutrients we need. Thus, we should remember that it is more important to provide the population the minimum conditions of access to housing, health, service, transport, work and a healthy diet than to furnish them with fortified foods.

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Received on: 14/4/2004
Final version resubmitted on: 25/2/2005
Approved on: 18/4/2005