

Vitamin A stability in salt triple fortified with iodine, iron, and vitamin A

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Abstract

Background. Dietary micronutrient deficiencies, which lead to diseases such as iodine deficiency disorders, iron-deficiency anemia, and vitamin A deficiency, are serious public health problems in the developing world. Fortifying salt with iodine, iron, and vitamin A is an attractive approach to simultaneously reduce the deficiencies of these three micronutrients in the diet.

Objective. To explore the technical feasibility of producing triple-fortified salt fortified with iodine, iron, and vitamin A that would be stable under the climatic conditions of developing countries (i.e., high temperature and high humidity).

Methods. Triple-fortified salt was obtained by granulation and encapsulation of commercially produced vitamin A products, iodine, and iron compounds. Vitamin A retention was determined in the presence of five iron and two iodine compounds, in different combinations, under three different storage conditions. The influence of commercial stabilization techniques for the vitamin A palmitate source used (spray-dried or dissolved in oil), and the type of binder used for granulation on vitamin A retention in triple-fortified salt was studied. The influence of temperature, humidity, and chemical interactions on vitamin A stability in triple-fortified salt was also investigated.

Results. The most stable formulation retained 77.73% of vitamin A after 2 months of storage at 40°C, 60% relative humidity, and 95% under ambient conditions.

Conclusions. The results indicate that the production of a stable triple-fortified salt is technically feasible.

Key words: Salt fortification, vitamin A, iron, iodine

Background

More than two billion people in developing countries are at risk for iodine-deficiency disorders, iron-deficiency anemia, and vitamin A deficiency, at either clinical or subclinical levels, due to dietary deficiencies of iodine, iron, and vitamin A [1].

Inadequate iodine intake results in iodine-deficiency disorders that can include mental and physical retardation, goiter, cretinism, reproductive failure, and infant mortality. Low iron intake leads to anemia, which impairs the transport of oxygen and basic cell functions, affecting work performance and compromising immunocompetence [2]. Vitamin A deficiency has been shown to cause xerophthalmia, blindness, impaired growth and reproduction, and increased morbidity and mortality [3, 4]. The disorders caused by micronutrient deficiencies have huge social and economic costs to society, which could be eliminated by providing minute quantities of these nutrients daily. The most rapid, flexible, and economical way to increase the nutrient intake of a population is by food fortification. For example, iron fortification would cost only about US\$0.20 per capita per year, iodine fortification about US\$0.10 per capita per year, and vitamin A fortification about US\$0.20 per capita per year [1]. Therefore, food fortification with all three of these nutrients could be achieved for about US\$0.50 per person per year (in 2005).

However, the success of fortification programs depends on the food selected for fortification. The carrier selected for micronutrients has to be consumed by the vast majority of the target population, at a constant level every day, regardless of socioeconomic status, and have a low potential for excessive intake. Salt is a food ingredient that fulfills all of these conditions. Moreover, the salt iodization programs that are currently operating in about 110 countries have resulted in a significant decrease in iodine-deficiency disorders, proving the efficacy of salt as a food vehicle. Since the infrastructure

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for salt iodization exists in many countries, adding iron and vitamin A together with iodine to the salt would be the most efficient solution to increase the population's micronutrient intake. Moreover, the synergistic effects between iodine-deficiency disorders and iron-deficiency anemia [5] and between iron-deficiency anemia and vitamin A deficiency [6] suggest that the best approach to eliminate these deficiencies is to simultaneously fortify salt with all three micronutrients.

Our experience with double-fortified salt [7, 8] showed that **when iron is introduced along with iodine into the salt, the interaction between iodine and iron results in a loss of iodine**. Moreover, the ferrous iron is oxidized to ferric iron, which is less bioavailable and has a rusty color. Alkaline conditions, oxidizing agents, high temperature, and high humidity accelerate these reactions. Stable double-fortified salt was obtained by granulating iron and iodine compounds with an inert binder and microencapsulating the resulting particles with a polymer or fat. The granulation step is necessary to distribute the recommended daily dosage of iodine more evenly in the average daily consumption of 10 g of salt, and at the same time to increase the size of iodine and iron particles to that of salt crystals. The goal of encapsulation is to protect the nutrients in the core. By forming a physical barrier between the reactive components, microencapsulation improved iodine stability and eliminated problems related to the oxidation of iron.

Vitamin A is also a labile compound when exposed to high temperature, humidity, trace minerals, oxygen, or light.

Objective

The objective of this study was to test the use of microencapsulation for protecting commercially produced vitamin A formulations in salt in the presence of iodine and iron under expected conditions of salt production and distribution. We assessed the stability of vitamin A in triple-fortified salt prepared by using combinations of iron and iodine compounds, at three storage temperatures and humidities. The influence of three diluents, mannitol, lactose, and calcium sulfate dihydrate, on vitamin A stability in the presence of ferrous fumarate was determined. Two types of commercially produced vitamin A palmitate products were tested: spray-dried vitamin A palmitate starch coated supplied by Watson Foods, West Haven, CT, USA, and vitamin A palmitate dissolved in oil provided by BASF Corporation, Mount Olive, NJ, USA.

Materials and methods

Materials

Noniodized salt was obtained from Cargill Foods, Minneapolis, MN, USA. Laboratory-grade potassium iodide and electrolytic iron were purchased from BDH Chemicals, Toronto, Canada; potassium iodate, ferric sodium ethylenediamine tetraacetic acid, (FeNaEDTA), i.e., ethylenediaminetetraacetic iron (III), sodium salt hydrate, and iron (II) D-gluconate dihydrate were obtained from Aldrich Chemical Company, Milwaukee, WI, USA; and ferrous sulfate heptahydrate and ferrous fumarate were purchased from Sigma Chemical Company, St. Louis, MO, USA. The vitamin A sources were commercially manufactured vitamin A palmitate powder (250,000 IU/g) from Watson Foods and vitamin A palmitate oil from BASF Corporation. For vitamin A determination, vitamin A USP reference standard was purchased from USP Rockville, MD, USA; pyrogallol, isopropanol, and ethanol were obtained from Aldrich Chemical Company; hexane was supplied by EM Science, Gibbstown, NJ, USA; and potassium hydroxide was supplied by Caledon Laboratories, Georgetown, CA, USA. Hydroxypropyl methylcellulose was received from Dow Chemical Company, Toronto, and polyvinyl pyrrolidone was supplied by Sigma Chemical Company, St. Louis, MO, USA.

Soy stearine was supplied by CanAmera Foods, Toronto. The antioxidants butylated hydroxyanisole (BHA) and butylated hydroxytolouene (BHT), supplied by Sigma Chemical Company, were incorporated into the soy stearine at a level of 0.02%.

Equipment

Granulation and encapsulation were performed in two rotating stainless-steel coating pans with diameters of 26 cm and 13 cm respectively, each equipped with a variable-speed drive. Both the rotation speed of the pan and the pan inclination could be adjusted. A hand sprayer bottle of about 250 mL, purchased from Aldrich Chemical Company, was used for spraying the granulation solution and the encapsulant onto the particles from the pan. For particle separation, U.S. Tyler sieves and a Ro-Tap sieve shaker were used.

Premix preparation

Salt was double fortified with either potassium iodide or potassium iodate and one of the five iron compounds, ferrous fumarate, ferrous sulfate heptahydrate, ferrous gluconate, electrolytic iron, or FeNaEDTA. The required daily iodine intake is provided by approximately 15 ppm in salt, but industrial practice in most

countries is to provide a significant excess, 100 ppm, for example, in North America, and 50 ppm in many developing countries. We chose 50 ppm as a conservative addition level, which also made the analysis more accurate. The methods selected for vitamin A introduction into salt were as follows:

- » Creating a new particle by granulation and encapsulation that contains vitamin A as active ingredient;
- » Introducing vitamin A together with iron into one particle so that the influence of the iron compound on vitamin A stability can be observed;
- » Introducing vitamin A together with iodine into one particle; thus, triple-fortified salt will contain two particles: one that combines iodine and vitamin A and the other that contains iodine;
- » Incorporating all three nutrients into a single particle.

The filler and binder used in this segment of the experiments was dextrin from Aldrich Chemical Company. The nutrient and the binder were first well mixed in a jar, followed by agglomeration with water in the pan. After granulation and recovery of particles in the 300- to 800- μ m size range, the granules were pan encapsulated with 40% soy stearine, a fully hydrogenated vegetable fat. The resulting premixes were tested for iodine and vitamin A stability, where appropriate. Triple-fortified salt was prepared by adding the encapsulated ingredients to salt at a ratio of approximately 1:150 to obtain target levels for the micronutrients in salt: vitamin A approximately 250 IU/g salt, iron 1,000 ppm, and iodine 50 ppm. The list of formulations used in the final trials is presented in **table 1**.

Packaging and storage

Samples of about 100 g of triple-fortified salt were packed in Ziploc polyethylene bags. Samples of triple-fortified salt were stored under three different conditions: ambient temperature and humidity ($\sim 22^\circ\text{C}$,

50%–70% relative humidity, light), high temperature and medium humidity (40°C and 60% relative humidity, dark), and high temperature and high humidity (40°C and 100% relative humidity, dark). The environmental chambers used did not allow us to control lighting. Because light contributes to vitamin A degradation, the observed stability may be higher than in samples exposed to light. This problem could be prevented in the field by distributing salt in cardboard or using another light barrier, as it is in North America. Storage in the dark was not expected to greatly affect the conclusions of a preliminary study.

The samples were analyzed for vitamin A content immediately after mixing and after storage. We deliberately used extreme conditions for testing the system to get a feel for the maximum loss that could be expected. We have published the results of field tests with double-fortified and triple-fortified salt samples that were put through the commercial salt distribution system in Kenya. The results indicate that the assumptions made in this work regarding the expected temperatures and humidities are valid [9]. The sampling times were dictated by our ability to complete analyses, and therefore samples were not pulled after exactly 30, 60, 90, and 120 days, as would be ideal.

Influence of binders used for granulation on vitamin A retention

Vitamin A palmitate beadlets from Watson Foods were granulated with and without iodine with different binders: mannitol, lactose, and calcium sulfate dihydrate. Hydroxypropyl methylcellulose (HPMC) and polyvinyl pyrrolidone (PVP) were used to enhance the binding. The granulated particles were encapsulated with approximately 40% soy stearine. The iron source used was microencapsulated ferrous fumarate prepared in pilot scale tests we performed at Glatt Air

TABLE 1. Vitamin A retention (%) in triple-fortified salt where different fillers were used for granulation—vitamin A encapsulated separately^a

Time (days)	Vitamin A retention (%)			
	Vitamin A granulated with mannitol and HPMC (I-1)	Vitamin A granulated with mannitol and PVP (II-1)	Vitamin A granulated with lactose and HPMC (III-1)	Vitamin A granulated with calcium sulfate dihydrate and HPMC (IV-1)
0	100	100	100	100
23	57.5	33.6	26.6	75
37	56	21.7	19.4	50
68	11	5.6	3.8	17.6
90	8	3.2	1.09	4.3

HPMC, hydroxypropyl methylcellulose; PVP, polyvinyl pyrrolidone

a. Source of iron: ferrous fumarate from Glatt Air Technique; source of iodine: potassium iodide from coating place. All types of granulations were coated in soy stearine (40%).

Techniques, Ramsey, NJ, USA. When vitamin A was granulated only with the binder without iodine, micro-encapsulated potassium iodide prepared in pilot-scale tests we performed at Coating Place, Madison, WI, USA, was used as the source of iodine. The salt was triple fortified at the target levels. Samples of triple-fortified salt were stored under conditions of high temperature and humidity. Samples were analyzed for vitamin A content immediately after mixing and four times during storage. Iodine content was determined once a month for a period of 3 months.

Vitamin A palmitate dissolved in oil

BASF Corporation supplied vitamin A palmitate oil stabilized with BHT (1.7 million IU/g), which is usually used for fortification of margarine and oils. Vitamin A palmitate dissolved in oil was introduced in the fat shell that protects the core containing potassium iodate and mannitol. The granules were coated with soy stearine in concentric layers: first a layer of soy stearine without vitamin A was applied, followed by another layer of soy stearine containing vitamin A, and finishing with another layer of soy stearine. Samples of triple-fortified salt made with the vitamin A and iodine premix and ferrous fumarate encapsulated at Glatt Air Techniques were stored at high humidity and temperature.

Analytical methods: Determination of vitamin A

Bags of salt were removed for analysis at three time intervals. The whole bag was subdivided with a two-necked funnel after remixing, with one of the streams representing half of the sample always rejected. A fluorometric method was used for vitamin A determination [10, 11] The method depends on excitation of the sample at 330 nm and measurement of retinol fluorescence at 480 nm. The intensity of the fluorescent emission was measured with a Perkin-Elmer Lumi-

nescence Spectrometer, LS 50B. To avoid exposure of vitamin A to light, the actinic glassware used in determination was covered with aluminum foil.

Since preliminary tests indicated no loss of iron and only small losses of iodine, the results for these micro-nutrients are not included in this article.

Results and discussion

Effects of iron and iodine compounds, temperature, and humidity on vitamin A stability

After 2 months of storage, the samples stored at ambient conditions and those stored at high temperature and moderate humidity were unchanged in color. All of the samples stored at high temperature and humidity changed color except the combinations in which FeNaEDTA was the iron source. The presence of the premix or premixes did not affect the caking of the salt, and the physical state of the salt had no effect on vitamin A retention. Adding an antislaking agent could resolve a caking problem in the field, but this was outside the scope of this study in any case.

Vitamin A retention for all combinations is presented in **table 2**. In 22 of 27 combinations, vitamin A retention under ambient conditions was higher than vitamin A retention at 40°C and 60% relative humidity or 40°C and 100% relative humidity, despite exposure to light under ambient conditions.

When all nutrients were encapsulated separately, the losses of vitamin A at high temperature and 60% relative humidity were 20% to 53% higher than the losses under ambient conditions, except for the combinations in which ferrous sulfate was used. When the active ingredients were encapsulated separately, the losses of vitamin A at 40°C and 100% relative humidity were 35% to 65% higher than under ambient conditions. This is not unexpected, since it is known from the

TABLE 2. Vitamin A retention (%) in triple-fortified salt where different fillers were used for granulation—vitamin A encapsulated with KIO₃^a

Time (days)	Vitamin A retention (%)			
	Vitamin A and KIO ₃ granulated with mannitol and HPMC (I-2)	Vitamin A and KIO ₃ granulated with mannitol and PVP (II-2)	Vitamin A and KIO ₃ granulated with lactose and HPMC (III-2)	Vitamin A and KIO ₃ granulated with calcium sulfate dihydrate and HPMC (IV-1)
0	100	100	100	100
17	61.8	61.9	26.5	64.8
38	37	27	11.6	53
65	7.65	5.9	0.6	12.7
91	1.4	0.69	0.3	3.26

KIO₃, potassium iodate; HPMC, hydroxypropyl methylcellulose; PVP, polyvinyl pyrrolidone

a. Source of iron: ferrous fumarate from Glatt Air Technique. All types of granulations were coated in soy stearine (40%).

literature [12] that the dominant degradation reaction for vitamin A ester is heat-induced formation of kitols, which follows a second-order rate law. The rate of reaction increases significantly with temperature. Losses are significant (> 10%/month) even at 1°C in vitamin A acetate protected by a gelatin coat [13].

In combinations in which vitamin A was granulated with potassium iodate or potassium iodide, vitamin A retention was better than in cases where the nutrients were encapsulated separately. The best vitamin A retention at 40°C and 100% relative humidity, for all iron compounds, was obtained when vitamin A palmitate was granulated together with iodide. This is somewhat unexpected, since both potassium iodide and vitamin A are reducing agents susceptible to oxidation, whereas potassium iodate is an oxidizing agent. Dextrin might improve the stability of potassium iodide [14].

Halverson and Hendrick [15] reported that vitamin A loss was greater when trace minerals ($\text{MnSO}_4 \cdot \text{H}_2\text{O}$, $\text{FeSO}_4 \cdot 7\text{H}_2\text{O}$, $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$, and $\text{CoSO}_4 \cdot 6\text{H}_2\text{O}$) were present. In a feed concentrate, a vitamin A loss of 5.7% occurred during 150 days of storage in the absence of minerals, whereas the loss was 34.4% in the presence of minerals. Other authors [12] suggested that the presence of minerals does not greatly affect vitamin A retention. They observed a vitamin A loss of 70% without minerals and 64% with minerals after 16 weeks of storage. Clearly, metals in reactive forms would increase vitamin A degradation at a rate that depends on other conditions, such as moisture and temperature.

When vitamin A samples granulated with different iron compounds were stored at high temperature and humidity, the vitamin A retention was less than when vitamin A was granulated alone. Therefore, vitamin A is destabilized by iron present in the premix particle. Moreover, the most soluble types of iron, ferrous sulfate and ferrous fumarate, almost entirely destroyed the vitamin A. Vitamin A retention was higher in combinations in which more stable iron compounds were used, such as electrolytic iron, ferrous gluconate, or FeNaEDTA. The best vitamin A retention at high temperature and humidity was obtained with FeNaEDTA. This can be explained by the fact that the EDTA group is a chelating agent that binds tightly to the iron.

When vitamin A was encapsulated together with iodine compounds, the best vitamin A retention was obtained in the presence of potassium iodate for all types of iron compounds and under all storage conditions. When vitamin A was encapsulated together with iron compounds, the best vitamin A retention was obtained for FeNaEDTA, for both potassium iodide and potassium iodate under all storage conditions. Consequently, commercially produced vitamin A palmitate was granulated together with potassium iodate and FeNaEDTA, and the granules were encapsulated with approximately 40% soy stearine. Salt was fortified with this premix and stored under three

different conditions. After 136 days of storage under ambient conditions, vitamin A retention was about 47%; at high temperature and 60% relative humidity, vitamin A retention was about 22%; and at 40°C and 100% relative humidity, vitamin A retention was only about 10%. By using FeNaEDTA as the iron source and potassium iodate as the iodine source, triple-fortified salt with barely adequate stability can be made with a single-component premix.

The salt did not discolor. The disadvantages of FeNaEDTA are its low iron content (about 15.2%), and high price.

Influence of binders used for granulation on vitamin A retention

Most commercially produced vitamin A products are fine powders. To increase the bulk size of the nutrient to the size of salt crystals, a granulation step is required. Another reason for the granulation step is to dilute the nutrient so that it is uniformly distributed in 10 g of salt. The properties of the binder, which comes in close contact with vitamin A, may influence vitamin A stability. Therefore, in selecting the binders, their abilities to retain water and their reactivity were considered. The first category of binders selected included mannitol and calcium sulfate dihydrate. These have a very low affinity for water and are used especially in combinations where moisture may be a problem. The second category includes lactose. Lactose is hygroscopic but has good stability and does not interact with the other components of the particle. It could be a suitable binder in particles that have adequate encapsulation. **Figure 1** depicts vitamin A retention in triple-fortified salt when vitamin A was granulated alone using the binders mentioned above. **Figure 2** presents vitamin A retention when vitamin A was granulated with potassium iodate, using the same binders as when encapsulated alone. Vitamin A degradation followed different degradation kinetics with each type of binder used in granulation. For the nonhygroscopic binders mannitol and calcium sulfate dihydrate, the destruction of vitamin A seems to be linear, whereas for lactose vitamin A destruction seems to follow a second-order rate law. Both mannitol and calcium sulfate dihydrate resulted in slightly higher vitamin A retention, and mannitol resulted in less salt discoloration.

Slightly less vitamin A was retained when it was granulated with potassium iodate than when it was granulated alone, but this difference was not statistically significant. An analysis of variance (ANOVA) with type of introduction of iodine, i.e., separate and together with vitamin A, and type of binder showed that the type of binder has a very significant effect on vitamin A retention ($P_{\max} = 99.9\%$), and by comparison the way that iodine is introduced into the system does not affect vitamin A retention ($P_{\max} < 75\%$).

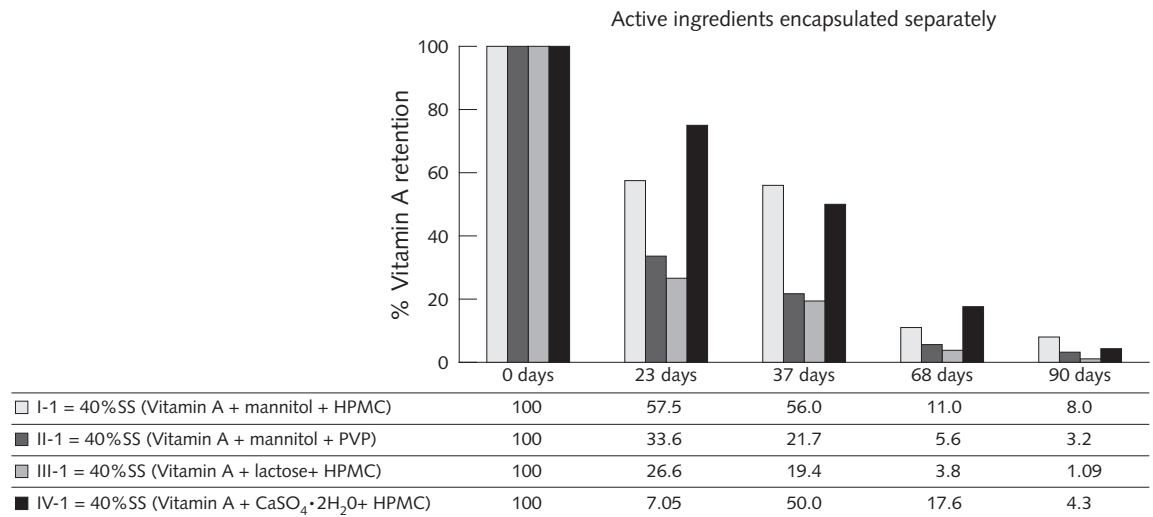


FIG. 1. Vitamin A retention (%) in triple-fortified salt where different fillers were used for granulation. Source of iron: ferrous fumarate from Glatt Air Technique; source of iodine: potassium iodide from Coating Place. KIO₃, potassium iodate; HPMC, hydroxypropyl methylcellulose; PVP, polyvinyl pyrrolidone; SS, soy stearine

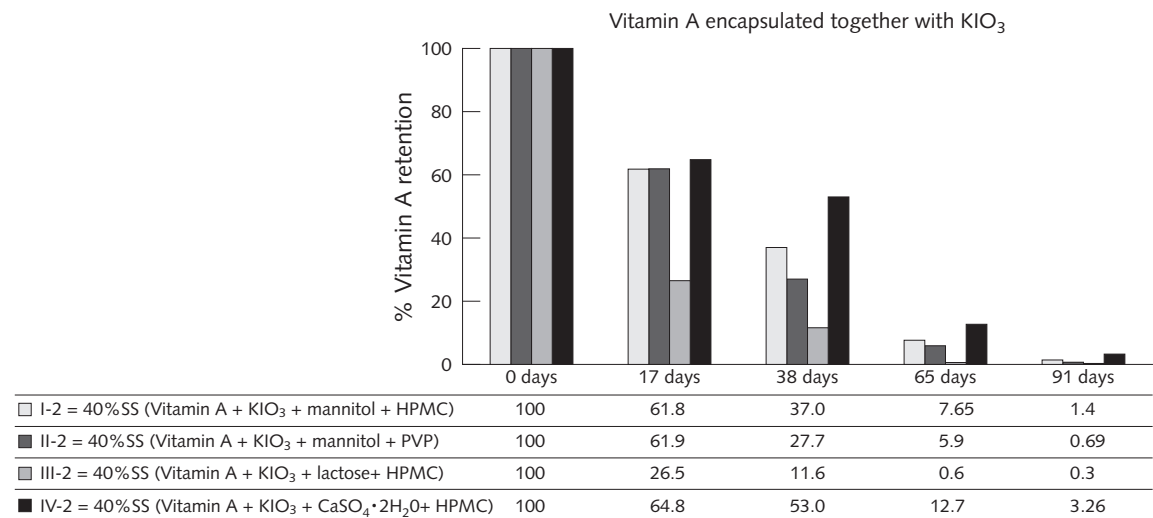


FIG. 2. Vitamin A retention (%) in triple-fortified salt where different fillers were used for granulation. Source of iron: ferrous fumarate from Glatt Air Technique. KIO₃, potassium iodate; HPMC, hydroxypropyl methylcellulose; PVP, polyvinyl pyrrolidone; SS, soy stearine

Spray-dried versus oil-dissolved vitamin A palmitate

Vitamin A retention in triple-fortified salt when vitamin A palmitate dissolved in oil was introduced into the fat shell that protected the potassium iodate–mannitol core was compared with vitamin A retention where vitamin A palmitate spray-dried was introduced into the core along with potassium iodate and mannitol. The vitamin A retention is presented in **figure 3**.

After 53 days of storage at 40°C and 100% relative humidity, the retention was 9.5% for vitamin A palmitate oil and 12% for spray-dried vitamin A palmitate.

The graph indicates that initially the vitamin A in the soy stearine degraded slower than the vitamin A in the core. Apparently the antioxidants (BHT+BHA) incorporated into soy stearine intercepted oxygen before it could react with the vitamin. After depletion of the antioxidant, the retinyl palmitate became vulnerable to oxidation. This explains why the vitamin A palmitate dissolved in oil degrades slowly at the beginning and more rapidly later. The fact that the vitamin A degraded more rapidly in the core than in the soy stearine is probably due to encapsulation imperfections. Water and trace minerals could get into the core through

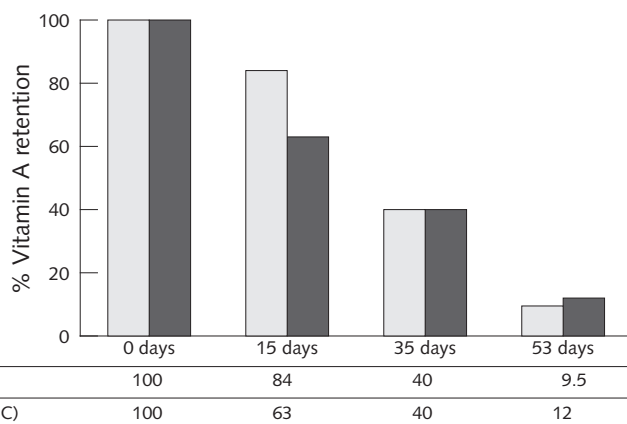


FIG. 3. Vitamin A palmitate spray-dried versus dissolved in oil in triple-fortified salt, under high temperature and humidity. Source of iron: ferrous fumarate, 1,000 ppm as Fe. KIO₃, potassium iodate; HPMC, hydroxypropyl methylcellulose; SS, soy stearine

the coat's cratering and attack vitamin A in the core, destroying it more easily than the vitamin A incorporated in the fat.

While bioavailability was not addressed in this work, using a digestible fat for encapsulation should have no effect on the bioavailability of the micronutrients. During cooking the micronutrients will be released, and will behave exactly as the added components: some vitamin A loss will occur during food preparation. Quantitation of this effect is beyond the scope of this work.

Conclusions

Under ambient conditions and 2 months of storage, we obtained the following vitamin A retention: 95% for triple-fortified salt made by two premixes, vitamin A palmitate + FeNaEDTA encapsulated together and potassium iodide (KI) encapsulated separately; and approximately 80% for vitamin A palmitate and potassium iodate (KIO₃) encapsulated together and separately encapsulated FeNaEDTA. At high temperature and humidity, vitamin A was rapidly destroyed. The best vitamin A retention (approximately 60%) after 2 months of storage at 40°C and 100% relative humidity was obtained in salt fortified with vitamin A palmitate granulated with potassium iodate and dextrin and coated with soy stearine, with FeNaEDTA used as the iron source. Premixes containing all three micronutrients in a single particle were less stable than premixes made with iodine and vitamin A in one particle and iron in a separate particle. The types of iron and iodine compounds used for fortification had a significant influence on vitamin A retention. We found that potassium iodate and ferric NaEDTA formed the most stable triple-fortified salt in terms of vitamin A retention.

The type of binder influences vitamin A retention, but the ultimate role in vitamin A stability is played by the quality of the coating. Nonhygroscopic fillers such as mannitol and calcium sulfate dihydrate gave better vitamin A retention than lactose. Spray-dried vitamin A palmitate was more stable than vitamin A palmitate dissolved in oil, but incorporating the vitamin A into the soy stearine provides reasonable vitamin A protection.

The best formulation retained 77.73 % of vitamin A after 2 months of storage at 40°C and 60% relative humidity. Considering that the time salt spends in distribution is typically 2 to 3 months, a substantial (9% to 50%) retention indicates that in an appropriately optimized system reasonable vitamin A retention of 75% or more should be achievable. With process and product optimization, which are beyond the scope of this preliminary survey, we expect to achieve even higher retention, resulting in the need for a smaller overage in a realistic system. Although there have been great increases in the average quality of salt, the effect of salt impurities must be investigated further. On the basis of our experience with double-fortified salt, this is not expected to be an insurmountable hurdle.

Commercial processing will require simple solid mixing equipment in the typical salt plant and central processing of the premix. Although the cost of the encapsulation system itself is only 1 to 3 US cents per kilogram of salt, the added cost of the micronutrient will have a large impact on the cost of the salt, unless the salt is subsidized from savings of current or contemplated supplementation methods.

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