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Double fortification of salt with folic acid and iodine

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ABSTRACT

Salt fortification is an effective strategy to reduce micronutrient deficiency in developing countries because salt is consumed universally and at constant levels irrespective of socioeconomic status. The demonstrated efficacy of salt iodization resulted in a major international program to achieve universal salt iodization. To address the widespread deficiency in folic acid, the objective of this research was to develop a stable formulation of salt fortified with both folic acid and iodine. The fortification process will use a single solution that will be sprayed onto salt using existing salt iodization equipment and infrastructure. Optimal salt formulations were prepared by spraying a pH 9 carbonate buffer solution containing 1%–3% (weight per volume) iodine, as potassium iodate, and 1%–2% (weight per volume) folic acid. After fortification, the optimal formulations prepared using refined salt, retained >80% of the folic acid and >90% of the iodine after 12 months of storage at ambient conditions.

1. Introduction

Two billion people in the developing world are directly affected by micronutrient malnutrition (WHO, 2007). The most extensive problems arise in developing countries where people consume micronutrient-poor cereal and tuber diets which do not provide a sufficient amount of iodine, iron, folic acid, vitamin A, or zinc (FAO, 2002). Food fortification is an ideal method for dealing with this issue as it is more quickly implemented, less costly, and requires less (if any) behavioral change from target populations than alternative methods (i.e. dietary diversification and supplementation). Salt is an ideal vehicle for fortification because its consumption is universal and stable throughout the seasons irrespective of economic status, it is centrally processed with established distribution channels, and is generally purchased as opposed to bartered (WHO, 2008). To combat micronutrient deficiency, salt iodization has been used since the 1920s (Adamson, 2004). Now over 70% of households in developing countries have access to iodized salt (Mannar, 2007). In conjunction with the most prevalently known iodine health issue, goitre (swelling of the thyroid gland), severe iodine deficiency also causes birth defects such as cretinism. This severe form of fetal neurological damage is characterized by mental retardation, stumped growth, and deaf mutism (National Academy of Sciences, 2001). Furthermore, iodine deficiency is the most common cause of mental impairment (Mina et al., 2011). Where iodine is sufficient, measured intelligence is increased by an average of 13 IQ points (Micronutrient Initiative, 2009).

Considering the success of salt iodization it is logical to add more micronutrients and therefore combat further deficiencies though salt fortification. One such micronutrient, folic acid, has been added to grain products (WHO, 2006). In 1998 it became mandatory in the United States to fortify grain products with folic acid which led to a 26% reduction in neural tube birth defects (WHO, 2006). These birth defects result from the improper development of the spinal cord and brain during early pregnancy. The two common neural tube birth defects are spina bifida (which causes lower body paralysis) and anencephaly (which usually leads to death within hours of birth) (FAO, 2002). Now more than 30 countries fortify their flour with folic acid (WHO, 2006).

Unfortunately the foods that have been fortified are not universally consumed and many people in developing countries are not benefiting. Therefore we aimed to engineer a novel formulation of fortified salt such that it contains both iodine and folic acid. The production of which is only to require the use of existing salt iodization equipment and infrastructure allowing for simple inexpensive implementation. Thus, allowing for the prevention of birth defects as well as other consequences derived from deficiencies in these micronutrients.

Both crude, coarse grained salt and more refined, fine grained salt are common in developing countries. Of the three major salt

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iodization technologies (dry mixing, drip feed addition and spray mixing), spray mixing is the only method suitable for both coarse and fine grained salts (Holman, 1958). Furthermore, it is simple to implement in both large scale and small local scale facilities (Mannar and Dunn, 1995). Spray mixing involves a solution of iodine being sprayed as a fine mist onto salt that is continually mixed. Potassium iodide (KI) and potassium iodate (KIO_3) are the most common forms of iodine used for salt iodization. KIO_3 is recommended for use where the salt is less refined and stored in warmer temperatures because KI is less stable (Holman, 1958). KI oxidizes to elemental iodine and is then quickly lost through sublimation under conditions of warm temperature, high moisture, in the presence of impurities, sunlight, and acidity. Therefore, our research explored the feasibility of incorporating folic acid into the existing spray mixing method of salt iodization using KIO_3.

The spray solution containing iodine and folic acid must maintain its micronutrients in a functional and solubilized form for at least 1 month. This duration was determined based on small scale plants processing iodized salt, which typically replenish their spray solution every 2–4 weeks. It must also contain 1%–5% weight per volume (w/v) iodine in accordance with current practice and at least 1%–3% w/v folic acid so as to make a significant nutritional contribution. The target fortification level for iodine is 200% of the recommended dietary allowance (RDA), or 30 ppm (Health Canada, 2010). For folic acid 25%–75% of the RDA should provide suitable nutritional improvement (10–30 ppm) (Health Canada, 2010). The salt must demonstrate acceptable retentions of micronutrients, 75%–90% over a 12 month storage period. Micronutrients are added at an overage to allow for this expected loss.

A few predominant challenges arise from the addition of folic acid to iodized salt production. Folic acid has poor solubility in water (0.16% w/v at 25 °C), is heat-labile, and photosensitive. Solubility is an important factor for ease of implementation and cost, as mixing would be required in order to maintain a well dispersed suspension. Significant losses of iodine have also been observed in a previous attempt on double fortification of salt, where a folic acid solution was sprayed onto iodized (KIO_3) salt (Li et al., 2011). This might have been due to low pH caused by the presence of folic acid. Iodate in acidic pH is more susceptible to degradation (by way of reduction) into elemental iodine and subsequent sublimation. In alkaline solution, the solubility of folic acid is greatly increased. It has been reported that the anionic form of folate dominates under these conditions, which improves its stability (Akhtar et al., 1999). Therefore, the use of an alkaline solution to solubilize and stabilize the micronutrients was investigated.

There are three primary inexpensive food-safe buffer formulations that have a pH range suitable for this study: citrate-phosphate (pH 3–8), phosphate (pH 6–8), and carbonate (pH 9–11) (FAO/WHO, 2016; Sigma-Aldrich, 2011). However, phosphate has been shown to decrease folic acid stability (O'Broin et al., 1975). Therefore carbonate buffer was selected at the lowest pH of its useful buffering range (pH 9) to minimize the impact on the salt. The stability of the spray solutions and fortified salt were monitored. Furthermore, the appearance and possible dosing issues due to grain size distribution within the salt were also investigated.

Ultimately, a novel formulation of fortified salt was engineered such that it contains both iodine (KIO_3) and folic acid. This fortified salt is to be prepared using existing spray mixing salt iodization equipment and infrastructure. Addition of only sodium carbonate, sodium bicarbonate, and folic acid to the existing spray solution will be required. This formulation will be easily implemented into salt fortification plants in the developing world, allowing folic acid fortification to reach populations that currently do not have access to sufficient folate.

2. Materials and methods

2.1. Materials

Folic acid (FA) was purchased from Bulk Pharmaceuticals Inc., Canada. Potassium iodate (KIO_3), sodium carbonate, and sodium bicarbonate were obtained from Sigma-Aldrich Chemicals, Canada. Refined Canadian salt (~400 μm diameter grain size) was purchased from Sifto Canada (Compass Minerals Canada Corp., Ontario, Canada). Two coarse salt samples from India were provided from the Micronutrient Initiative. The sample from Orissa, India, had a grain size of approximately 2–3 mm. The other sample was of coarse sea salt with a large range of crystal sizes (from <0.1 mm to >3 mm). All formulation components used in this study were food grade. Analytical chemicals including hydrochloric acid, sodium hydroxide, sodium nitrite, zinc granules, and potassium iodide were purchased from Caledon Laboratories Limited, Canada. The remaining chemicals: 3-aminophenol, sulfamic acid, sulfuric acid, sodium thiosulfate, and starch indicator were acquired from Alfa Aesar, Sigma-Aldrich, EMD, BDH, and LabChem Incorporated respectively. All chemicals used for analytical testing were ACS grade.

2.2. Spray solution preparation and storage

Spray solutions and control spray mixtures (solutions/suspensions) were prepared using reverse osmosis purified water. Spray solutions were prepared at pH 9 using a buffer composed of sodium carbonate and sodium bicarbonate, referred to as a carbonate buffer. Although potassium iodate is the form of iodine used for fortification, the content of iodine in all samples is reported on an iodine (I) basis.

The first set of spray solutions were prepared with 0.35% w/v of each micronutrient so as to allow the buffering capacity of a 0.1 M carbonate buffer solution (60% v/v 0.1 M sodium carbonate, 40% v/v 0.1 M sodium bicarbonate) to counteract the shift in pH that would be caused by the addition of folic acid. Also, three varieties of control spray mixtures were prepared: 0.35% w/v folic acid, 0.35% w/v iodine, and 0.35% w/v of both micronutrients. The preparation of solutions containing lower concentrations of iodine than is used in current practice while maintaining a concentration of carbonate expected to be useful in the final formulations was done so as to more clearly evaluate the impact of carbonate itself on the stability of iodine and folic acid. Control spray mixtures and spray solutions were stored in dark ambient conditions (approximately 25 °C) and tested for micronutrient stability for four months.

To adhere to current salt fortification procedures, spray solution concentrations were increased. In order to not influence pH, three component buffering solutions composed of folic acid at 1% w/v, 2% w/v, 3% w/v and varying volumetric ratios of 0.1 M or 0.2 M sodium carbonate and sodium bicarbonate were used to attain pH 9 solutions (see Table 1). Solutions of 2%–3% w/v folic acid in a 0.1 M carbonate buffer solution were not able to attain pH 9 due to the acidity of folic acid. Therefore, these solutions were not considered

Table 1
Ratio of carbonate to bicarbonate required for pH 9 solution.

Folic acid (% w/v)	Carbonate/bicarbonate molarity	Carbonate solution (% volume)	Bicarbonate solution (% volume)
1	0.1	80	20
2	0.1	Did not reach pH 9	Did not reach pH 9
3	0.1	Did not reach pH 9	Did not reach pH 9
1	0.2	50	50
2	0.2	80	20
3	0.2	100[a]	0[a]

[a] Did not reach pH 9, however was close at pH 8.84.