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A Pinch of Salt: Fortification with Iodine and Iron

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Introduction

The proper growth and development of all organisms, including humans, requires a complex dietary intake of nutrients. These nutrients act as cofactors, building blocks, and metabolites in biological systems and play essential roles in many biological pathways. To further compound the matter, not only must these nutrients be available in the diet of organisms but they must also be in a bioavailable form. Merriam-Webster defines bioavailability as the degree or rate of uptake of a substance into an organism or the degree and rate at which it is made available at the site of physiological activity. What this means in simplified terms is that a nutrient must be both present in the diet and in a form that is biologically compatible for integration into the organism consuming the nutrient.

Among the more common issues in underdeveloped and developing countries are nutrient deficiencies in the dietary intake. Underdeveloped and developing regions are often characterized by the decreased availability and bioavailability of nutrients, which translates into dietary deficiencies and adverse health conditions. These adverse health conditions, in turn, generate a decreased social health that hampers the development of the countries - creating a complex handicap for the culture based on dietary inadequacies. In an effort to combat this issue, science has been researching the effectiveness of fortification programs for nutrient supplementation.

Many issues must be considered when designing a method of nutrient fortification if a robust and effective supplementation program is to be achieved. To develop a program that is both ethically and economically acceptable, the social and economic structure of the population must be considered. The choice of vector must be able to coincide with the social and economic concerns and most importantly, the product must have an adequate nutritional value. With these parameters in mind, the fortification of salt has been emerging as a successful forerunner in the battle to eradicate nutrient deficiencies.

Socio-Economic Issues Surrounding Nutrient Supplementation

Climate and resources can define each region of the globe. As a result of these characteristics, and the specific population density of the region, complex socio-economic issues arise that generate constraints for nutrient supplementation programs. Unfortunately, the generation of programs tailored to the constraints of each individual region does not represent a feasible approach to nutrient supplementation from both a functional and economic viewpoint. To compensate for this, a robust supplementation program must be designed that can be tailored to the needs of the three general global constraints: diet, resources, and accessibility.

Dietary needs are dependent on the region that supports a population. Many regions of the world have insufficient availability or bioavailability of nutrients in the environment, leading to deficiencies in dietary intake. Human culture often exceeds the carrying capacity of the environment and this creates additional environmental stresses, which translate into decreased nutrient availability per capita. This necessitates a flexible fortification program that can include levels of dietary nutrients that are beneficial to the population, neither exceeding nor falling below what is required for normal biological development. The dietary constraints further extend to the aesthetic characteristics of the product as well. The supplementation must be bioavailable yet not discolour the food or alter food flavour and odour. If the population chooses not to consume the supplement due to aesthetic issues, a properly engineered product will still fail. It is just

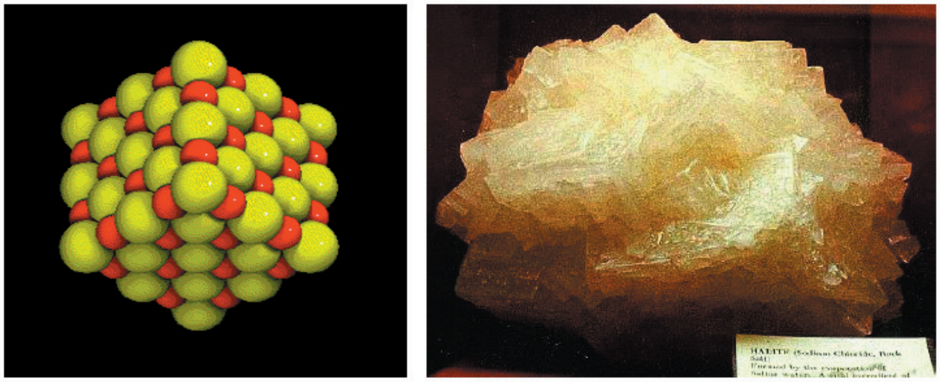


Figure 1 The crystal-packing lattice of NaCl and the appearance of Halite

as important to design a product that the population will be comfortable consuming as one that effectively meets dietary needs.

Resources play a critical role in dietary issues primarily due to their economic impacts. The availability of infrastructure to support a population is instrumental in the development of a region but, in many cases, the more prominent dietary deficiencies occur in underdeveloped or developing countries. The economic feasibility of supplementation programs is a hefty component this topic. Often, regions cannot support a local production facility for a fortification program. This can be due to insufficient raw material availability, insufficient capital to invest and maintain the industry, or a lack of resources to distribute the product. Even if these economic difficulties are addressed, many regions of the globe lack adequate storage facilities for most food reserves. A major handicap to diet is the lack of refrigeration in many regions, which means that items do not have adequate shelf lives due to degradation and decomposition. This requires an initiative to design fortified products that are stable under high temperature or humidity conditions. Such fortified products would have long shelf lives to ensure a positive return on the investments in nutrient supplementation programs.

Product accessibility is the third constraint of nutrient supplementation programs. A successful supplementation program necessitates uniform availability and consumption of the product to all segments of the population. The nutrients must be accessible and distributed to the general public on a regular, consistent, and uniform basis regardless of social status. The product must also be in a form that is effectively incorporated into standard diets on a regular basis without adverse effects. Based on these criteria, the fortification of salt has been a promising avenue for scientific research into combating dietary nutrient deficiencies.

Salt

Salts are ionic crystalline molecules that display a diverse array of speciation and packing matrices. The most simplified forms of salts are the elemental salts like sodium chloride (common table salt) which are formed by the ionic bonding of a cation and anion in equal ratios. This face-centered cubic lattice can be obtained through mining of rock salt called halite or by evapoconcentration from soluble salt reservoirs (Figure 1). Sodium chloride is a ubiquitous component of homeostasis in biological systems and also finds many applications in both industry and society. For this reason, salt has become an integral part of not only daily life, but also the fabric of the many different human societies.

Sodium chloride has a critical role in homeostasis primarily as an electrolyte that balances the osmotic pressure of cells and drives many electrochemical potentials such as neuronal signaling. The importance of this role is emphasized by the wealth of references to salt in human culture. In Roman times, many wages were paid partially in supplies of salt and this carries through even in current culture. An individual may be described as “worth 'his' salt" or it may be suggested to take events “with a pinch of salt”. These examples clearly illustrate the value of salt to, and the intrinsic place it has taken in, human culture.

Human culture not only uses salt for biological purposes, but also in both daily and industrial applications. Many of the common aspects of society rely on the properties and availability of salt. As society becomes more industrialized, the daily applications often become industrial ones. Salt is used as a food preservative and flavour, for curing hides, and for the dying of textiles. These are daily applications that can be performed by individuals but are now being done more often on an industrial scale, to provide a service to a growing population. Other, more industrial, applications of salt are: use in control of ice formation, the optimization of smelting and metallurgy purification, and water softening treatments. Salt occupies a piv-

Figure 2 Goiter formation associated with Iodine Deficiency Disorders

otal position in not only the homeostasis of biological systems but also in the homeostasis of industrialized society as a global organism.

As described above, salt is easily refined and purified by several techniques, and is a global commodity. In addition to this, the energetics of the sodium chloride crystal lattice, or packing matrix, make salt stable for long periods of time even in humid conditions. These properties of sodium chloride, in addition being biologically ubiquitous, make salt an appealing vector for nutrient supplementation. Scientists have been experimenting with the nutrient supplementation of salt since the early 1900s. Initial studies concentrated on supplementation of salt with a single nutrient, such as iodine. More recently, technological advances have focused research on the introduction of multiple nutrients within salt, such as iodine and iron.

Iodine

Iodine is a nutrient required for the proper functioning of the thyroid, a gland located at the base of the neck. The thyroid gland is responsible for the biogenesis of hormones and these hormones are in turn responsible for regulating many key biological pathways by stimulating cellular activity. Unfortunately, environmental levels of iodine can vary drastically between different environments and habitats. Iodine is found in both water and soil but the bioavailability of soil-bound iodine is relatively poor. As a result, geographical regions that have low soil-bound iodine levels often yield nutrient deficient crops. This translates into dietary iodine deficiencies for the population within these regions. To correct this deficiency, a research group led by David Marine supported by the Michigan State Medical Society launched a prevention program for iodine deficiency disorders (IDD) using iodized salt in 1924.

The effects of iodine deficiency disorders (IDD) can range from simple physiological manifestations to severe developmental disorders. Iodine is critical for the biosynthesis of thyroid hormones and these hormones are required for the coordinated stimulation of cells. Iodine deficiencies resulting in thyroid diseases are typically characterized by an endemic swelling of the thyroid soft tissues (Figure 2) but other, more prominent, developmental symptoms can arise from lack of dietary iodine. Research from the supplementation studies by the Marine group identified IDD as the cause of not only goiters but also that iodine deficiency resulted in a 10-15% reduction in a population's IQ capability, mental retardation and cretinism. Development of the central nervous system for normal intellectual functioning depends on an adequate supply of thyroid hormones, which require iodine for biosynthesis. In addition to goiter formation and mental retardation, developmental issues associated with IDD can include lethargy, physical disabilities, stillbirths, and neonatal deaths. Supplementation of salt with iodine successfully decreases the adverse effects induced by IDD and prevention programs using iodized salt are now globally accepted.

Supplementation programs must be robust so that they are effective under the range of environmental conditions encountered globally. Two primary approaches are used for iodine supplementation depending on environmental conditions. The most common form of iodine supplementation is the use of potassium iodide (KI). This is a relatively stable salt complex that is inexpensive to produce and easily dissolves for bioavailability in the digestive system. Unfortunately, KI becomes unstable and readily degrades to release elemental, non-bioavailable iodine (I_2) in regions of high temperature and humidity. Another formulation used to combat iodine deficiencies is potassium iodate (KIO_3).

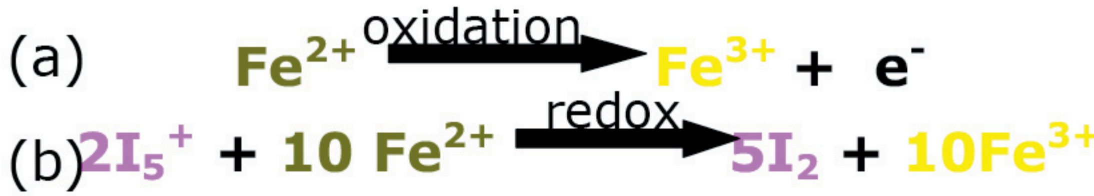


Figure 3 Redox reactions associated with iron bioavailability

This supplement is slightly more costly to produce than KI but exhibits a similar bioavailability profile. The benefit of using KIO3 is an increased stability over KI under humid conditions, resulting in a longer product shelf life. The use of these two approaches, by the three main producers of iodized salt, has been implemented to design robust and efficient iodine supplementation programs. Education programs implemented by organizations such as the World Health Organization (WHO) have stimulated many underdeveloped and developing countries in the world to enacted legislation making the use of iodized salt a legal requirement. These programs have made iodized salt available to the general population, regardless of the socio-economic factors, and have effectively eradicated iodine deficiency disorders in the global population.

Iron

Another essential nutrient for growth and development is iron. Iron deficiency anemia (IDA) affects approximately two billion people worldwide. This disorder, more prominent in women and young children, is common in underdeveloped and developing regions due to stresses placed on the carrying capacity of the environment resulting in dietary deficiencies of iron. This results in a significantly decreased work capacity that in turn generates more stress on the population and further hampers the development of the region. Health organizations have prompted the investigation of iron fortification of salt in an effort to resolve some of the concerns associated with iron deficiencies in the developing worlds.

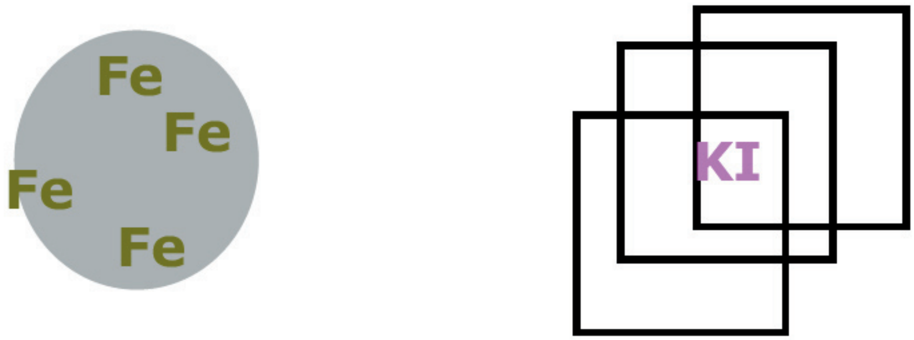
The primary effect of iron deficiency is decreased oxygen tension and transport within the body. Iron is a critical cofactor in the function of hemoglobin, acting as a redox cofactor to allow the covalent ligand docking of oxygen and carbon dioxide for gas transport from the lungs to the tissues and vice versa.

Decreased levels of dietary iron can lead to anemia, which results in the decreased transport of oxygen and carbon dioxide and leads to a lack of cellular respiration. This can generate reduced work capacity due to increased fermentative respiration and a depletion of cellular energy reserves; this lack of energy is manifested in decreased work capacity of muscles. Severe cases of anemia develop into tissue hypoxia and necrosis due to lack of cellular respiration. This can lead to adverse birth outcomes such as fetal mortality, low birth-weight, pre-term births, and maternal mortality. Approximately 20% of maternal mortality during birth can be attributed to IDA. IDA also causes decreased thermal regulation and an impaired ability to maintain body temperature in cold conditions due to a decrease in the secretion of thyroid-stimulating hormone and thyroid hormone.

In addition to its role in cellular respiration, iron is an important cofactor in other cellular functions. Numerous enzymes and cellular functions are iron-dependent and both a lack and an excess of iron can result in unbalanced homeostatic function. Neuropsychological disturbances such as developmental delay, behavioural disturbances, and attention deficits have been associated as characterizations of iron deficiencies. The proper development and signaling of cells is a complex process that involves iron. Also, iron deficiencies have been correlated with reduced disease resistance. Iron plays a role in the cell-mediated immune response against pathogens and many microorganisms deplete cellular iron levels as a common tactic to gain an advantage over the immune system.

The homeostatic process is also severely hampered by low iron levels and a decrease in bioavailable iron reserves has been associated with increased heavy metal absorption and hormone biosynthesis, as previously mentioned. Iron deficiency is compensated for by increased gastrointestinal iron uptake. The uptake mechanism for iron is not highly selective and also results in uptake of toxic heavy metals such as lead, cobalt, and cadmium. The success of the iodized salt initiative has prompted much research into combining both iodine and iron into a salt supplement. However, this endeavour has been problematic due to the redox potential and reactivity of iron.

The bioavailability of iron is a complex issue. Iron has a reactive redox potential and can occupy two valency states. These states are the reduced ferrous ($Fe2+$) and the oxidized ferric ($Fe3+$) (Figure 3a). Ferrous iron is significantly more bioavailable than ferric and is a preferable iron supplement not only for this reason but also because ferric iron has a more prom-



Chelation
(Sodium hexametaphosphate)

Encapsulation
(dextrin [dextrose])

Figure 4 Methods to physically inhibit iodine and iron interactions

inent colour and odour. To maintain product quality in conjunction with the dietary constraints outlined in previous paragraphs, product quality of both ferrous fumarate and sulfate compounds was investigated. Results indicated that ferrous fumarate generated a more pleasing odour than ferrous sulfate making it the iron compound of choice.

Alkaline and oxidizing impurities such as air, humidity, MgCl, and MgSO4 readily convert ferrous iron to the ferric form resulting in unpleasant discolouration and odour of the product. In addition to these impurities, iodine readily reacts with iron evolving into elemental iodine (I2) and generating a non-bioavailable ferric iron product (Figure 3b). To prevent this redox reaction, stabilizers must be used in the formulation. These stabilizers also must not produce undesired colouration or flavouring of the product.

Research into stabilizers has driven insight into multiple methods of fortifying salt with both iodine and iron without inducing loss of nutrient bioavailability. Prolonged storage of the standard dually fortified salt encounters two main problems. Interactions between the two nutrients result in a decreased availability of iodine and a decreased bioavailability of iron (see Figure 3). This is a result of the redox potential of iron, salt moisture and impurity content, relative humidity and temperature. The chemical properties of iron cannot be altered, but to circumvent this issue, stabilizers can be added to the salt product to reduce unwanted side reactions. The most effective approaches to solving this problem have been the use of physical barriers to prevent iron interactions with salt components and the environmental conditions (Figure 4).

These physical barriers have been proven to be effective at preventing the interaction of the iron and iodine supplements. A sodium hexametaphosphate (SHMP) capsule can be employed as an iron chelator that occupies the valence potential of the iron preventing redox reactions. A dextrin or gelatin coating can be used to encapsulate the iodine nutrient inhibiting interactions with iron. For both methods, ingestion and digestion liberates the nutrients for uptake within the digestive system providing bioavailable nutrient supplementation. Gelatin microencapsulation yielded an unacceptable sticky product while SHMP chelating of iron retained a shelf life of approximately three months. Dextrin microencapsulation products retained a shelf life of at least one year and generated the most promising formulation of a salt fortified with both iodine and iron.

Conclusion

Nutrient deficiencies pose a serious threat to the development of a global community. However, nutrient supplementation is a realistic and successful means of dietary regulation. The engineering of adequate supplementation programs can address socio-economic issues surrounding nutrient deficiencies. Dietary fortification of salt with nutrients has been shown to be an effective means of overcoming these issues when coupled with scientific advances in nutrient fortification technology.

Salt iodification, and the dual fortification of salt with iodine and iron using chelating and microencapsulating processes are pioneering the field of nutritional supplementation. Results of these applications indicate that both iodine and iron can be maintained in a stable, bioavailable state for dietary supplementation. The diversification of the research field is also actively generating relatively robust alternatives that provide an opportunity to tailor products to better suit various environmental conditions. Salt fortified dietary supplementation represents a feasible means of combating the nutrient deficiencies encountered in the varied ecosystems colonized by human societies. These salt products could be readily available but will only be successful in combating dietary nutrient deficiencies if governments, health agencies, and industry combine their resources and work together.

References

(1) http://www.chem-eng.toronto.edu/~diosady/sltdbl.html

(2) http://dieoff.org/page110.htm

(3) http://www.emporia.edu/earthsci/museum/salt.jpg

(4) http://www.idrc.ca/books/reports/1992

(5) http://www.idrc.ca/nayudamma/malnusalt_e.html

(6) http://images.google.ca/imgres?imgurl=www.domsalt.co.nz/images/refinery.jpg&imgrefurl=http://www.domsalt.co.nz/profile.html&h=210&w=160&prev=/images%3Fq%3Dsalt%2Brefinery%26svnum%3D10%26hl%3Den%26lr%3D%26ie%3DUTF-8%26oe%3DUTF-8

(7) http://www.saltinstitute.org/37.html

(8) http://www.sph.emory.edu/PAMM/iron.htm

(9) http://www.unu.edu/unupress/food/8F151e/8F151E06.htm6/17-01e.html

(10) http://www.m-w.com/home.htm

All sites were available as of 24 February 2003