

**Review Article****Fortification: A key role in Micronutrient Deficiency****Anitha Nandagopal\*, Syeda Maryam Danisha***Department of Pharmacology, Sultan-ul-Uloom College of Pharmacy, Road no.3, Banjara Hills, Hyderabad-500 034, Telangana, India.*<https://doi.org/10.31024/ajpp.2018.4.2.3>

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**Abstract**

Micronutrients are an essential component of a healthy diet and are indispensable to the normal growth, development and wellbeing of a human being. Micronutrient deficiencies, also known as 'Hidden hungers' currently affect more than 2 billion people worldwide, resulting in poor growth, impaired physical and mental development and increased rate of morbidity and mortality, thus having a long term effect on the progress of societies and nations. Food fortification, which involves adding micronutrients to food, is an effective method to combat this epidemic. Numerous studies have demonstrated the effectiveness and feasibility of such interventions and their potential to improve a populations' nutritional status. This article reviews the prevalence of micronutrient deficiencies with focus on Vitamin A, iron, iodine and folate deficiencies, fortification processes and successful examples of fortification interventions.

**Keywords:** Fortification, micronutrients, malnutrition, micronutrient deficiencies

**Introduction**

Micronutrients are the components that are present in small quantities in food and include various vitamins and minerals. They are an essential component of a healthy diet. Although required in minute quantities by the human body, they are indispensable to the normal growth and development, including physical and mental health and wellbeing of human populations (Hunter, 2011).

Micronutrient deficiencies currently affect about more than 2 billion people worldwide, (Allen et al., 2006) and are especially common among children and women of low and middle income countries. They result in perinatal complications, poor growth, impaired physical and mental development and increased rate of morbidity and mortality, all of which impair the economic development and productivity of countries affected (UNICEF, 2013).

Since micronutrient deficiencies are mostly prevalent among populations belonging to low and middle income countries, an economically feasible solution with high cost – benefit ratio is to be implemented in order to effectively combat this epidemic.

Food fortification, which involves adding micronutrients to food, is one such effective method.

**Food fortification**

According to WHO, Fortification is the practice of deliberately increasing the content of an essential micronutrient, i.e. vitamins and minerals (including trace elements) in a food, so as to improve the nutritional quality of the food supply and provide a public health benefit with minimal risk to health (Allen et al., 2006). The Codex General Principles for the Addition of Essential Nutrients to Foods defines "Fortification", as "the addition of one or more essential nutrients to a food whether or not it is normally contained in the food, for the purpose of preventing or correcting a demonstrated deficiency of one or more nutrients in the population or specific population groups" (Codex Alimentarius, 1994).

The first ever mention of what today is called food fortification was by a Persian physician Melampus in 400 BC who suggested addition of iron fillings to wine to increase soldiers' potency and strengthen their resistance to spears and arrows (Mejia, 1994; Darnton-Hill, 1998).

In 1831 the French physician Boussingault urged adding iodine to salt to prevent goitre (Mejia, 1994). During 1921, from American Medical Association (AMA) convention, two Ohio doctors presented findings from their clinical trial demonstrating the effectiveness of sodium iodide treatments for the prevention of goitre in Akron school girls.

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After the publication of this study, Michigan was the first state to introduce iodised salt. An extensive educational campaign resulted in increased consumer awareness and demand for iodised salt increased so much that by 1924 iodised salt became widespread (Bishai and Nalubola, 2002).

Around the same time Switzerland also introduced iodised salt (Hess et al., 2001). Between the First and Second World Wars (1924-1944) widespread fortification was established as a measure either to correct or prevent nutritional deficiencies in populations or to restore nutrients lost during food processing. Thus, during this period the process of adding of iodine to salt, vitamins A and D to margarine, vitamin D to milk, and vitamins B1, B2, niacin, and iron to flours and bread was established by various industrialized countries (Mejia, 1994).

Food fortification is one of the three main approaches to address micronutrient deficiencies (Venkatesh Mannar, 2003). It has been identified by the World Bank as one of the most cost effective micronutrient interventions. (World Bank, 1993) .It involves addition of nutrients during production stage to the staple foods consumed by the target population in order to reduce the nutrient deficiency in the population. This process provides nutritional benefit to the population without them having to change their dietary habits or purchasing patterns, thus making it more effective than the other interventions to deal with micronutrient deficiencies like micronutrient supplementation dietary diversity etc., (WHO, 1999).

### **Micronutrients**

Micronutrients, that include vitamins and minerals, are called so because they are required in minute quantities by the body. However, they are indispensable to the overall health and wellbeing of human beings as they are essential components of various hormones, enzymes and have an important role in life processes.

### **Types of micronutrients**

**Vitamins:** Vitamins are organic compounds that are essential to sustain life and prevent diseases. They have a wide range of biochemical functions in the body; they act as regulators of processes like mineral metabolism, cell and tissue growth and differentiation (Bender, 2003), while others function as antioxidants and cofactors or precursors of various enzymes (Bolander, 2006).

**Minerals:** Minerals are substances of chemical origin that are required by the body as nutrients. Minerals are not produced in the body and thus need to be obtained from diet. They are essential in performing various functions like forming blood, growth and maintenance of bones, transmission of nerve impulses etc. (Kraemer et al., 2011).

### **Micronutrient deficiencies**

Micronutrients are essential for maintenance of optimum health

and nutrition. They have a significant role in advancement of physical and intellectual health of human populations and thus have a long term effect on the progress of societies and nations. Of all the micronutrients, Vitamin A, iron, iodine, folate and zinc are critical as nearly one third of the world's population is deficient in them (Maberly, 1994).

Despite the growing awareness of the importance of micronutrients in maintaining health, micronutrient deficiency remains widely prevalent. About 1.1 million children under the age of five die every year as a result of vitamin A and zinc deficiencies alone. Every year, 115,000 women die during pregnancy due to iron-deficiency anaemia, which also accounts annually for approximately 600,000 stillbirths and deaths of babies within the first week of life. Each year, 18 million babies are born with a mental impairment due to maternal iodine and iron deficiency during pregnancy, while 150,000 babies are born with neural tube defects resulting from an inadequate intake of folate by their mothers before and during pregnancy. Vitamin A deficiency causes a staggering 350,000 children to become blind every year (Kraemer et al., 2011).

### **Causes**

Micronutrient deficiencies are a form of malnutrition. When compared to micronutrient deficiencies, other forms of malnutrition are easily visible, thus micronutrient deficiencies are also known as the 'hidden hungers'. They occur due to insufficient intake or sufficient intake combined with impaired absorption of nutrients due to diseases, infections etc. Infant deficiencies are as a result of maternal micronutrient deficiencies. The factors responsible for micronutrient deficiencies include.

1. Basic causes: Sociocultural, economic and political instability.
2. Underlying causes: Food insecurity, poor/negligent feeding practices. Unhealthy environment and lack of health services.
3. Immediate cause: Inadequate dietary intake and disease state.

The root of micronutrient deficiencies seems to be poverty. However, micronutrient deficiencies are not confined to developing and low income nations; it exists in developing nations also. While the poor populations suffer from deficiencies irrespective of where they live, micronutrient deficiencies occur in developed nations due to the lack of education and poor dietary choices made by people (Allen et al., 2006). The following micronutrients are significant because of their utmost importance in the physical and mental development of human beings, and as well as due to the large number of people afflicted by their deficiencies.

**Vitamin A:** The most widely occurring vitamin A deficiency problems are related to the eye. Xerophthalmia, night blindness, conjunctival xerosis, Bitot's spot, corneal xerosis. Vitamin A deficiency blindness is the most preventable cause of blindness worldwide. Xerophthalmia and vitamin A deficiency is associated with increased mortality and severe morbidity due to respiratory and GI diseases (WHO, 2009). WHO estimates that about 250-500 million children are blind due to vitamin A deficiency and half of these children will die within an year of vision loss (Bailey et al., 2015).

**Iron:** Iron deficiency is the most common micronutrient deficiency, effecting about 30% of the world's population (Ahad et al., 2010). It is severely manifested among young children and women- especially accounting for monthly menstrual losses, increased demand during pregnancy and losses during child birth. Anaemia occurs as a result of decreased capacity of haemoglobin to carry oxygen due reduced amounts of iron available to the body. In extreme cases anaemia may lead to tissue hypoxia and heart failure leading to death in young children and pregnant women. Anaemia aggravated by haemorrhage and sepsis is the leading cause of maternal deaths worldwide. Anaemia in less severe stages markedly reduces the physical capability and performance of adults, decreasing their productivity. Other consequences of iron deficiency include neurophysical disturbances, impaired immunity etc., (WHO, 2009).

**Iodine:** Iodine is present in the body in minute amounts mainly in thyroid gland where it has a role in the synthesis of thyroid hormones. It is a vital micronutrient required at all stages of life. Mental retardation caused by iodine deficiency is the most preventable cognitive impairment. During pregnancy and lactation, the average requirement of iodine nearly doubles. Iodine deficiency during pregnancy causes spontaneous abortions, still births, congenital anomalies etc. Infants born to iodine deficient mothers may develop endemic cretinism. Iodine deficiency in children results in slow or retarded physical and mental development, low IQ levels and impaired performance. Adults with iodine deficiency are characterised by apathy, reduced mental functioning, lack of physical energy and reduced work output, all contributing to poor quality of life. Iodine deficiency represents a significant threat to social and economic development of nations.

**Folate:** Folate is the synthetic form of Vitamin B9. It is involved in synthesis of nucleotides and thus has an important role in cell multiplication and tissue growth. Folate deficiency causes megaloblastic or macrocytic anaemia and increases the likelihood for pregnancies affected by neural tube defects. The global prevalence of anaemia secondary to folate deficiency is very low. Folate deficiency in pregnancy has also been associated

with low birth weight, preterm delivery and foetal growth retardation. Globally, only about 30% of women take folic acid supplements prior to conception (Allen et al., 2006).

#### **Types of food fortification programmes**

**Mass fortification:** It refers to the addition of one or more micronutrients to the food that is consumed by majority of the population, such as cereals, condiments etc., that is introduced, mandated and regulated by the government. Mass fortification is usually the best strategy to deal with widespread micronutrient deficiencies in majority of the population.

**Targeted fortification:** In this, foods consumed by the specific target population are fortified as opposed to the entire population. This includes foods targeted towards children and pregnant women.

**Market-driven fortification:** In this, manufacturers take a business oriented initiative and decide to add micronutrients to processed foods. This is voluntary but must be done within government set limits.

**Other types of fortifications:** Newer approaches towards food fortification include house-hold fortification that includes addition of micronutrients to food using micronutrient tablets, powders, spreads etc., and bio fortification that is the breeding of staple foods to either increase quantity or absorption of nutrients (Allen et al., 2006).

#### **Development of a food fortification programme**

A significant public health risk due to a micronutrient deficiency must be established using appropriate criterion, prior to introduction of a food fortification programme.

#### **Selection of appropriate food vehicle**

The success of a food fortification program depends upon selection of a suitable vehicle for fortification. Usually foods having the following characteristics are suitable for fortification-

- Consumed by a relatively large proportion of population and specifically by the target population.
- Consumed regularly in relatively consistent amounts.
- Centrally processed foods are generally preferred so that quality control procedures are effectively implemented.
- The stability and bioavailability of added micronutrients must not change under standard storage and usage conditions.

- The process of fortification should be economically feasible and should not affect the cost of the food.
- Consumption patterns of particular foods are required to be studied before deciding a vehicle for fortification. Also the knowledge of consumption levels is necessary to determine the amount of fortificant that can be added safely to the vehicle.
- Marketing and distribution patterns of the vehicle must be known so that the fortified food can reach the population uniformly.

#### **Selection of suitable fortificant**

The following are the major considerations while selecting a suitable form of micronutrient to be fortified.

- The fortificant must not cause any alterations to the organoleptic properties of the food. It should not separate out or cause any other stability problems that may decrease the consumer acceptability of the product.
- The probability of any potential interactions between the fortificant and any other micronutrient either present or added that may interfere with its absorption or may adversely affect its stability must be considered prior to designing a fortification programme.
- The cost of fortification must not affect the cost of the fortified vehicle.
- The bioavailability of the micronutrient obtained from the fortified food must be optimum enough to improve its levels in the target population.

#### **Determination of suitable form and quantity of fortificant**

After identifying the risk of a micronutrient deficiency and selection of a vehicle, a suitable form of fortificant must be selected mainly based on the cost, bioavailability and least potential of interactions or sensory changes.

The amount of fortificant to be added must be determined based on the level of daily consumption of the vehicle by target population to be sufficient for optimum absorption. The fortification should provide adequate levels of the micronutrient without any risk of overdose upon excessive intake.

#### **Developing a quality assurance system**

A good quality assurance system helps to maintain constant levels of fortification with minimal extra cost. Adequate technical expertise is to be developed and adequate testing under a range of real field conditions must be done.

#### **Monitoring and evaluating fortification programme**

Any fortification programme has limited success without the support of the government. Legislations should not be restrictive, rather should facilitate and ensure that fortification while maintaining an open market with minimal cost increase to the consumer. Fortification programmes should be constantly monitored to ensure that the target populations are receiving

adequate amounts of fortified foods. They must be evaluated periodically to track the progress and benefits of the intervention. Periodic evaluations help to design appropriate interventions or changes to be implemented to ensure success of the programme (Allen et al., 2006; WHO, 2009; De Benoist et al., 2008).

#### **Food fortification- successful examples**

##### **Salt Iodization**

The greatest story of progress in food fortification has been that of salt iodization, demonstrating how well government commitment, market opportunity and social responsibility can be combined for improved health. Salt is consumed throughout the world in small, fairly consistent amounts on a daily basis. Because of this, it is an ideal vehicle for fortification with micronutrients. In most countries, potassium iodate is added to salt after it is refined and dried and before it is packed. Between 1993 and 2007, the number of countries in which iodine deficiency disorders were a public health concern reduced by more than half – from 110 countries to 47 (UNICEF, 2008). These striking public health results are clearly linked to expanded salt iodization. In 1990, less than 20% of households in the developing world were consuming iodized salt (UNICEF, 2009). Today that figure has increased to 70 % (UNICEF, 2008).

34 developing countries have achieved the universal salt iodization goal (Maberly, Stanley, 2005), and an additional 38 countries are considered 'on track' for elimination of iodine deficiency disorders. These are countries that have either shown increases in coverage of at least 20% over the previous decade or that have reached between 80% and 89% coverage with no indication of possible decline (Bailey et al., 2015).

Potassium iodate is preferred to potassium iodide for salt iodization because it is more stable. The benefits of correcting iodine deficiency far outweigh the potential risks of fortification. Iodine-induced hyperthyroidism and other potential adverse effects can be almost entirely avoided by adequate and sustained quality assurance and monitoring of iodine fortification (Allen et al., 2006).

##### **Flour fortification**

For more than 60 years, flour fortification has proven effective in the reduction of vitamin and mineral deficiencies. Flour fortification provides a platform to increase folic acid, iron, zinc, and other B vitamins in the diet of the population. Regular consumption of bread, noodles and other flour products fortified with such micronutrients can contribute to improving a deficient diet. By 2009, 30% of the world's flour produced in large roller

mills was being fortified (Maberly, 1994). Flour fortifications with iron, folic acid and, in some cases, other nutrients were taking place in at least 63 countries. In the United States, Canada, Chile, and South Africa, studies have shown great reductions in numbers of children born with a neural tube defect since nationally mandated flour fortification with folic acid came into effect in the late 1990s. Rates have dropped by 26% in the United States, 42% in Canada, 40% in Chile, and 30% in South Africa (USAID, 2017).

### **Fortification of vegetable oils and fats**

Vegetable Oils are suitable as vehicles for vitamins A, D and E fortification, as the production and refining of oils is a centralized process. As vitamins A, D and E are fat soluble, they can be uniformly distributed in oil. The stability of vitamin A is greater in oils than in any other food and it facilitates the absorption of vitamin A by the body. Vegetable Oils are consumed by almost everyone, thus, it is possible to improve people's access to fat soluble vitamins through fortification of oils and fats.

The prevalence of Xerophthalmia in Denmark declined drastically in 1918 and disappeared in 1919, following the introduction of butter rationing (which made butter available at a low price and diminished consumption of non-enriched margarine). Xerophthalmia reappeared in 1920 when butter rationing was discontinued, thus eliminating access to an important source of natural vitamin A. Such observations eventually led to the enrichment of margarine with Vitamin A (Allen et al., 2006).

### **Other Vehicles for Vitamin A fortification**

Vitamin A is an essential nutrient and its deficiency is associated with adverse health effects. Since vitamin A is fat-soluble, it is easily added to fat-based or oily foods. When the food vehicle is either dry or a water-based liquid, an encapsulated form of the vitamin is needed.

Sugar fortification presents an important intervention for improving the vitamin A status of at risk populations. Guatemala was one of the first countries to implement a sugar fortification program to ensure an adequate intake by the population. Given the success of the relatively long-running programme to fortify sugar with vitamin A in Central America, where the prevalence of vitamin A deficiency has been reduced considerably, similar initiatives are being attempted in other world regions. Asian countries are also considering sugar fortification.

Rice is an important staple in many countries where the prevalence of vitamin A deficiency is high; hence vitamin A fortification of rice has the potential to be an effective public health strategy for the elimination of Vitamin A deficiency.

Other foods that have been fortified successfully with Vitamin A include: dry milk, complementary foods for infants and young

children, biscuits and beverages, which are sold commercially or used in school feeding programmes such as those implemented in Indonesia, Mexico and other countries in Central America and South Africa (Allen et al., 2006).

### **Iron Fortification**

The effectiveness of iron fortification has been demonstrated in several world regions. Iron fortification of infant formulas has been associated with a fall in the prevalence of anaemia in children aged less than 5 years in the United States (Yip et al., 1987; Fomon, 2001). In Venezuela, wheat and maize flours have been fortified with iron (as a mixture of ferrous fumarate and elemental iron), vitamin A and various B vitamins since 1993. A comparison of the prevalence of iron deficiency anaemia pre- and post-intervention showed a significant reduction in the prevalence of these conditions in children (Layrisse et al., 1996). Fortification of milk with iron and vitamin C in Chile produced a rapid reduction in the prevalence of iron deficiency in infants and young children (Stekel et al., 1988; Hertrampf et al., 2002).

The effectiveness of the fortification of soy sauce with iron is currently being evaluated in a population of 10000 Chinese women and children with a high risk of anaemia. Preliminary results of the 2-year double-blind placebo-controlled study have shown a reduction in anaemia prevalence rates for all age groups after the first 6 months.

For most food vehicles, the recommended iron fortificant, in order of preference, are: ferrous sulfate, ferrous fumarate, encapsulated ferrous sulfate or fumarate, electrolytic iron (at twice the amount), and ferric pyrophosphate (at twice the amount). The co-addition of ascorbic acid in a 2:1 molar ratio is recommended in order to enhance iron absorption. This applies to infant foods and market-driven foods. Ferric sodium EDTA is recommended for the mass fortification of high-phytate cereal flours and for sauces with high peptide content (e.g. fish sauce, soy sauce). For liquid milk products, ferrous bisglycinate, micronized ferric pyrophosphate and ferric ammonium citrate are the most appropriate fortificants (Allen et al., 2006).

### **Advantages of food fortification**

Food fortification offers a number of advantages over other interventions aimed at preventing and controlling micronutrient deficiencies.

- If consumed on a regular and frequent basis, fortified foods will maintain body stores of nutrients more efficiently and more effectively than will intermittent supplements.
- Fortified foods are also better at lowering the risk of the multiple deficiencies that can result from

seasonal deficits in the food supply or a poor quality diet.

- Fortification of widely distributed and widely consumed foods has the potential to improve the nutritional status of a large proportion of the population, both poor and wealthy.
- Fortification doesn't require any changes in existing food patterns.
- When properly regulated, fortification carries a minimal risk of chronic toxicity.
- Fortification is often more cost-effective than other strategies, especially if the technology already exists and if an appropriate food distribution system is in place (Allen et al., 2006 ; Yip et al., 1987).

### Limitations of food fortification

Food fortification can have an enormous positive impact on public health; however, it has some limitations.

- While fortified foods contain increased amounts of selected micronutrients, they are not a substitute for a good quality diet that supplies adequate amounts of energy, protein, essential fats and other food constituents required for optimal health.
- A specific fortified foodstuff might not be consumed by all members of a target population. Conversely, everyone in the population is exposed to increased levels of micronutrients in food, irrespective of whether or not they will benefit from fortification.
- Infants and young children, who consume relatively small amounts of food, are less likely to be able to obtain their recommended intakes of all micronutrients from universally fortified staples or condiments alone.
- Fortified foods often fail to reach the poorest segments of the general population who are at the greatest risk of micronutrient deficiency. This is because such groups often have restricted access to fortified foods due to low purchasing power and an underdeveloped distribution channel.
- Technological issues relating to food fortification have yet to be fully resolved, especially with regard to appropriate levels of nutrients, stability of fortificants, nutrient interactions, physical properties as well as acceptability by consumers including cooking properties and taste.(Allen et al., 2006).

### Conclusion

Micronutrients are essential to sustain life and for optimal physiological function. Widespread global micronutrient

deficiencies exist, with pregnant women and their children less than 5 years at the highest risk. Iron, iodine, folate, vitamin A, and zinc deficiencies are the most widespread micronutrient deficiencies, and all these deficiencies are common contributors to poor growth, intellectual impairments, perinatal complications, and increased risk of morbidity and mortality.

Fortification of food with micronutrients is a valid technology for reducing micronutrient malnutrition as part of a food-based approach. National, mandatory fortification programs hold great potential for impacting widespread change in a populations' nutritional status with numerous studies demonstrating its effectiveness and feasibility. A successful programme requires private-sector involvement, public-sector support, willingness of both sectors to enforce quality assurance, good data on consumption patterns, social acceptability of the fortified food and minimal increase in cost.

Food fortification based on sound principles and supported by clear policies and regulations can play an important role in the progress towards prevention and control of micronutrient malnutrition.

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### Conflicts of interest

Authors report no conflict of interest.

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