



Review

The importance of minerals in human nutrition: Bioavailability, food fortification, processing effects and nanoencapsulation



Seyed Mohammad Taghi Gharibzahedi ^a, Seid Mahdi Jafari ^{b, *}

^a Young Researchers and Elites Club, Science and Research Branch, Islamic Azad University, Tehran 14778-93855, Iran

^b Department of Food Materials and Process Design Engineering, Gorgan University of Agricultural Sciences and Natural Resources, Gorgan, Iran

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ABSTRACT

Background: As minerals have diverse functionalities and potentials in the body's metabolism and homeostasis, deficiency of these bioactive constituents can result in an abundant incidence of common disorders and disease symptoms. Maintenance knowledge of the mineral content in terms of safe food fortification and processing techniques can significantly increase their absorption and bioavailability rate. **Scope and approach:** This overview mainly discusses current investigations about the identification of high-available sources and remarkable functions of mineral elements, quantification methods for the bioavailability assessment, and influence of different processing practices and usual fortification strategies on mineral content and quality of staple food products.

Key findings and conclusions: The most dominant minerals to fortify various food preparations are iron, calcium, zinc and iodine. Utilization of isotopic approaches can sensitively determine the bioavailability values of food minerals. Modern processing techniques (e.g., high pressure and sonication) compared with the conventional processes have lower negative impacts on the content of micro- and macro-minerals. Accumulation of mineral elements in the edible tissues of crops using agrobiotechnological techniques (e.g., gene overexpression and activation control) and their direct fortification into formulation of processed foods along with nanoencapsulation could enhance the concentration and bioaccessibility of these bioactive ingredients.

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1. Introduction

Micronutrients include vitamins and minerals because small amounts of these components are needed for the body. Minerals are extensively divided into major minerals (macro-minerals) and trace minerals (micro-minerals). Major minerals are including calcium (Ca), magnesium (Mg), potassium (K), sodium (Na), chloride (Cl), phosphorus (P) and sulfur (S); while trace minerals are iodine (I), zinc (Zn), selenium (Se), iron (Fe), manganese (Mn), copper (Cu), cobalt (Co), molybdenum (Mo), fluoride (F), chromium (Cr) and boron (B). Various food sources of major and trace minerals and their functions in the body are explained in Table 1. For a good and balanced nutrition, different plant (vegetables and fruits) and animal sources can be consumed to receive a number of important minerals (Table 1). Although the needed amounts of minerals in the body are not a sign of their significance, less amount of trace

minerals for the body is needed compared with major ones. As a result, a balanced diet can commonly support all essential minerals for the body (Lukaski, 2004).

Minerals have key roles in our body to do necessary functions - from building strong bones to transmitting nerve impulses - for healthy and lengthy life. Existence of a series of minerals not only can make different hormones, but also can regulate a standard heartbeat. Some macro- and micro-elements are found in the structure of teeth (Ca, P and F) and bones (Ca, Mg, Mn, P, B and F), whereas most micro-elements (Cu, Fe, Mn, Mg, Se and Zn) play a vital role as a structural part in many enzymes (Table 1). Macro-elements (Ca, Mg, P, Na and K) compared with micro-ones (I) have a lot more considerable functions in nerve cells (transmission and signaling). Although microelements have key roles in the formation of erythrocyte cells (Co, I and Fe), regulation of the glucose levels (Cr), and their protection via activation of antioxidant enzymes (Mo), macro minerals such as, Ca and K have a high potential to control blood pressure (Table 1). Minerals also involved in immune (Ca, Mg, Cu, Se and Zn), and brain (Cr and Mn) systems (Table 1).

* Corresponding author.

E-mail address: smjafari@gau.ac.ir (S.M. Jafari).

Table 1
Main sources and functions of essential minerals.

Minerals	Main sources	Main functions
<i>Macro-minerals</i>		
Calcium (Ca)	<i>Vegetable:</i> Greens (broccoli, mustard greens), legumes <i>Animal:</i> Milk and dairy products, fortified tofu and fortified soy milk, canned fish with bones (salmon, sardines)	Important for healthy bones and teeth; Helps to relax and contract the muscles; Important in nerve functioning, health of immune system, blood clotting and blood pressure regulation
Chloride (Cl)	<i>Vegetable/Fruit:</i> Seaweed, rye, tomatoes, lettuce, celery, olives; <i>Animal:</i> Meats, small amounts in milk; <i>Other:</i> Table salt, soy sauce; large amounts in processed foods, breads	Required to have a good balance in body fluids, An essential part of digestive (stomach) juices
Magnesium (Mg)	<i>Vegetable:</i> Nuts and seeds, legumes, artichokes, leafy and green vegetables; <i>Animal:</i> Milk and dairy products, seafood; <i>Other:</i> Chocolate, "hard" drinking water	Found in bones; Needed for the formation of protein, muscle contraction, immune system health and nerve transmission; Assists to avoid constipation
Phosphorus (P)	<i>Vegetable:</i> Seeds (pumpkin & squash), nuts (Brazil nut), legumes (beans & lentils); <i>Animal:</i> Meat (lean sirloin, lean beef), fish (salmon), shellfish (scallops), poultry, eggs, milk, low fat dairy (non-fat yogurt), cheese (Romano); <i>Other:</i> Processed foods (soda pop), soya foods (tofu)	Found in every cell; Needed for the body to make proteins providing the cell growth, maintenance, and reparation; ATP and energy production; Important for healthy bones and teeth; Part of the system that maintains acid-base balance; Works with the B vitamins to help kidney performance, muscle constrictions, regular heartbeat and nerve signaling
Potassium (K)	<i>Vegetable/Fruit:</i> Fresh and dried fruits and vegetables, whole grains, legumes; <i>Animal:</i> Meats, fish (salmon), milk, yogurt (plain, skim/non-fat); <i>Other:</i> Baked potato and acorn squash	Needed for proper fluid balance, nerve transmission, muscle contraction, suitable maintenance of blood pressure and waste elimination
Sodium (Na)	<i>Vegetable:</i> Pickles (cucumber), canned vegetables (sweet peppers); <i>Animal:</i> Cured meat & fish (bacon, cooked), small amounts in milk, cheese (Roquefort); <i>Other:</i> Table salt, breads, large amounts in processed foods; such as, soy sauce, instant soups (beef noodle), roasted and salted nuts & seeds (pumpkin seeds), snacks (pretzels), fast foods (egg & ham biscuit)	Needed for appropriate maintenance of electrolyte balance and fluid balance, heart function and specified metabolic activities, muscle contraction and nerve transition
Sulfur (S)	<i>Vegetable:</i> Cruciferous (broccoli, cauliflower, cabbage, kale, Brussels sprouts, turnips, Bok Choy, kohlrabi), and allium (garlic, onions, leeks, chives) vegetables, legumes, nuts; <i>Animal:</i> Meats, poultry, fish, eggs, milk; <i>General:</i> Occurs in foods as part of protein	Found in protein molecules; Helps resist bacteria and protects against toxic substances; Necessary for proper development of connective tissue; Helps skin to maintain structural integrity.
<i>Micro-minerals</i>		
Boron (B)	<i>Vegetable/Fruit:</i> Broccoli, carrots, onions, potatoes, Bananas, red grapes, peaches, pears, apples, avocados, olives, dried fruit (prunes, raisins), nuts (especially almonds, peanuts, hazelnuts), peanut butter, legumes (lentils, beans), wheat and oat bran; <i>Other:</i> Fruit juices, honey, bee pollen	Handles other minerals (e.g., Mg and P), Improving the estrogen concentrations in post-menopausal women and healthy men (estrogen is useful in keeping healthy bones and mental performance), Removes yeasts producing vaginal infections in common form of boric acid; Embryonic development; Important in maintaining cellular and organ membrane functions
Chromium (Cr)	<i>Vegetable/Fruit:</i> Whole grains, wheat germ, nuts, green peppers, apples, bananas, spinach, black pepper, molasses; <i>Animal:</i> Beef, liver, eggs chicken, oysters, cheese, butter; <i>Other:</i> Brewer's yeast, unrefined foods	Important in the metabolism of fats and carbohydrates; Important for brain function and other body processes; Stimulates fatty acid and cholesterol synthesis; Works closely with insulin to regulate blood sugar (glucose) levels
Cobalt (Co)	<i>Vegetable:</i> Cereals (oats), green leafy vegetables (broccoli, cabbage, lettuce, turnip and spinach), nuts, mushrooms (especially shiitake), figs; <i>Animal:</i> Meat, liver, kidneys, milk, oysters, mussels, fish, shellfish	As a part of the vitamin B12 is used in <i>pernicious anemia</i> by improving blood because it promotes the formation of red blood cells (erythrocytes); Help to solve the cases of fatigue, and digestive and neuromuscular issues
<i>Micro-minerals</i>		
Copper (Cu)	<i>Vegetable/Fruit:</i> Legumes (cooked beans and chickpeas), nuts (cashew nuts), seeds (sesame), whole grains, raw kale, mushrooms (shiitake, cooked), dried fruit (prunes), avocados; <i>Animal:</i> Organ meats, seafood (oysters, cooked); goat cheese (soft); <i>Other:</i> Drinking water, fermented soy foods (tempeh)	A structural part in many enzymes; Desirable for Fe and protein metabolism; Essential to the proper functioning of organs and metabolic processes; Stimulates the immune system to fight infections; Repairs injured tissues; Promotes healing; Helps to neutralize free-radicals causing intense cell damage
Fluoride (F)	<i>Vegetable:</i> Most teas; <i>Animal:</i> Seafood (fish, shellfish), mechanically deboned meat/chicken, <i>Other:</i> Drinking water (either fluoridated or naturally containing fluoride), processed cereals, beverages (beer, wine, Juice), & other foods (canned fish and shellfish)	Involved in bones and teeth development; Helps to prevent tooth decay; Help to reduce cavities in children by more than half by adding fluoride to tap water (called fluoridation); Help maintain bone structure and slows-down bone density loss
Iodine (I)	<i>Vegetable/Fruit:</i> Foods grown in iodine-rich soil, bananas, cranberries, dried prunes, organic strawberries, organic navy beans, organic potatoes; <i>Animal:</i> Seafood (cod fish, shrimp, lobster), dairy products (milk, organic yogurt and raw, organic cheese, Cheddar cheese), baked turkey breast, boiled eggs; <i>Other:</i> Iodized salt, bread, baked potatoes, canned tuna, canned corn	A vital component of hormones produced by the thyroid gland which are responsible for a number of key activities in body, including growth, development, metabolism, reproduction, nerve and muscle function, production of blood cells, adjustment of body temperature and generally the speed of body processes
Iron (Fe)	<i>Vegetable/Fruit:</i> Squash and pumpkin seeds, nuts (cashew, pine, hazelnut, peanut, almond), beans and pulses (white beans, lentils), whole grains, bran, dark leafy greens (spinach, Swiss chard), dried fruits; <i>Animal:</i> Liver (chicken), seafood (oysters, mussels, clams), beef and lamb (lean chuck roast), eggs, poultry; <i>Other:</i> Dark chocolate, cocoa powder, Fe-enriched breads and cereals, tofu	Needed for the formation of hemoglobin in red blood cells, which carries oxygen from the lungs to the body cells; Needed for energy metabolism; A transport medium for electrons within cells; An integrated part of important enzyme systems in various tissues
Manganese (Mn)	<i>Vegetable/Fruit:</i> Nuts (hazelnuts), seeds (pumpkin), beans (butter/lima beans, cooked), spinach (cooked), whole grains (brown rice), tea (black, brewed); <i>Animal:</i> Seafood (mussels, cooked), fish (bass, cooked); <i>Other:</i> Bread (whole-wheat), tofu (firm, raw) <i>General:</i> Widespread in foods, especially plant foods	Part of many enzymes; Important for the normal functioning of the brain and proper activity of nervous system throughout the body; Vital for proper and normal growth of human bone structure; Useful for post-menopausal women and preventing osteoporosis
Molybdenum (Mo)	<i>Vegetable/Fruit:</i> Legumes (beans, peas, lentils), whole grains, chokeberry, leafy vegetables (spinach), Swiss chard, nuts, sunflower seeds, wheat flour, cucumber; <i>Animal:</i> Eggs, liver, milk, cheese, organ meats (lamb); <i>Other:</i> Pasta, breads	Cell protection through activation of enzymes that have antioxidant roles in blood; Needed for permitting cells to generate energy within the mitochondria, or powerhouse of the cells, with the help of broken-down macronutrients; To activate enzymes required to remove waste in the body

Table 1 (continued)

Minerals	Main sources	Main functions
Selenium (Se)	<i>Vegetable/Fruit:</i> Leafy and green vegetables (broccoli, cabbage, spinach), seeds (chia, sunflower, sesame, flaxseed), Brazil nuts, whole grains (rye), lima/pinto beans, brown rice, common mushrooms; <i>Animal:</i> Seafood (oysters - cooked), fish (tuna - cooked), beef & lamb (lean beef steak - cooked), chicken and turkey (turkey, back or leg meat cooked), pork (lean tenderloin - cooked); <i>Other:</i> whole-wheat bread; Se-enriched yeast	Making special proteins, called antioxidant enzymes that play a role in protecting the body from the damaging effects of heavy metals, free radicals and other harmful substances; Stimulation of the immune system; Forms part of the enzyme that activates the thyroid hormone; Protecting the organism from various viruses (e.g. HIV-1); Helps to detoxification processes
Zinc (Zn)	<i>Vegetable/Fruit:</i> Leavened whole grains, wheat germ (toasted), spinach, pumpkin and squash seeds, nuts (cashews), beans (cooked chickpeas), white mushrooms (cooked); <i>Animal:</i> Seafood (cooked oysters), beef and lamb (cooked lean beef shortribs), fish, poultry, pork (cooked lean pork shoulder); <i>Other:</i> Chocolate, cocoa powder	An important part in structure of many enzymes; Needed for making protein and genetic material; Has a main function in taste perception, wound healing, sperm production, normal fetal development, normal growth and sexual maturation and immune system health; Enhances smell; Improves digestion

In recent years, a large number of scientific and technological attempts have been focused to overcome mineral malnutrition in industrial and developing countries, because the deficiency of Fe, Zn, I, and Se in the world's population is about 60, 30, 30 and 15%, respectively. Moreover, deficiency of Zn, Fe and I along with shortage of vitamin A can lead to a ~20% death rate in children less than 5 years old (Bronner, 1998; White & Broadley, 2009). Deficiency of Fe in the body by decreasing levels of hem proteins (e.g., hemoglobin) and enzymes (having Fe as a cofactor) causes anemia prevalence or a decrease in the quantity of red blood cells (RBCs). The reduced use of Fe from digested foods and accordingly its inadequate dietary intake can also lead to a lower rate of growth and cognitive ability in children, more disorders during pregnancy period and a poorer working efficiency in adult people (Martinez-Navarrete, Camacho, Martinez-Lahuerta, Martinez-Monzo, & Fito, 2002). Deficiency of Zn can bring many adverse effects such as, growth (weight and hair loss), digestive (diarrhea, appetite loss, and taste variations), and immunity (postponed wound-healing and high susceptibility to infections), sexual (delayed sexual-maturation, lessened spermatogenesis, male hypogonadism and impotence) problems (Badii, Nekouei, Fazilati, Shahedi, & Badiei, 2012). An iodine deficiency can also lead to the enlargement of the thyroid gland "goiter" and the avoidable intellectual incapacity (Leung, Braverman, & Pearce, 2012). An enhanced overall mortality has been associated with poor immunity, incidence and development of viral diseases/infections and unalterable brain injury (Rayman, 2012).

Presentation of potential strategies is thus required to reduce mineral deficiencies and related adverse disorders/diseases (Gharibzahedi, Emam-Djomeh, Razavi, & Jafari, 2014; Gharibzahedi, Mousavi, Jafari, & Faraji, 2012). Biofortification is an excellent breeding process for enhancing quantity and quality of nutrients in agricultural crops such as rice, wheat, maize, common beans and some other cereals and legumes. This process can highly improve the mineral density of staple crops via common plant breedings and contemporary bio-technology in order to attain an extraordinary and dramatic impact on human health. Formulation enrichment of processed foods with minerals is also considered as an effectual way for decreasing occurrence of their deficiency with a substantial enhancement in absorption and bioavailability levels (Bouis & Welch, 2010; Zimmermann et al., 2004). This review highlights the food sources, biological functions, absorption mechanisms, bioavailability assessment methods and some enrichment solutions of minerals. The effect of various processing and storage technologies on the mineral content of some important food products has also been precisely reviewed.

2. Bioavailability of minerals

Although the total quantity of a mineral in a food does not

reflect its available amount in the body via absorption, only a certain quantity is bioavailable (Jafari & McClements, 2017). The biological accessibility or bioavailability of macro- and micro-minerals is defined as the fraction of the ingested mineral that is absorbed and consequently used for usual physiological functions (Fairweather-Tait & Hurrell, 1996). Fairweather-Tait (1993) earlier introduced three main steps in the bioavailability of a nutrient (e.g. a mineral) including (I) nutrient absorption by improving its accessibility in the intestinal lumen, (II) maintenance and/or absorption/uptake in the body, and (III) utilization (consumption) by the body. As a principal rule, the bioavailability level is highly dependent on digestion, release from the food matrix, absorption rate of the target ingredient by intestinal cells, and its transport amount to body cells.

2.1. Quantification methods of minerals bioavailability

It is very important to consider different bioavailability techniques in understanding interactions between minerals and food components in gastrointestinal (GI) tract; e.g., ascorbic acid increases Fe absorption, while tannins have an inhibitory effect. There are three general methods to quantify bioavailability level including *in vitro* tests, bioassays and balance investigations (Fairweather-Tait, 1993; Watzke, 1998). Measurements of solubility, dispersibility, fractional dialysability and also investigations of the mineral uptake in experimental animals can be carried out by *in vitro* studies. Thus, a reliable knowledge on the effects of luminal parameters (including enzymes and pH), nature of the food matrix, and food preparation and processing practices on absorbability of nutrients like minerals is needed.

Furthermore, this procedure compared to the human or animal investigations is a cheaper and quicker way and proposes improved control of experimental variables (Sandberg, 2005). Balance studies according to the difference estimations between the fed (input) and the excreted (output) quantity of the nutrient can evaluate the bioavailability in a mass balance-like mode from the apparent absorption/uptake (Watzke, 1998). In bioassay experiments, absorption/uptake and utilization of a mineral is assessed based on the response of the experimental animal or man by directly determining the metabolites in urine, blood, or tissues (Fairweather-Tait, 1993; Watzke, 1998).

However, scientific attempts are steadily in progress to develop and refine techniques determining dietary mineral absorption in body. One of these important attainments is application of isotopes (radio and stable) for labeling some minerals to follow their metabolic paths and to estimate the fractional absorption from the consumed foods. Therefore, several novel methods based on isotopes are developed to assess mineral absorption which include whole body retention (γ -emitting isotopes), plasma appearance/disappearance (based on the curve (AUC) deconvolution), isotope

balance (faecal and urinary monitoring), urinary excretion (double isotope method), and hemoglobin incorporation (especially for Fe) (Lowe & Jackson, 2001). Analytical methods of atomic absorption spectroscopy (AAS) and inductively coupled plasma mass spectrometry (ICP-MS) have been recently used to exactly determine the mineral isotopes for assessing their bioavailability. Selecting a technique responsible for evaluating mineral bioavailability depends on the various parameters such as the mineral under study and the objective of the investigation, location, type of volunteers and available reserves (Harvey, 2001). Some isotopic methods conducted for the bioavailability quantification of minerals in foods is summarized in Table 2.

2.2. Mechanisms of mineral absorption

In general, all minerals present in GI secretions and ingested foods that enter into the intestine are absorbed. Nonetheless, there are some exceptions; for example, Fe and Ca are absorbed in the duodenum. Since deficiencies of Fe and Ca have been significantly led to health problems all over the world, in here, we obviously clarify the mechanisms involved in absorption of these minerals.

2.2.1. Absorption of Fe

Although it is vital to absorb sufficient amounts of Fe in the duodenum, significant amounts of this mineral is not absorbed from the diet. Moreover, antacids or other conditions that interfere with gastric acid secretion and also presence of some chelating agents can interfere with Fe absorption. Women compared to men have approximately four times more Fe transport proteins in the intestinal epithelial cells because menstruation cycle in women causes a great loss in Fe concentration. Disorders of Fe-lack in the body; such as, anemia are happened by its inadequate uptake (Fuqua, Vulpe, & Anderson, 2012). Nonetheless, high amounts of Fe can be dangerous because mammals do not have a physiologic pathway for its elimination (Fuqua et al., 2012; Saini, Nile, & Keum, 2016).

Absorption of ionic Fe into mucosal cells for the hemoglobin production is done through active transport under acidic conditions. Complexes of Fe-ferritin storing Fe are formed by bonding between the ionic Fe and ferritin protein in these cells. Fe^{3+} is reduced to Fe^{2+} in the duodenal lumen via the ferrireductase activity. Fe is co-transported with a proton into the enterocyte through the divalent metal transporter DMT-1. This transporter type is non-specific for Fe which transports many divalent metal ions (Saini et al., 2016). Fe inside the enterocyte follows one of two major pathways depending on a complex cell programming based on both dietary and systemic Fe loads: (I) Fe within the enterocyte under abundance conditions is trapped by its incorporating into ferritin and so is not transported into blood. This Fe is lost when the enterocyte dies and is shed, and (II) Fe is exported out of the enterocyte under limiting conditions by a ferroportin transporter located in the basolateral membrane and then links to the Fe-carrier transferrin to transport in all the body. On the other hand, heme-Fe form is simply absorbed via ingestion of hemoglobin/myoglobin. It looks as if intact heme in such conditions is taken up by the small intestinal enterocyte by active transport of endocytosis. Fe once inside the enterocyte is liberated, and essentially follows the same pathway for export as absorbed inorganic Fe. Some intact molecules of heme may be transported into the circulation (Miret, Simpson, & McKie, 2003).

Liver synthesizes a Fe-regulating small peptide “hepcidin” containing 25 amino acids to retain homeostasis of this essential mineral in the body. The hepcidin production and release is usually

adjusted with factors such as cytokines involved in inflammation particularly interleukin (IL)-6, presence of bacterial lipopolysaccharide, amount of Fe-reservoirs and Fe requirement for erythropoiesis (Bergamaschi et al., 2016). Systemic Fe-metabolism can be adjusted through interaction of hepcidin with the transmembrane protein “ferroportin”. Hecpudin by inactivating ferroportin presence in membranes of enterocyte, macrophage, and hepatocyte can significantly decrease Fe overload under normal conditions via its absorption, recycling and storage actions (Rossi, 2005). As mentioned earlier, an important reason for the reduction of Fe absorption and also effectiveness of Fe-enriched foods is inflammation and infectious disorders possibly due to a rise in hepcidin synthesis in the exposure to acute-phase reactions by inflammatory cytokines. Having broken down ferroportin at the increased concentrations of hepcidin, the Fe-regulatory hormone clogs the crossing path of Fe from the intestinal cells to the plasma. This inherent immune response can constrain the growth of pathogens or infectious agents by limiting Fe supply (Hurrell, 2012). Adversely, a high Fe-release rate by the down-regulating liver hepcidin production can be obtained with an enhancement in enterocyte Fe-absorption, Fe-recycling onto plasma transferrin by macrophages and hepatocyte Fe-storage (Rossi, 2005).

2.2.2. Absorption of Ca

Two distinguished mechanisms can comprehensively explain Ca-absorption from the intestinal lumen. The accessible quantity of free-Ca for absorption can relatively assess level of its importance. These absorption paths are including (Bronner, 1998):

- I Active transcellular absorption (TCA): this pathway occurs only in the duodenum at the time that intake of Ca is low. TCA process includes import of Ca into the enterocyte, transport across the cell, and finally export into extracellular fluid and blood. Using voltage-insensitive (TRP) channels, Ca moves in the intestinal epithelial cells and is pumped out of the cell via a Ca-ATPase system. Ca-transport across the epithelial cell is the restricting portion of TCA, which is significantly increased by calbindin protein carrier. Calbindin synthesis is tremendously reliant on the presence of vitamin D in the body.
- II Passive paracellular absorption (PCA): this pathway happens greatly in the jejunum and ileum. Nevertheless, PCA route in colon is developed to a slighter degree in dietary levels of Ca which are moderate or high. Ca^{2+} through close-fitting junctions moves into the basolateral regions around enterocytes, and thus into blood. PCA is responsible for the bulk Ca absorption when Ca availability is high because of the very short time available for active transport in the duodenum.

2.2.3. Absorption of Se

A different absorption rate for Se in human and rat populations was reported between various forms of organic (seleno-methionine and seleno-cysteine) and inorganic (selenate and selenite) Se. Although organic forms of Se are wholly maintained in the body, they have a lower intake amount compared to inorganic ones. However, the form of Se existing in plasma is a determining factor in metabolism of absorbed Se. After moving different forms of Se to the selenide pool, two metabolic routes for this essential mineral are predicted including (i) its use to synthesize the seleno-protein, and (ii) its excretion as a seleno-sugar in the urine. Meanwhile, seleno-methionine (main Se form in meat) via the methionine replacement can straightly be combined to protein structures. In the brassica and allium vegetable family, a distinct metabolic path

Table 2
Isotopic methods for assessing bioavailability of some essential minerals.

Minerals	IMN ^a	Isotopic method	Food	Subjects	Bioavailability	Reference
Calcium (Ca)	⁴⁰ Ca (96.94)	Isotope (⁴⁴ Ca) balance	Semi-purified diet containing inulin Calcium <i>L</i> -threonate Mineral water	Rats Healthy Chinese Men, premenopausal and postmenopausal women	Inulin intake increased Ca Good bioavailability (26.49%) Good bioavailability (21.62–23.15%)	Coudray et al. (2005b) Wang, Hu, and Jiang (2013) Bacciottini et al. (2004)
	⁴² Ca (0.647)	Double-label stable isotope (⁴⁴ Ca and ⁴² Ca)				
	⁴³ Ca (0.135)	Single-isotope (⁴⁴ Ca) method, ICP-MS				
	⁴⁴ Ca (2.086)					
	⁴⁶ Ca (0.004)					
Magnesium (Mg)	²⁴ Mg (78.99)	Isotope (²⁵ Mg) balance	Semi-purified diet containing inulin Organic and inorganic Mg salts	Rats Rats	Sufficiently bioavailable except Mg gluconate	Coudray et al. (2005b) Coudray et al. (2005a)
	²⁵ Mg (10.00)	Isotope (²⁶ Mg) balance				
	²⁶ Mg (11.01)					
Chromium (Cr)	⁵⁰ Cr (4.345)	AAS/ICP-MS (⁶³ Cu)	Breast milk	Lactating women	Not detected	Mohamedshah et al. (1998)
	⁵² Cr (83.79)					
	⁵³ Cr (9.501)					
	⁵⁴ Cr (2.365)					
Copper (Cu)	⁶³ Cu (69.17)	Faecal monitoring (⁶⁵ Cu), ICP-MS	Red wine, soybeans, mushrooms, sunflower seeds Wheat flour	Norwich females/males <i>In-vitro</i> digestion	Good for red wine, mushrooms and sunflower seeds; poor for soybeans Excellent (61–80%) Good bioavailability	Harvey et al. (2005) Erdemir and Gucer (2016)
	⁶⁵ Cu (30.83)	AAS/ICP-MS (⁶³ Cu and ⁶⁵ Cu)				
Iodine (I)	¹²⁷ I (100)	Substoichiometric isotope dilution analysis	Drinking water, milk and commercial salts	Turkish people	Good bioavailability	Uenak, Yurt, and Biber (2000)
Iron (Fe)	⁵⁴ Fe (5.85)	Hemoglobin incorporation (radio- and stable isotopes; the best method); Faecal monitoring (radio- and stable isotopes); Whole-body counting (⁵⁹ Fe) Single-isotope (all isotopes of Fe) method, ICP-MS	Ferrous salts, Iron glycine; Ferritin; Polysaccharide iron complexes Aqueous form, Fe-enriched meat	British men and women Healthy non-pregnant women	Sufficient bioavailability High absorption (8–45%)	Fairweather-Tait (2001) Barrett, Whittaker, Fenwick, Williams, and Lind (1994)
	⁵⁶ Fe (91.75)					
	⁵⁷ Fe (2.12)					
	⁵⁸ Fe (0.28)					
Manganese (Mn)	⁵⁵ Mn (100)	Single-isotope (⁵⁵ Mn) method by ICP-MS	Spinach leaves	Turkish men	Good (45–47%) bioavailability	Erdemir and Gucer (2013)

Minerals	IMN ^a	Isotopic method	Food	Subjects	Bioavailability	Reference
Molybdenum (Mo)	⁹² Mo (14.77)	Isotope dilution method (⁹⁴ Mo, ⁹⁶ Mo, ⁹⁷ Mo, ¹⁰⁰ Mo)	Soy and kale	Women and men	Kale Mo highly bioavailable, soy Mo less bioavailable	Turnlund et al. (1998)
	⁹⁴ Mo (9.23)					
	⁹⁵ Mo (15.90)					
	⁹⁶ Mo (16.68)					
	⁹⁷ Mo (9.56)					
	⁹⁸ Mo (24.20)					
	¹⁰⁰ Mo (9.67)					
Selenium (Se)	⁷⁴ Se (0.89)	Stable isotope (⁷⁴ Se, ⁷⁶ Se) method, and GC/MS Faecal monitoring, Urinary excretion (⁷⁴ Se, ⁷⁶ Se, ⁷⁷ Se, ⁷⁸ Se, ⁸² Se)	Commercialized Se supplements Fish, Yeast, (selenized)	French population British men	Bioavailability of 76% Fish Se highly bioavailable, yeast less bioavailable compared with selenate	Ducros, Favier, and Guigues (1991) Fox et al. (2004)
	⁷⁶ Se (9.37)					
	⁷⁷ Se (7.64)					
	⁷⁸ Se (23.77)					
	⁸⁰ Se (49.61)					
	⁸² Se (8.73)					
Zinc (Zn)	⁶⁴ Zn (48.27)	Faecal isotope (⁶⁸ Zn, ⁷⁰ Zn) balance	Chicken meat/soy protein isolate	Health men	Higher absorption of ⁶⁸ Zn than ⁷⁰ Zn	Janghorbani, Istfan, Pagounes, Steinke, and Young (1982)
	⁶⁶ Zn (27.98)					
	⁶⁷ Zn (4.10)					
	⁶⁸ Zn (19.02)					
	⁷⁰ Zn (0.63)					

^a Isotope mass number (IMN) as % abundance is given in parenthesis.

is observed because of the presence of γ -glutamyl methylselenocysteine. This organic component is initially transformed to Se-methylselenocysteine and then enzymatically is transmuted to methyl-selenol with β -lyase. The final compound is mainly warded off through breath and urine, but can also go in the selenide pool (Fairweather-Tait, Collings, & Hurst, 2010; Rayman, 2012).

2.2.4. Absorption of other minerals

As earlier mentioned, intestinal absorption is a key regulatory step in homeostasis of minerals (e.g., P, Cu, Zn, Na, and K). Absorption of phosphorus is generally done in top parts of small intestine. This essential element enters into epithelial cells via a cotransport mechanism with Na. Vitamin D can highly potentiate transporters expression of this macro-mineral (Prasad & Bhadauria, 2013). Absorption of Cu can be explained according to two processes of rapid (low-capacity system) and gentle (high-capacity system) which are comparable to the two processes described in Ca absorption. Clarification of unknown details in the molecular level in relation to Cu absorption is of particular importance. However, it has been revealed that defect existence in intestinal uptake of Cu causing Menkes disease can be due to the disabling mutations of gene encoding of an intracellular Cu-ATPase. It has been demonstrated some dietary factors; such as, considerable dietary intake of either Zn or Mo can notably provide secondary Cu deficiency conditions (Lutsenko, Gupta, Burkhead, & Zuzel, 2008).

Absorption and loss of zinc in the small intestine can be considered as a regulation mechanism for Zn homeostasis. In villiform epithelial surface, a set of Zn-transporters and Zn-binding proteins are present. Nonetheless, in association with the molecules involved in Zn absorption, worthy and detailed studies have not performed yet. Intestinal exclusion of this mineral is befallen through pancreas cells and biliary secretions by shedding of epithelial cells. Some nutritional issues; such as, specified animal proteins and chelating phytates present in dietary plant tissues are key factors to adjust Zn absorption. Generally, one of the main reasons of Zn deficiencies in human body is use of phytate-rich diets in food patterns. Also, co-transport mechanisms during absorption process cause the accumulation of Na ions inside the cells, whereas anti-transport ones reduce K ion concentration inside the cells. A Na-K pump requiring ATP essentially pumps Na out and K in to reinstate the Na-K gradient across the cell membrane (Palfrey & Rao, 1983).

2.3. Effect of the food matrix on mineral absorption

Phytates and polyphenols are two dominant compounds in staple agricultural crops (e.g., cereals and legumes). These inhibitory agents by forming strong chelates and complexes with micro- (e.g., Zn and Fe) and macro- (e.g., Ca) elements can remarkably reduce their absorption and cause malnutrition in vegetarians. Since humans are unable to hydrolyze phytates in their stomach, mineral chelation by these anti-nutritional compounds can lead to a mineral deficiency in the body. In addition, there is a significant decrease in absorption rate of minerals by producing the insoluble complexes between these micronutrients and phenols in GI tract. Chemical structure of polyphenols can be a determining parameter for absorption rate of the formed complexes, so that the most powerful chelators for Fe were proanthocyanidins containing catechol and galloyl groups and hydrolyzable tannins having galloyl groups (Saini et al., 2016). Absorption of calcium can be positively/negatively affected in the presence of soluble fibers such as thickening galactomannan gums used in formulation of some milk products. Use of locust bean gum and high methoxyl pectin could decrease (~12%) the absorption and *in vitro* bioavailability of Ca, whereas an increase in these bioparameters was found by

supplementing inulin (~30%) (Bosscher, Van Caillie-Bertrand, Van Cauwenbergh, & Deelstra, 2003). A stronger synergistic inhibitory impact for water-soluble fibers on Fe-absorption was obtained in the presence of casein compared to whey proteins in dairy infant formulas. According to the numeric results, there was a significant difference in the Fe-dialyzability of formulas developed with casein- (0.32%) and whey-proteins (1.45%) by incorporating 0.42 g locust bean gum (Bosscher, Van Caillie-Bertrand, & Deelstra, 2001). A similar finding was observed by Drago and Valencia (2004), who found a higher Fe absorption in the presence of whey proteins compared to caseins. Also, absorption and bioavailability of minerals especially Ca can be substantially decreased by forming Maillard reaction products (MRPs). The overheated milk due to higher MRPs levels than the UHT one showed a lower Ca solubility and *in vitro* digestion (Seiquer, Delgado-Andrade, Haro, & Navarro, 2010).

2.4. Impact of food processing on the mineral bioavailability

Use of processing ways that can preserve the beneficial structures and nutrients for good biological functions after their consumption and assimilation was emphasized at the beginning of early 1980s. For this reason, foods are preferably processed at reduced temperatures, but may be a requirement to process at higher temperatures for long-term storage. Although many nutrients are sensitive to heat, oxygen, or water, and other physical operations, shelf-life extension of processed foods is possible with implementing high temperatures and low moisture contents in order to control or kill harmful organisms. Moreover, processing can also improve accessibility of micronutrients by decreasing anti-nutrients levels. These days, people incline to choose palatable and suitable foods that provide added advantages; such as, improved health, beauty, longevity and liveliness. Watzke (1998) divided unit operations in food production based on their functions into three distinct groups including separation of food ingredients after harvesting step and during processing or home preparations, the incorporation of food functional components into the formulated foods, and preservation of the final products. Stability and bioavailability rate of functional ingredients can be changed in each of three mentioned classes.

Minerals compared with vitamins are more resistant to industrial production processes. However, these components cannot tolerate alterations after exposure to light, moisture, heat, or oxygen during the processing and storage of food materials. Also, Cu, Fe and Zn may be lost by reacting with a large variety of interactive food constituents; such as, carbohydrate and protein biopolymers (Hazell, 1985). The formed interactions should relatively be considered as a network of exchange reactions permitting the minerals to change binding sites and carriers during processing and thus to decrease their bioavailability levels. Since various processing techniques; such as, heating, soaking, grinding, germination/malting, fermentation etc. are utilized to prepare the processed foods, thermal and non-thermal processing treatments can have a substantial influence on the mineral bioavailability (Gibson, Perlas, & Hotz, 2006). Minerals especially micro-ones are removed/reduced irreversibly during food processing. Nevertheless, processing depending on the certain plants and minerals can have a useful effect on mineral bioaccessibility because it causes minerals in food matrix to be more diffusible and biologically uptakable (Gibson et al., 2006; Watzke, 1998).

Negative and positive impacts of various food operations on the mineral content of some agricultural crops and food products/ingredients are shown in Table 3. The heat treatments; such as, boiling, drying, frying, pressure cooking, steaming and sterilization can meaningfully decrease/destroy some macro- (Ca, Mg, P, K, Na)

Table 3
Influence of different food processes on the mineral availability.

Food processing	Food	Impacts on mineral amounts	Impact type (±)	References
Autoclaving	Lentils grown in Egypt	Considerable reduction in Ca, K, Mg, P, Na, Fe and Cu	–	Hefnawy (2011)
Baking	Fortified whole wheat flour	Decrease of Mn, Fe, Cu and Zn contents	–	Akhtar, Anjum, Rehman, and Munir (2010)
Baking	Bread from Se-enriched whole meal/white flour	No significant reduction in seleno-methionine content after processing and production of bread was found.	+	Hart et al. (2011)
Blanching	Spinach/amaranth leaves	Increasing HCl extractability of Zn and Ca	+	Yadav and Salil (1995)
Boiling ^a	Meat (block, sliced, and cubed)	Reduction of phosphorus content	–	Ando, Sakuma, Morimoto, and Arai (2015)
Cooking	Carrots enriched with minerals	Improving the contents of micro- and macro- minerals	+	Biezanowska-Kopeć et al. (2016)
Pressure cooking	Iodized salt	Iodine decrease (22%)	–	Geetanjali, Karmarkar, Umesh, and Jagannathan (1995)
Canning	Different processed foods	Complex destruction	–	Ranhotra and Bock (1988)
Debitting	Lupin (<i>Lupinus albus</i> L.) seeds	High decrease in minerals, Phytic acid removal (71.4%)	±	Ertaş and Bilgiçli (2014)
Dehydration	Cabernet and Merlot grapes	Increasing the contents of micro- and macro minerals	+	Panceri et al. (2013)
Drying	Egg white	Maillard reaction, Denaturation of binding proteins	–	Leahy and Thompson (1989)
Extrusion	Extruded foods	Inactivation/deactivation of phytase enzyme	–	Mercier (1993)
Fermentation	Pearl millet	Hydrolysis reaction, Decrease of phytate content	–	Alka, Kapoor, and Sharma (1996)
Freezing ^b	Leafy vegetables (kale, spinach)	High retention of mineral constituents	+	Lisiewska, Gebczynski, Bernas, and Kmiecik (2009)
Frying	Iodized salt	Reducing iodine in shallow (27%) and deep (20%) frying	–	Geetanjali et al. (1995)
Germination	African yam bean	Decreasing content of phytic acid	+	Ene and Obizona (1996)
Grilling	African catfish	Increasing mineral contents	+	Ersoy and Özeren (2009)
High pressure	Milk/soy-smoothies	No significant changes after the treatments and storage	+	Andrés et al. (2016)
Microwave cooking	Iodized salt	Reducing iodine content (27.13%)	–	Rana and Raghuvanshi (2013)
Microwave cooking	Lentils cultivated in Egypt	Lesser decrease of minerals than other preparation methods	+	Hefnawy (2011)
Microwave cooking	Common cereals, pulses and green leafy vegetables	A significant decrease in the bioaccessibility of Se, SeMet and SeCys ₂ . ^c	–	Khanam and Platel (2016)
Peeling	Cooked carrots	A lower, unchanged or higher content of mineral ingredients	±	Biezanowska-Kopeć et al. (2016)
Pressure cooking	Common cereals, pulses and green leafy vegetables	An overall significant decrease in the Se content	–	Khanam and Platel (2016)
Radiation	Cucumber	A better effect to retain various Se-forms than microwave cooking	–	Rahman, Roy, Sajib, Sarkar, and Hussain (2015)
Roasting	Iodized salt	Reducing iodine content up to 6%	–	Geetanjali et al. (1995)
Soaking	Brown rice cultivar	High loss of Fe (50%) and Zn (>64%)	–	Albarracín, González, and Drago (2013)
Sonication	Apple juice	Mineral contents (Na,K,Ca,P,Mg,Cu,Zn) notably increased	+	Abid et al. (2014)
Steaming	Iodized salt	Iodine decrease (20%)	–	Geetanjali et al. (1995)
Storage ^d	Fruits and vegetables	Reducing Ca, Mn, Fe, Zn and Cu during storage period	–	Bouzari, Holstege, and Barrett (2015)

^a Different boiling methods (normal pan and pressure cooker).

^b Higher mineral contents in the frozen products using the modified technology (cooking-freezing-defrosting-heating in a microwave oven), compared to the traditional method (blanching-freezing-cooking).

^c SeMet and SeCys₂ are and, respectively.

^d Refrigerated and frozen storage.

and micro - (Fe, Zn, Cu, Mn) minerals (Table 3). It seems that the maximum loss of minerals can happen during common heating in the kitchen because these essential components can readily leach into hot cooking fluids. Heat-induced chemical reactions like Maillard-browning reaction which happens between reducing sugars and amino acids or proteins can form compounds that bind minerals tightly. The resulted products from this reaction will be more resistant to digestion process in GI tract and subsequently their mineral-binding characteristics will remain intact (Hazell, 1985). In addition, heating treatments can significantly deteriorate vitamin C which is considered a main component in increasing Fe uptake (Hallberg, 1981). But, Hefnawy (2011) by scrutinizing the effect of processing methods on mineral composition and anti-nutritional factors in lentils found that microwave cooking (MWC) compared with boiling and autoclaving led to a lower decrease in Ca, Mg, K, Na, P, Fe and Cu values. This researcher proposed MWC for lentil preparation, not only for improving nutritional quality, but also for reducing cooking time (Hefnawy, 2011). A rise in content and bioavailability of micro- and macro-minerals was reported for dehydrated Cabernet and Merlot

grapes (Panceri, Gomes, De Gois, Borges, & Bordignon-Luiz, 2013). Furthermore, Yadav and Salil (1995) earlier demonstrated that blanching of spinach leaves can remarkably improve HCl-extractable Ca and Zn, so that this fact can appear in the acidic environment of the stomach (Table 3). Use of novel processing techniques; such as, sonication and high pressure has shown positive effects on food liquids of apple juice, milk and soy-smoothies (Abid et al., 2014; Andrés, Villanueva, & Tenorio, 2016).

One of the most important concerns in the processing of mineral rich foods is formation of strong complexes between bivalence elements (e.g., Ca²⁺, Mg²⁺, Zn²⁺, Fe²⁺, Cu²⁺), and, phytate, fiber, and compounds of tannin and lectin. Dephytization introduced as a good process to break-down the phytates of infant cereals to improve the uptake efficacy; transport level and release rate of minerals such as Fe, Zn and even Ca (Frontela, Scarino, Ferruzza, Ros, & Martínez, 2009). Earlier examinations revealed that debittering of pea seeds and germination of African yam beans can potentially result in the decrease/removal in phytic acid and accordingly can increase the bioavailability of minerals present in these raw materials (Ene & Obizona, 1996; Ertaş & Bilgiçli, 2014).

However, Mercier (1993) found that the extrusion process can inactivate phytase enzyme in the processed foods.

As well, oxalic acid and its partially or fully ionized salts (oxalates) can create the soluble - (at pH = 2; K⁺, Na⁺ and NH⁴⁺) and insoluble - (at pH = 6; Ca²⁺, Mg²⁺ and Fe²⁺) complexes with mineral elements. Therefore, foods containing oxalates can reduce absorption of main macro- and micro-minerals in the body. However, Zn absorption was not affected by oxalic acid added to the diets of Zn-deficient rats (Welch, House, & Van Campen, 1977). As pH is an essential factor to form the oxalate complexes, their acid sensitivity should be considered. Noonan and Savage (1999) pointed out that the high content of oxalates in tea leaves, spinach and cocoa (300–2000 mg oxalic acid/100 g) can be significantly decreased using their soaking or cooking processes.

3. Mineral biofortification

Biofortification is an excellent breeding process for enhancing quantity and quality of nutrients in a specific crop such as rice, wheat, maize, common beans and some other cereals and legumes. Generally speaking, the agricultural crops at the growing phase are mainly targeted to implement mineral biofortification (Dwivedi et al., 2012). This process is taken into account as an economical and sustainable solution to address malnutrition in poor and developing countries because it targets staple foods that are daily consumed. Dwivedi et al. (2012) listed three major biofortification strategies including agronomic (soil amendments or foliar application), conventional breeding (radiation and chemically induced mutagenesis), and transgenesis (recombinant DNA and genetic engineering). Although most mineral biofortification works have been performed via conventional breeding based on the application of transgenic technology, breeding pipelines using standard varieties and non-genetically modified organism methods are used to form the first delivery products (Pfeiffer & McClafferty, 2007).

Since Fe, Zn, Ca, Se and I are considered as the most limiting mineral micronutrients in the plant-based diets, many researchers

have focused on biofortification of these essential minerals. For instance, Goto, Yoshihara, Shigemoto, Toki, and Takaiwa (1999) Fe-fortified rice seeds via overexpressing a soybean ferritin gene and increased the Fe accumulated in the endosperm three-times higher than non-fortified rice seeds. Biofortification of carrots with increasing Ca content was also performed by Morris, Hawthorne, Hotze, Abrams, and Hirschi (2008) via the gene overexpression of CAX1. They claimed that consumption of the modified carrots can twice deliver the Ca amount into the bones of experimental animals due to higher amounts of Ca maintained in the edible portion, and subsequently improved the amount of the Ca absorbed in human body by just over 40%. Similar Ca-fortifications have been conducted through the overexpression of CAX1 gene from Arabidopsis for potato tubers (Kim et al., 2006; Park et al., 2005a) and tomatoes (Park et al., 2005b). Overexpression of CAX1 gene has favorable potentials to enhance the bioavailability of other minerals because the Ca/H⁺ anti-porter transports other minerals besides Ca. The results obtained by Park et al. (2005a) and Kim et al. (2006) also showed that Ca-fortification can highly extend shelf life of the modified formulations. Blasco et al. (2008) demonstrated the possibility of considering I (mainly under the form of I₂) at certain rates to increase the antioxidant response in lettuce and, thus, the nutritive quality, sans inflicting phytotoxic impacts. Also, White and Broadley (2009) examined aspects of soil science, plant physiology and genetics supporting crop biofortification programs, as well as agronomic and genetic approaches done to bio-fortify food crops with the mineral elements most commonly lacking in human diets including Fe, Zn, Cu, Ca, Mg, Se and I. A list of mineral biofortification mechanisms for selected agricultural crops is illustrated in Table 4.

Haas et al. (2005) evaluated the effectiveness of consuming high-Fe rice during a 9-months feeding trial with a double-blind dietary intervention in Filipino women. They concluded that the consumption of biofortified rice without any other dietary variations is valuable in improving Fe stores of women with Fe-poor diets in the developing countries. Hama et al. (2012) studied

Table 4
Mineral biofortification strategies for some agricultural crops.

Mineral	Crop	Biofortification strategy	Reference
Fe	Rice	Overexpressing a soybean ferritin gene	Goto et al. (1999)
Fe	Rice/barely	<i>Nicotianamine</i> synthase gene expression	Higuchi et al. (2001)
Fe	Rice	Activation of the <i>nicotianamine synthase</i> gene	Lee et al. (2009)
Fe	Rice	Introduction of multiple Fe homeostasis genes	Masuda et al. (2012)
Fe	Cowpea	Using Fe fertilizers in the form of FeSO ₄ (25 μM/L)	Márquez-Quiroz, De-la-Cruz-Lázaro, Osorio-Osorio, and Sánchez-Chávez (2015)
Fe/Zn	Durum wheat	Whole usage of Zn fertilizers/transgenic methods for the Fe-dense crop	Cakmak, Pfeiffer, and McClafferty (2010)
Zn	Durum wheat	Soil- and foliar- applications of nitrogen and Zn fertilizers	Kutman, Yildiz, Ozturk, and Cakmak (2010)
Fe/Zn	Rice	Fundamental overexpression of the gene family of osnas	Johnson et al. (2011)
Fe/Zn	Rice	Introducing barley genes involved in the synthesis of phytosiderophore	Masuda et al. (2008)
Zn	Wheat/rice/bean	Application of foliar Zn fertilizer	Ram et al. (2016)
Ca	Carrot	Overexpressing the CAX1 gene	Morris et al. (2008)
Ca	Tomato	Overexpressing the CAX1 gene from Arabidopsis (<i>Arabidopsis thaliana</i>)	Park et al. (2005b)
Ca	Potato tube	Overexpressing the CAX1 gene from Arabidopsis	Kim et al. (2006)
Ca	Potato tube	Expressing the CAX gene from Arabidopsis	Park et al. (2005a)
Se	Lettuce	The use of nutritive solution of Seas selenate at low contents	Ramos et al. (2010)
Se	UK-grown crops	Application of foliar Se fertilizer (Na ₂ SeO ₃ and Na ₂ SeO ₄) ^a Breeding and genetic variations for different species	Broadley et al. (2006)
Se	Chickpea	Application of foliar Se fertilizer (Na ₂ SeO ₃ and Na ₂ SeO ₄)	Poblaciones, Rodrigo, Santamaria, Chen, and McGrath (2014)
Se	Pea	Foliar nutrient solution with Na ₂ SeO ₃ and Na ₂ SeO ₄	Poblaciones, Rodrigo, and Santamaria (2013)
Se	Lentil	Foliar nutrient solution with Na ₂ SeO ₃ and Na ₂ SeO ₄	Thavarajah et al. (2015)
I	Wheat	Fertigation (5% KIO ₃ solution)	Ren, Fan, Zhang, Zheng, and DeLong (2008)
I	Lettuce	Nutrient solution (13–129 μg/L I ⁻ or IO ₃ ⁻)	Voogt, Holwerda, and Khodabaks (2010)

^a Sodium selenite (Na₂SeO₃), Sodium selenate (Na₂SeO₄).

capacity of non-GMO biofortified pearl millet (*Pennisetum glaucum*) for increasing Fe and Zn contents and estimated their bioavailability during abrasive decortication in terms of the molar ratio of phytate to mineral. The Fe (6.7–7.2 mg/100 g DM) and Zn (4.1–5.6 mg/100 g DM) contents in the biofortified varieties were much higher than in the common ones. These scientists obtained no incredible enhancement in Fe bioavailability in the biofortified varieties because phytate and other chelating factors were only partially removed during decortication process. However, Zn absorption with regard to phytate-to-Zn ratios of 6–18 could be improved by using these biofortified varieties in the production of processed foods. Kodkany et al. (2013) by isotope extrinsic labeling techniques and analyses of duplicate diets also determined the absorption of Fe and Zn from pearl millet biofortified with two micronutrients in Indian young kids. They concluded that absorbed quantities of Fe and Zn are more than adequate to meet the physiological requirements for these micronutrients when Fe- and Zn-biofortified pearl millet is fed to the children.

Poblaciones and Rengel (2016) have recently applied soil and foliar Zn biofortification in field pea and then investigated the Zn accumulation and bioavailability in raw and cooked seeds. As pea seeds could noticeably improve Zn content in the human food chain, they found that field pea may be a suitable crop to be included in Zn biofortification schedules. In addition, their findings proved that the use of 8 mg ZnSO₄·7H₂O/kg soil and 0.25% (w/v) ZnSO₄·7H₂O foliarly was the most suitable combination for increasing Zn content in pea grains (>40 mg Zn/kg) with an ideal bioavailability. Even though the cooking process led to a significant loss in Zn content (about 30%); its bioavailability value stayed well. An earlier study on Zn-biofortification (as ZnSO₄ solution) of soybean sprouts and its bioaccessibility in the sprouts was done by Zou, Xu, Hu, Pang, and Xu (2014). This research demonstrated that the edible portions of Zn-enriched soybean sprouts significantly had more total content, bioaccessible content and bioaccessibility rate of Zn than those of water-germinated soy sprouts. Even if soaking leaks of Fe, Mn and Cu from soybeans to steeping media happened to some degrees, there were no significant differences in content of these minerals in edible portions of soybean sprouts between ZnSO₄ solution and water germinations (Zou et al., 2014).

Ca-biofortification and Ca-bioaccessibility in soilless production of “baby leaf” vegetables (BLVs) including basil, mizuna, tatsoi and endive was studied by D’Imperio et al. (2016). Using agronomic approaches, they applied a floating system containing the nutrient solution with two levels of Ca (100 and 200 mg/L) to produce the biofortified BLVs and evaluated Ca-bioaccessibility based on an *in vitro* digestion test. A significant improvement in Ca-enrichment (9.5%) was found in the highest level used of Ca (200 mg/L) without influencing BLVs growth rate, oxalate amounts and commercial quality. Applying Ca-biofortification process can increase release of Ca in the digested fluid of BLVs. While the enhancement degree of Ca release showed a significant growth or mizuna and basil by 25 and 33%, respectively, but there was no significant difference in Ca treatments between tatsoi and endive (D’Imperio et al., 2016).

4. Fortification of processed foods by direct addition of minerals

One of the most important global public health problems especially for preschool children and pregnant women in low-income countries is mineral deficiencies of Fe, Zn, Ca and I. Among multiple strategies to control deficiency of minerals, fortification is a current favorable technique to improve the intake of minerals without causing a change in the existing dietary patterns particularly in countries where existing food sources and/or limited access fail to supply adequate levels of micronutrients in the food

regime (Hurrell, 1997). Bouis, Hotz, McClafferty, Meenakshi, and Pfeiffer (2011) had represented that fortified staple foods compared to supplements or fortified food products cannot deliver equally high concentrations of minerals and even vitamins per day. According to a general principle, nutrient fortification not only should have no adverse effect on the sensory attributes of the final product, but also should not reduce the consumer demand for the consumption of fortified-food. This process should effectively increase the nutrient absorption and bioavailability and should subsequently have a positive effect on the consumer’s healthiness. Nevertheless, development and design of a fortification technology that makes the bioavailable mineral sources more compatible with the food vehicle has been remained a challenge.

Fe deficiency arises when physiological demands are not met because of scarce ingestion, uptake or usage, or ample Fe dissipations. The most current reason of anemia - a deficiency of RBCs—also is Fe-poor diets and other Fe deficiencies that can result in complications; such as, fatigue, shortness of breath, and even heart failure (Zimmermann et al., 2004). Consistent with the data of Martinez-Navarrete et al. (2002), recommended daily intake (RDI) of dietary of Fe for normal infants, children, adult male and female, postmenopausal women, enceinte and lactating mothers are 1, 10, 12, 15, 10, 27 and 10 mg daily, respectively. Although Fe salts are usually applied to fortify the food formulations, their bioavailability amounts and pro-oxidant properties are dissimilar.

Fe salts used in fortification of food materials are classified into three groups (Hurrell, 1997):

- (I) Freely water-soluble (e.g., ferrous sulfate (FeSO₄), ferrous gluconate (C₁₂H₂₄FeO₁₄), and ferrous lactate (C₆H₁₀FeO₆)). These salts have high bioavailability, however, freely interact with fortified foods can highly change the sensory attributes because Fe catalyzed oxidation processes and thus accelerate fat rancidity speed. The nutritional value of a food component can be considerably decreased by the formation of catalytic oxidation reactions because it may react with other nutrients like vitamins, amino acids and much more.
- (II) Poorly water-soluble or soluble in a dilute acid (e.g., ferrous fumarate (C₄H₂FeO₄), and ferrous succinate (C₄H₄FeO₄)). Ideal solubility and bioavailability rates along with negligible undesirable influences on the organoleptic properties are benefits of components present in this class. Nonetheless, precipitation of these salts in neutral liquids owing to the solubility lack is taken into account as a main disadvantage. Therefore, use of these salts is suitable for solid dehydrated foods like infant cereals and chocolate drink powders.
- (III) Water-insoluble or poorly-soluble diluted acids (e.g., elemental Fe, and, ferric orthophosphate (FeO₄P) and pyrophosphate (Fe₄O₂₁P₆)). Though these Fe-based compounds do not change sensory or nutritional value of the foods, they have a low solubility and bioavailability.

The Zn-RDI is about 15 mg for growth and development in healthy adults (Food and Nutrition Board, 2001, pp. 37–46). Gülsereen, Fang, and Corredig (2012) declared that deficiency of this essential mineral is estimated more than 40% in the world whole population. It can therefore be said that Zn insufficiency is the most common micronutrient deficiency after Fe-deficiency, in the world particularly in developing countries. The low consumption of animal-source foods with high Zn bioavailability and *vice versa*, high consumption of plant diets based on cereals and legumes with very low Zn-bioavailability (due to high amounts of phytate) are led to the high occurrence of Zn deficiency in these countries (Gibson, 1994).

Zn deficiency can be characterized by growth retardation,

appetite loss, and weakened function of immune system like delayed healing of wounds. Undesirable difficulties including eye and skin lesions, hair loss, weight loss or impotence, delayed sexual maturation, diarrhea, taste abnormalities, and mental lethargy can be also occurred in more critical cases of Zn shortage (Maret & Sandstead, 2006).

There are a number of accessible Zn salts to fortify food products; such as, zinc oxide (ZnO), zinc sulfate (ZnSO₄), zinc acetate (C₄H₆O₄Zn) and zinc chloride (ZnCl₂). Yet, ZnO and ZnSO₄ are most commonly Zn-salts used in the food industries because of their low cost. Although ZnSO₄ is more expensive, this salt due to its better solubility can theoretically provide more reliable absorption than ZnO (Kahraman & Ustunol, 2012).

Heaney (1993) reported that Ca-RDI (mg/kg/day) to be beneficial to bone mass at all stages of life for adolescent, pregnant and nursing women, and people aged more than 65 years is between 1200 and 1500. Satisfactory ingestion of this water-soluble element not only can decrease osteoporosis risk by reducing Ca release rate from bone fractions, but also can prevent certain diseases and disorders; for example, colon cancer, kidney stones, hypertension and lead uptake (Sirisoontarak, Limboon, Jatuwong, & Chavanalikit, 2016). It is very important to fortify food products in order to increase Ca absorption and availability. Yet, fortification process of foods with this macro-mineral may lead to the unwanted interactions including protein coagulation and precipitation providing unfavorable defects like chalkiness and bitter taste in the final food formulations (Singh, Bohidar, & Bandyopadhyay, 2007).

A number of properties accompanying with the particular foods; such as, solvability, Ca level, taste sensory character and bioavailability rate are usually considered to select the suitable Ca source for food enrichment. Another important factor to assess the best Ca-fortifying source is economic considerations. Based on reference of Münchbach and Gerstner (2010), the usual Ca sources to fortify milk and dairy products include the following:

- (I) Inorganic salts; such as, calcium carbonate (CaCO₃), and calcium phosphate (Ca₃(PO₄)₂),
- (II) Ca from animal origin (e.g., calcium from milk; mainly composed of Ca₃(PO₄)₂) or vegetables (e.g., seaweed Ca; mostly composed of CaCO₃)
- (III) Organic salts; for example, tri-calcium citrate (C₆H₅O₇)₂Ca₃·4H₂O), calcium lactate (C₆H₁₀CaO₆), calcium lactate gluconate (C₉H₁₆CaO₁₀), and calcium gluconate (C₁₂H₂₂CaO₁₄).

Iodine (I) is an essential micronutrient for the production of thyroid hormone. Tulyathan and Prunglumpu (2009) demonstrated that inadequate use of this essential mineral can result in an enlargement in the thyroid gland or goiter disorder. Age and life stage highly affect the RDI of I. For instance, I-RDI (μg/day) for the adult women and men (19–70 years old), pregnant women and lactating mothers is 150, 15, 220 and 270, respectively. A stable, effective and cheap way to ensure sufficient intake of I in the body is the salt fortification with I salts; such as, potassium iodate (KIO₃) and potassium iodide (KI). Of course, I stability in salt is highly depended on the different environmental and storage conditions. The FDA recommended range for salt fortification is 46–76 mg iodide/kg, but iodized salt in the U.S. is fortified at 45 mg iodide/kg (Dasgupta, Liu, & Dyke, 2008). Sometimes, the salt iodization is an unfeasible process in some regions of the world. For this reason, other iodized foods (rice or wheat-breads, biscuits, etc.), and/or administered oral or intramuscular iodized oil supplements is suggested (Leung et al., 2012).

Low dietary Se intake can lead to a number of deficiency symptoms including hair loss and skin and fingernail discoloration,

low immunity, permanent fatigue, foggy head anxiety symptoms, depression concentration problems, reproductive issues in women and men and hypothyroidism disease (Lockitch, 1989). Se-RDI (μg/day) for the adult men and women (>14 years old), pregnant women and lactating mothers is 55, 55, 60 and 70, respectively. Se enrichment for food products is not extensively applied, except for clinical products including enteral and parenteral nutrition products and infant formulas. However, some foods are fortified with sodium selenite (Na₂SeO₃ or Na₂O₃Se), and sodium selenate (Na₂O₄Se) to decrease the Se deficiency and also to obtain *in vivo* data about their bioaccessibility, absorption, maintenance and health risk by human subjects (Van Dael, Davidsson, Åoz-Box, Fay, & Barclay, 2001).

Practical fortification of several agricultural and food products by direct incorporation of Fe, Zn, Ca, I and Se is given in Table 5. This Table also represents the bioavailability of minerals and their negative quality effects on the final fortified-products. In general, mineral fortification could improve the bioavailability and absorption of these bioactive elements. No substantial variations have been found in the quality attributes determined for the fortified and non-fortified products. Nonetheless, analysis of thiobarbituric acid (TBA) for fortified yogurts (El-Kholy, Osman, Gouda, & Gharee, 2011), and Feta cheese (Jalili, 2016) showed an increase in the oxidation values by increasing concentration of incorporated minerals. Similarly, fortification of Zn indicated a small attenuator effect on texture characteristics of the Cheddar cheese and chapattis baked based on whole wheat flours (Table 5). The mineral fortification causes a disapproving taste in some fortified-products. Therefore, taste masking of unfavorable food tastes through encapsulation techniques can be a key strategy in developing of food formulations. On the other hand, the stability and bio-accessible content of minerals in the fortified products can be significantly reduced during the storage period. This fact was observed for finger millet flour fortified with Fe₄O₂P₆, basmati rice grains fortified with ferric sodium ethylenediaminetetraacetate (NaFeEDTA) and FeSO₄ and parboiled milled rice fortified with KI and KIO₃ (Table 5).

5. Nanoencapsulation of minerals

Nanoencapsulation is considered as a novel technology to cover bioactive substances into a matrix at a size lower than 1000 nm. This method can possibly present new delivery systems for minerals and other functional ingredients with enhanced physico-chemical stability, water-solubility, bioaccessibility and bioavailability (Katouzian and Jafari, 2016; Faridi Esfanjani and Jafari, 2016). Since use of mineral nanocapsules can considerably increase the production of novel functional food formulations, a high focus on the design of applicable approaches has been recently done to nanoencapsulate minerals for fortifying food products (Jafari & McClements, 2017). Investigations also show that the development of mineral ions/salts-nanocapsules has been based more on chemical processes (nanoliposome, nanoemulsification, cyclodextrin inclusion, solid lipid nanoparticles, biopolymeric nanoparticles, ionotropic gelation and complex coacervation) rather than physico-mechanical ones. In our appraisal, we realized the chemical processes much more practical (>95%) than the physico-mechanical ones to produce the mineral nano-particles.

With regard to the current disadvantages in fortifying food products with mineral salts through direct addition/mixing, application and incorporation of minerals nanoencapsulated with a variety of coatings into food and drug formulations can provide unique benefits in developing novel functional products with improved physicochemical and sensorial characteristics. Nano-encapsulated mineral salts can have advantages; such as, inhibition

Table 5
Mineral fortifications of some agricultural and food products and their effects on the quality and bioavailability.

Foods	Mineral type/form	Negative quality impacts and bioavailability amount	Reference
Ready-to-eat milk-based formula	Se: selenite/selenate	Selenite and selenate administered within normal dietary intake ranges were equally well retained in healthy men, but high differences in absorption and urinary excretion was observed.	Van Dael et al. (2001)
Yogurt	Fe: FeCl ₃	Slightly higher scores of oxidized flavor than the control sample	Hekmat and McMahon (1997)
Yogurt Domiati cheese with buffalo milk	Fe: NH ₄ Fe(SO ₄) ₂ ; (NH ₄) ₂ Fe(SO ₄) ₂ ·6H ₂ O No significant effect on the chemical composition and organoleptic traits by fortifying all the mineral salts Declining sensory scores by enriching Zn and Fe salts at high levels	Increasing the oxidation speed assessed by TBA test Zn: ZnSO ₄ , Zn(O ₂ CCH ₃) ₂	El-Kholy et al. (2011) El-Din, Hassan, El-Behairy, and Mohamed (2012)
Edam cheese	Zn: Zn(O ₂ CCH ₃) ₂ (H ₂ O) ₂ , ZnCl ₂ , ZnSO ₄	Promotion of human dietary Zn intake. Adding ZnSO ₄ in comparison with two other Zn-salts was less effective in improving sensory properties.	Abd-Rabou, Zaghoul, Seleet, and El-Hofi (2010)
Petit suisse cheese	Fe: C ₁₂ H ₂₄ FeO ₁₄	A high rate in Fe bioavailability for the industrial fortified sample was obtained	Janjetic et al. (2006)
Cheddar cheese	Zn: ZnSO ₄	Zn-fortified cheese with 5 times more Zn than the control had firmer texture, but there were no variances in their organoleptic attributes and overall quality.	Kahraman and Ustunol (2012)
Feta cheese	Fe: FeSO ₄ , FeCl ₃	A slight rise in lipid oxidation (using TBA test) was found	Jalili (2016)
Finger millet flour	Fe: C ₄ H ₂ FeO ₄ ; Fe ₂ O ₂₁ P ₆ Co-fortificants: EDTA and folic acid	Decreasing the bio-accessible Fe content in the flour fortified with Fe ₄ O ₂₁ P ₆ after 30 d-storage. Insertion of EDTA and folic acid, with the Fe salts, significantly increased the Fe-bioaccessibility. Heat processing of the flours improved the Fe- bioaccessibility from the unfortified and fortified flours.	Tripathi and Patel (2010, 2011)
Milled rice seeds	I: KI	Iodine enrichment of in the milled seeds using flour gel coating technique Washing/cooking of the iodine-enriched rice resulted in about 99% and 94% retention of original iodine, respectively. Significant excretion of iodine in the urine of healthy male and female was found	Tulyathan and Prunglumpu (2009)
Milled rice seeds	Ca: C ₆ H ₁₀ CaO ₆	Acidification led to a decrease in lightness and cooked rice hardness and an increase in total solid loss and pasting viscosity. Although panelists accepted the fortified rice, acetic acid taste retained. Enhancing soaking temperature induced higher Ca-penetration to rice kernels but Ca was lost more easily after washing.	Sirisoontarak et al. (2016)
Parboiled milled rice	I: KI, KIO ₃	Iodine content in the fortified rice decreased significantly after storage for 5 months, but it did not affect pasting attributes of parboiled milled rice.	Tulyathan, Laokuldiolk, and Jongkaewwattana (2007)
Basmati rice grains	Fe: NaFeEDTA; FeSO ₄	Quite stability of Fe; folic acid loss during the storage of edible-coated Fe-folate fortified rice.	Ahmed, Butt, Sharif, and Iqbal (2016)
Whole wheat flour	Zn/Fe: ZnO, Elemental Fe, ZnSO ₄ , NaFeEDTA	Fortificants had a small deteriorative impact on textural properties of chapattis	Akhtar, Anjum, Rehman, Sheikh, and Farzana (2008)
Chapatti (Bread)		The flour enriched with NaFeEDTA in mixture with ZnSO ₄ or ZnO stored under controlled conditions had the highest organoleptic acceptability for chapattis fortified with the minerals.	Akhtar and Anjum (2007)
Bread	Zn: H ₁₄ O ₁₁ SZn	A significant increase in serum Zn and Fe levels in all groups except in the control Zn- and Fe-absorption in the group consuming high-Zn bread was significantly greater than that in the group that received low-Zn bread.	Badii et al. (2012)
Oat biscuits	Premix (11 minerals and 13 vitamins)	Less liked than commercial ones, due to flavor imparted by whey protein fortification	Tsikritzi, Moynihan, Gosney, Allen, and Methven (2014)

of interactions with substances present in the created matrix, discoloring avoidance, off-flavor reduction by masking of taste and smells, controlled release of the mineral components, perfect preservation in the production and storage processes and improvement of the product's physical properties (Gharibzahedi and Jafari, 2017).

During the recent two decades, most studies of researchers have been concentrated on the mineral fortification of dairy products and table salt with nanoencapsulated minerals especially Fe, Ca, Zn and I. Fe encapsulated forms used as core materials in fortifying dairy products are electrolytic-Fe, FeSO₄, FeSO₄·7H₂O, C₄H₈FeN₂O₄, NH₄Fe(SO₄)₂ and C₆H₁₀FeO₆. Encapsulated forms of two Ca-salts of tricalcium phosphate (Ca₃(PO₄)₂) and calcium citrate (Ca₃(C₆H₅O₇)₂) have also been applied to fortify soy-yogurt and soy-milk. The most popular encapsulated formulas of iodine and Fe for fortifying edible salts are KI and KIO₃, and, C₄H₂FeO₄ and FeSO₄,

respectively. Nevertheless, some attempts have been made to develop fortified bakery products based on flours nano-encapsulated with minerals as suitable vehicles (Gharibzahedi and Jafari, 2017).

6. Conclusions and future trends

This study was an updated and critical review on functions, absorption and bioavailability/bioaccessibility mechanisms, quantitative approaches determining bioavailability rate (especially isotopic methods) and some food enrichment strategies of minerals. Mineral bioavailability can be enhanced through bio-fortification of agricultural crops and direct fortification of processed foods (cereals, dairy and bakery products) with different minerals. Mineral bioavailability in human groups who have consumed biofortified crops has been variable due to the presence

or absence of interactions between essential minerals and some antinutritional components; such as, phytates, oxalates and other chelating agents. Although a significant difference in sensory attributes (astringency, metallic taste, smell, appearance/color and general acceptability) between the products fortified with direct addition of minerals and the control ones is found, this enrichment process do not affect notably other critical quality characteristics. This drawback can be successfully solved using polymeric and non-polymeric coating materials to micro/nanoencapsulate the target essential minerals. Crucial functionality of minerals with an improved release control can be sufficiently provided using encapsulation techniques. This promising process has been recently employed to produce some mineral-fortified foods with the prolonged shelf life and decreased nutritional and sensory quality losses. The novel and stable delivery systems with the highest bioavailability rate can be thus designed based on current technical progresses in terms of efficient micro/nanoencapsulation techniques for a wide range of minerals.

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