Iron (Fe)

Food:

	Total	Heme	Non-heme
	mg/100g	mg/100g	mg/100g
Beef steak prepared	2.8	1.8	1.0
Egg boiled	2.4	0.0	2.4
Bread wholemeal	1.7	0.0	1.7
Spinach boiled	2.4	0.0	2.4
Sausage pork prepared	1.2	0.5	0.7
Tuna cooked	0.9	0.2	0.7
Pasta wholemeal boiled	1.7	0.0	1.7

(Dutch Food Composition Database, NEVO)

Main functions:

- Stores and transports oxygen to all of the tissues
- Produces energy
- Protects cells against the damaging effects of free radicals
- Protects itself against bacteria by producing free radicals as part of the immune response

For scientific sources, please contact **info.nutritionscience@dsm.com.**

Iron (Fe)

Iron is involved in the formation of red blood cells and hemoglobin, oxygen transport, the immune system, and cognitive development and function. As it is not made in the body, sufficient levels must be absorbed from the diet. Iron deficiency is the number one nutritional disorder in the world, according to the World Health Organization.

Functions

'Heme' is an iron-containing compound found in a number of important proteins such as hemoglobin and myoglobin, which are involved in the transport and storage of oxygen. Hemoglobin, the primary protein found in red blood cells, carries oxygen from the lungs to body tissue, while myoglobin functions in the transport and short-term storage of oxygen in muscle cells, helping to match the supply of oxygen to the demand of working muscles. Since iron is a key component of both proteins, which are essential for oxygen transport throughout the body, low iron levels may compromise performance and intense physical activity and may lead to fatigue and tiredness.

'Cytochromes' are heme-containing compounds that are critical to cellular energy production through their roles as electron carriers in mitochondrial electron transport. Cytochrome P450 is a family of enzymes that functions in the metabolism of a number of important biological molecules, as well as the detoxification and metabolism of drugs and pollutants. Non-heme iron-containing enzymes are also critical to energy metabolism.

'Catalase' and 'peroxidases' are heme-containing enzymes that protect cells against potentially damaging highly reactive oxygen species (e.g., H2O2). In addition to such antioxidant effects, heme-containing enzymes can catalyse (increase the rate of a reaction) the production of reactive oxygen species used to kill bacteria as part of the immune response.

When cellular oxygen concentration drops below a critical threshold ('hypoxia'), as experienced by those who live at high altitudes or those with chronic lung disease, compensatory physiologic responses such as increased red blood cell formation, blood vessel growth, and production of certain enzymes, is induced. The activation of genes, coding for enzymes that play an important role in responses to inadequate oxygen supply, is an iron-dependent process.

In addition, an iron-dependent enzyme is required for DNA synthesis; thus, iron is required for a number of vital functions, including growth, reproduction, healing, and immune function.

The **European Food Safety Authority (EFSA)**, which provides scientific advice to assist policy makers, has confirmed that clear health benefits have been established for the dietary intake of iron in contributing to:

- Normal formation of red blood cells and hemoglobin
- Normal oxygen transport in the body
- Normal energy-yielding metabolism
- Normal function of the immune system
- Normal cognitive development
- Normal cognitive function
- Normal cell division
- The reduction of tiredness and fatigue

Dietary sources

Iron from food comes from two forms: heme and non-heme. Heme iron mainly comes from the hemoglobin and myoglobin in meat, poultry, and fish. In addition to heme iron, meat and fish products also contain some non-heme iron. Dried beans and peas, legumes, nuts and seeds, whole grains, dark molasses and green leafy vegetables, dairy products, and iron salts added to foods and supplements are all sources of non-heme iron.

Absorption and body stores

The amount of iron in food and supplements that is absorbed is influenced by many factors such as nutritional status of the individual, but more importantly by the food matrix and the form of iron that is consumed. Individuals who are anemic or iron deficient absorb a larger percentage of the iron they consume (especially non-heme iron) compared to those who are not anemic and have sufficient iron stores.

Heme iron, which is found in meat, poultry, and fish, is readily absorbed by the intestines and less affected by other dietary factors. The proper absorption of non-heme iron (form of iron in plant-based foods), on the other hand, is strongly influenced by the presence of anti-nutritional factors such as polyphenols and phytate in the same meal. Vitamin C, for example, helps the absorption of plant-based sources of iron, whereas calcium, bran, tea and unprocessed whole grain products inhibit iron absorption. Phytase is an enzyme that has been shown to increase absorption of iron when added to plant-based foods. It also provides additional benefits regarding phosphorus, calcium, zinc and amino acids. Phytase significantly decreased iron and zinc deficiency in children indicating the potential of this strategy for preventing and treating iron deficiency anemia.

Most of the iron in the body is found in the red blood cells that carry oxygen to all of the tissues (hemoglobin) and in muscle cells (myoglobin). Excess iron is stored in the liver, bone marrow, spleen, and muscles.

Physiological interactions

- Vitamin A supplementation has been shown to have beneficial effects on iron deficiency anemia and improve iron status among children and pregnant women.
- Adequate copper nutritional status appears to be necessary for normal iron metabolism (absorption and transport) and red blood cell formation.
- Phytate (occurring in plant-based diets, rice, flour), polyphenols (occurring in vegetables, fruits, some cereals and legumes, tea, coffee and wine), calcium, and proteins (in milk, eggs, soybeans) have been found to decrease absorption of non-heme iron when consumed together in a single meal.
- Ascorbic acid (vitamin C) increases the absorption of plant-based sources of iron.
- Minerals in plant-based foods are often bound to phytic acid. Phytase is an enzyme that has been shown to release the bound minerals from phytic acid to make them available for absorption. Therefore, phytase improves iron absorption when added to plant-based foods.

Deficiency

Significant iron deficiency leads to anemia (low levels of iron in the blood), which results in diminished oxygen transport. Iron deficiency is a major cause of nutritional anemia but nutritional anemia can also be caused by a lack of riboflavin, vitamin B6, folate, vitamin B12, and vitamin A. Iron deficiency can be the result of high requirements during pregnancy, heavy menstrual bleeding, or the rapid growth that takes place during infancy, early childhood, and adolescence. For this reason, pregnant women, young women during their reproductive years, and children tend to be the highest risk of becoming deficient in iron. Iron-deficiency affects 17% of the preschool children and 21% of the women of reproductive age worldwide. Iron deficiency or iron-deficiency anemia affects individuals from both high- and low-income countries. A vegetarian or vegan diet may be of concern for possible shortage of iron intake as animal-derived foods contain the most bioavailable form of this micronutrient.

The most common symptoms of anemia are weakness and fatigue, but may also include a rapid heart rate and rapid breathing on exertion. The condition can also impair the ability to maintain a normal body temperature on exposure to the cold. In cases of severe iron deficiency, symptoms may include brittle and spoon shaped nails, sores at the corner of the mouth and a sore tongue. While more advanced iron-deficiency anemia may cause difficulty in swallowing due to the formation of webs of tissue in the throat and gullet.

Possible reduction of disease risk factors

Impaired intellectual development in children

Several possible mechanisms link iron deficiency anemia with poor mental development in children. Studies have shown that compared to children without anemia, anemic children tend to move around and explore their environment less, which may lead to developmental delays, poor school achievement, and behavior problems. However, it is difficult to separate the effects of iron deficiency anemia from other types of deprivation in such studies.

Lead toxicity

A number of population studies have found iron deficiency to be associated with increased intestinal absorption and higher blood levels of lead in young children. The use of iron supplementation in lead poisoning should be reserved for those individuals who are truly iron deficient or who experience long-lasting lead exposure, such as continued residence in lead-exposed housing.

Pregnancy complications

Population studies provide strong evidence of a relationship between severe anemia in pregnant women and adverse pregnancy outcomes, such as low birth weight, premature birth, and maternal mortality. While iron deficiency can be a major contributory factor to severe anemia, evidence that iron deficiency anemia is a reason for poor pregnancy outcomes is still lacking.

Impaired immune function

Sufficient iron is critical to several immune functions, including the development and division of white blood cells, and the generation of free radicals, which are used for killing infectious agents (e.g. bacteria). Despite the critical functions of iron in the immune response, the role of iron in infections is controversial as there is debate about the possibility that iron supplements or iron-fortified foods may increase the incidence of certain types of infections. However, recent evidence suggests that iron supplementation does not adversely affect children when regular malaria surveillance and treatment are provided.

Restless legs syndrome

Restless Legs Syndrome (RLS) is a neurological movement disorder that is often associated with sleep problems due to unpleasant sensations, resulting in an irresistible urge to move the legs. RLS occurs in some people with iron deficiency and some RLS patients benefit from iron supplementation.

Recommended Daily Intake (RDI)

The recommended dietary intake of iron is dependent on age, gender, and other factors applied in individual countries. In Europe, many health authorities recommend daily iron intakes of 9 mg for adult males, and 15-20 mg for females of reproductive age to compensate for menstrual loss. In pregnancy, the recommended intake is 30 mg/day because of the increased iron requirement. In the U.S., health authorities recommend slightly different amounts, which can be found in the table. Vegetarians need almost twice as much iron as listed in the table, since they do not eat meat, poultry or fish, and consume less absorbable non-heme iron from plant sources mostly.

Recommended daily intakes (RDI)

Group	Life stage	Dose/day*
Infants	<6 months	0.27 mg**
Infants	7-12 months	11 mg
Children	1-3 years	7 mg
Children	4-8 years	10 mg
Children	9-13 years	8 mg
Males	14-18 years	11 mg
Females	14-18 years	15 mg
Males	19-50 years	8 mg
Females	19-50 years	18 mg
Adults	>51 years	8 mg
Pregnancy	<18 years	27 mg
Pregnancy	>19 years	27 mg
Breastfeeding	<18 years	10 mg
Breastfeeding	>19 years	9 mg

** Institute of Medicine (2001)*
*** Adequate intake (AI)*
If not otherwise specified, this table presents RDIs.

Safety

When consuming iron from dietary sources or fortified foods only, adults with normal intestinal function have a very low risk of iron overload. When taking iron supplements, it might help to take these after eating since some people may experience gastrointestinal symptoms. The low amount of iron in fortified foods is unlikely to trigger gastro-intestinal complaints.

U.S. health authorities have established that taking up to 45 mg iron/day is safe. However, the same guidance cannot be given for amounts above this level. The European Food Safety Authority (EFSA) has decided that the available data are not sufficient to establish an upper level for iron from dietary sources.

Supplements and food fortification

Iron supplements are indicated for the prevention and treatment of iron deficiency. Fortification is another widely used strategy in many parts of the world where iron deficiency is common. Frequently used foods, including wheat or maize flour, pasta, rice, milk, soy sauce, and fish sauce, are often chosen for fortification. Fortified foods and supplements can also help vegetarians reach their higher nutritional requirements for iron. Currently, some vegetarian or vegan alternatives are fortified. Many iron compounds are available for food fortification, but these compounds vary in bioavailability and may interact with other food compounds. Therefore, choosing the appropriate iron form needs proper attention. For most food products, ferrous sulfate, ferrous fumarate, encapsulated ferrous sulfate or fumarate, electrolytic iron (at twice the amount), and ferric pyrophosphate (at twice the amount) are recommended by the World Health Organization and Food and Agriculture Organization of the United Nations.