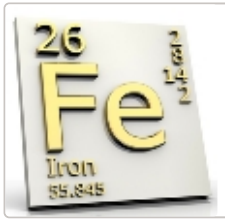

Iron

SCIENTIFIC NAME
Iron, Fe, Atomic number 26

FAMILY

Other Common Names

Overview

Iron is a trace mineral found in two ionic forms in the body. It exists in a reduced state as ferrous iron and in an oxidized state as ferric iron. Most of the iron in the body is found in the hemoglobin of red blood cells and in the myoglobin of muscle cells (1093). Iron is found in various foods, including beef, liver, lamb, pork, ham, chicken, fish, and beans (9540,9541). Historically, iron has been used to treat various skin conditions, cystitis, diarrhea, edema, excessive lacrimation, fevers, gout, hemorrhoids, perianal fistulas, tuberculosis, and other disorders (56539).

Safety

LIKELY SAFE ...when used orally and appropriately. For people age 14 and older with adequate iron stores, iron supplements are safe when used in doses below the tolerable upper intake level (UL) of 45 mg per day of elemental iron. The UL is not meant to apply to those who receive iron under medical supervision (7135,96621). To treat iron deficiency, most people can safely take up to 300 mg elemental iron per day (15). ...when used intravenously and appropriately. Ferric carboxymaltose 200 mg and iron sucrose 200 mg have been given intravenously for up to 10 doses with no reported serious adverse effects (91179). A meta-analysis of clinical studies of hemodialysis patients shows that administering high-dose intravenous (IV) iron does not increase the risk of hospitalization, infection, cardiovascular events, or death when compared with low-dose IV iron, oral iron, or no iron treatment (102861). A more recent meta-analysis of clinical studies of all patient populations shows that administering IV iron does not increase the risk of hospital length of stay or mortality, although the risk of infection is increased by 16% when compared with oral iron or no iron (110186).

LIKELY UNSAFE ...when used orally in excessive doses. Doses of 30 mg/kg are associated with acute toxicity. Long-term use of high doses of iron can cause hemosiderosis and multiple organ damage. The estimated lethal dose of iron is 180-300 mg/kg; however, doses as low as 60 mg/kg have also been lethal (15).

CHILDREN: **LIKELY SAFE** ...when used orally and appropriately (7135,91183). **LIKELY UNSAFE** ...when used orally in excessive amounts. Tell patients who are not iron-deficient not to use doses above the tolerable upper intake level (UL) of 40 mg per day of elemental iron for infants and children. Higher doses frequently cause gastrointestinal side effects such as constipation and nausea (7135,20097). Iron is the most common cause of pediatric poisoning deaths. Doses as low as 60 mg/kg can be fatal (15).

PREGNANCY AND LACTATION: **LIKELY SAFE** ...when used orally and appropriately. Iron is safe during pregnancy and breast-

feeding in patients with adequate iron stores when used in doses below the tolerable upper intake level (UL) of 45 mg daily of elemental iron (7135,96625,110180). **LIKELY UNSAFE** ...when used orally in high doses. Tell patients who are not iron deficient to avoid exceeding the tolerable upper intake level (UL) of 45 mg daily of elemental iron. Higher doses frequently cause gastrointestinal side effects such as nausea and vomiting (7135) and might increase the risk of preterm labor (100969). High hemoglobin concentrations at the time of delivery are associated with adverse pregnancy outcomes (7135,20109).

Adverse Effects

General: Orally or intravenously, iron is generally well tolerated when used appropriately.

Most Common Adverse Effects:

Orally: Abdominal pain, constipation, diarrhea, gastrointestinal irritation, nausea, and vomiting.

Serious Adverse Effects (Rare):

Orally: Case reports have raised concerns about oral or gastric ulcerations.

Cardiovascular

Endocrine

Gastrointestinal

Immunologic

Oncologic

Other

Effectiveness

EFFECTIVE

Anemia of chronic disease. Oral and intravenous iron in combination with erythropoiesis-stimulating agents (ESAs) are effective for treating anemia of chronic disease.

Details:

Iron deficiency anemia. Oral and intravenous iron are effective for treating or preventing iron deficiency anemia. The benefits of iron supplementation in people with iron deficiency without anemia are unclear.

Details:

Pregnancy-related iron deficiency. Oral iron is effective for preventing pregnancy-related iron deficiency.

Details:

POSSIBLY EFFECTIVE

Breath-holding attacks. Oral iron seems to be effective for reducing the frequency of breath-holding attacks in children with iron deficiency.
Details:

Cognitive function. Oral iron seems to be effective for improving cognitive function in children and adolescents with iron deficiency.
Details:

Heart failure. Intravenous iron seems to be effective for improving recovery in patients with heart failure and iron deficiency. It is unclear if oral iron is effective.
Details:

Restless legs syndrome (RLS). Oral and intravenous iron seem to be beneficial for RLS. The American Academy of Neurology recommends a combination of oral ferrous sulfate and vitamin C or intravenous ferric carboxymaltose for patients with RLS.
Details:

POSSIBLY INEFFECTIVE

Athletic performance. Oral iron does not seem to improve athletic performance.
Details:

Child growth. Oral iron does not seem to be beneficial for child growth.
Details:

Preterm labor. Oral iron does not seem to prevent preterm labor and may actually increase the risk in malaria-endemic regions.
Details:

INSUFFICIENT RELIABLE EVIDENCE to RATE

ACE inhibitor-induced cough. It is unclear if oral iron is beneficial in patients with this condition.
Details:

Attention deficit-hyperactivity disorder (ADHD). It is unclear if oral iron is beneficial in children with ADHD.
Details:

Child development. It is unclear if oral iron is beneficial for improving development in non-anemic children.
Details:

Esophageal cancer. It is unclear if oral iron is beneficial for esophageal cancer prevention.
Details:

Fatigue. It is unclear if oral iron is beneficial in patients with fatigue due to iron deficiency without anemia.
Details:

Inflammatory bowel disease (IBD). In patients with active IBD, intravenous iron may be more beneficial than oral iron due to impaired absorption. However, it may also increase the risk of infection in these patients.
Details:

Postoperative recovery. It is unclear if intravenous iron is beneficial for recovery following cardiac surgery.
Details:

Postpartum depression. Although there has been interest in using iron for postpartum depression, there is insufficient reliable information about the clinical effects of iron for this condition.

Prematurity. Enteral iron seems to be beneficial for some measures of development in preterm infants.
Details:

More evidence is needed to rate iron for these uses.

Dosing & Administration

- **Adult**

  Oral:

  General: For adults, the recommended daily allowance (RDA) for iron is 8 mg/day for males ages 19 and older, and females ages 51 and older. For females 19 to 50 years, the RDA is 18 mg/day. During pregnancy, the RDA is 27 mg/day. During lactation, the RDA is 10 mg/day for ages 14 to 18 years, and 9 mg/day for ages 19 to 50 (7135).

  Patients should not exceed the tolerable upper limit of 45 mg iron daily unless advised by a healthcare provider. See Effectiveness section for condition-specific information.

  Dietary or supplemental calcium may decrease the absorption of dietary or supplemental iron. However, in people with adequate stores of these minerals, this does not appear to have a clinically significant effect on long-term iron status (8875).

  Advise patients that iron should be taken on an empty stomach if possible. Taking iron supplements with food can decrease iron absorption by 40% to 75% (17500,110193). This is likely due to binding of iron in the gut by calcium, polyphenols, tannins, and other dietary constituents (8875,8887,9570,9571,9573,17497,17500). If iron must be taken with food to mitigate gastrointestinal side effects, advise patients to avoid taking iron at the same time as dairy, coffee, tea, or cereals (17497,17500).

  Intravenous/Intramuscular:

  Research is limited; typical dosing is unavailable.

- **Children**

  Oral:

  General: The adequate intake (AI) of iron for infants 6 months of age and less is 0.27 mg/day (7135). For older infants and children, the recommended daily allowances (RDAs) for iron are: 7-12 months, 11 mg/day; 1-3 years, 7 mg/day; 4-8 years, 10 mg/day; 9-13 years, 8 mg/day; males 14-18 years, 11 mg/day; females 14-18 years, 15 mg/day.

  For preventing iron deficiency in children, the American Academy of Pediatrics guidelines recommend iron supplements for some groups. For breast-fed infants, elemental iron 1 mg/kg/day is recommended from ages 4-6 months. Infants from 6-12 months should get 11 mg/day from food or supplements. For pre-term infants, 2 mg/kg/day for the first year is

recommended. This should be continued until the baby is switched to formula or otherwise getting enough iron from food sources. Formula-fed children get enough iron from infant formula. Toddlers aged 1-3 years usually get enough iron from foods; however, a supplement can be added as needed (17495,17496). Plain iron drops (Fer-In-Sol, Fer-Gen-Sol, etc) are usually preferred for children (17495).

Patients should not exceed the tolerable upper limit of 40 mg iron daily unless advised by a healthcare provider. See Effectiveness section for condition-specific information.

- **Standardization & Formulation**

  There are several formulations and salt forms of iron which contain different amounts of elemental iron:

  1 gram of ferrous gluconate = 120 mg elemental iron (12% iron)

  1 gram of ferrous sulfate = 200 mg elemental iron (20% iron)

  1 gram of ferrous fumarate = 330 mg elemental iron (33% iron)

  Efficacy and tolerability are similar for these different forms when used in equal doses of elemental iron. Manufacturers of some formulations such as polysaccharide-iron complex products (Niferex-150, etc) claim to be better tolerated than other formulations. However, there is no reliable evidence to support this claim. Enteric coated or controlled release iron formulations might reduce nausea for some patients; however, these products also have lower absorption rates (17500). Heme-iron polypeptide products (Proferrin ES, etc) are derived from the hemoglobin of animals and have better absorption compared to inorganic iron salts (17500). Carbonyl iron (Feosol with Carbonyl Iron, Iron Chews, etc) contains microparticles of 100% purified elemental iron. It is slowly absorbed which allows for controlled release over 1-2 days. It is not more effective than other forms, but is less toxic in cases of accidental ingestion (17500).

  Other forms include sodium iron ethylenediaminetetra-acetate (NaFeEDTA), iron(III)-hydroxide polymaltose complex (IPC), and iron proteinsuccinylate (20117,20118).

Interactions with Drugs

BISPHOSPHONATES
Interaction Rating = **Moderate** Be cautious with this combination.
Severity = Moderate • Occurrence = Probable • Level of Evidence = **D**

Iron reduces the absorption of bisphosphonates.

Details

CHLORAMPHENICOL
Interaction Rating = **Minor** Be watchful with this combination.
Severity = Moderate • Occurrence = Unlikely • Level of Evidence = **D**

Theoretically, taking chloramphenicol with iron might reduce the response to iron therapy in iron deficiency anemia.

Details

DOLUTEGRAVIR (Tivicay)
Interaction Rating = **Moderate** Be cautious with this combination.
Severity = Moderate • Occurrence = Probable • Level of Evidence = **B**

Iron might decrease dolutegravir levels by reducing its absorption.

Details

INTEGRASE INHIBITORS
Interaction Rating = **Moderate** Be cautious with this combination.
Severity = High • Occurrence = Possible • Level of Evidence = **D**

Theoretically, taking iron along with integrase inhibitors might decrease the levels and clinical effects of these drugs.

Details

LEVODOPA
Interaction Rating = **Moderate** Be cautious with this combination.
Severity = Moderate • Occurrence = Probable • Level of Evidence = **B**

Iron might decrease levodopa levels by reducing its absorption.

Details

LEVOTHYROXINE (Synthroid, others)
Interaction Rating = **Moderate** Be cautious with this combination.
Severity = Moderate • Occurrence = Probable • Level of Evidence = **B**

Iron might decrease levothyroxine levels by reducing its absorption.

Details

METHYLDOPA (Aldomet)
Interaction Rating = **Moderate** Be cautious with this combination.
Severity = Moderate • Occurrence = Probable • Level of Evidence = **B**

Iron might decrease methyldopa levels by reducing its absorption.

Details

MYCOPHENOLATE MOFETIL (CellCept)
Interaction Rating = **Moderate** Be cautious with this combination.
Severity = High • Occurrence = Unlikely • Level of Evidence = **D**

Theoretically, iron might decrease mycophenolate mofetil levels by reducing its absorption.

Details

PENICILLAMINE (Cuprimine, Depen)
Interaction Rating = **Moderate** Be cautious with this combination.
Severity = Moderate • Occurrence = Probable • Level of Evidence = **D**

Iron might decrease penicillamine levels by reducing its absorption.

Details

QUINOLONE ANTIBIOTICS
Interaction Rating = **Moderate** Be cautious with this combination.
Severity = Moderate • Occurrence = Probable • Level of Evidence = **D**

Iron might decrease levels of quinolone antibiotics by reducing their absorption.

Details

TETRACYCLINE ANTIBIOTICS
Interaction Rating = **Moderate** Be cautious with this combination.
Severity = Moderate • Occurrence = Probable • Level of Evidence = **D**

Iron might decrease levels of tetracycline antibiotics by reducing their absorption.
Details

Interactions with Supplements

ACACIA: Theoretically, taking iron together with acacia might lead to decreased absorption of iron or acacia.
Details

BETA-CAROTENE: Taking iron with beta-carotene might enhance dietary non-heme iron absorption and in people with anemia and Vitamin A deficiency.
Details

CALCIUM: Calcium can decrease iron absorption.
Details

CASEIN PROTEIN: Casein protein, but not hydrolyzed casein protein (casein peptides), seems to decrease iron absorption.
Details

LACTOBACILLUS: Theoretically, taking iron with lactobacillus might increase the absorption of iron.
Details

SOY: Soy protein seems to decrease iron absorption.
Details

VITAMIN A: Taking iron with vitamin A might enhance dietary non-heme iron absorption in people with anemia and Vitamin A deficiency.
Details

VITAMIN C: When ingested at the same time, supplemental or dietary vitamin C improves absorption of dietary non-heme iron. Its effect on iron supplements is unclear.
Details

YERBA MATE: Theoretically, concomitant use of iron and yerba mate may reduce the effectiveness of iron supplementation.
Details

ZINC: Iron and zinc can interfere with each other's absorption when taken on an empty stomach.
Details

Interactions with Conditions

ACHLORHYDRIA

DIABETES

HEMODIALYSIS

HEMOGLOBIN DISEASES

HEREDITARY HEMORRHAGIC TELANGIECTASIA (HHT)

PHYSICAL TRAINING

PREMATURE INFANTS

Interactions with Lab Tests

GUAIAC TEST

Nutrient Depletion

SOME DRUGS CAN AFFECT IRON LEVELS:

AMINOSALICYLIC ACID
Depletion Rating = **Moderate Depletion** Monitor for depletion; a supplement is needed in some patients.
Aminosalicylic acid reduces iron absorption and might decrease iron levels.
Details

ANTACIDS
Depletion Rating = **Insignificant Depletion** A supplement is not needed for most patients.
Antacids might modestly reduce iron absorption.
Details

CHOLESTYRAMINE (Questran)
Depletion Rating = **Insignificant Depletion** A supplement is not needed for most patients.
Cholestyramine might modestly reduce iron absorption and reduce iron levels.
Details

H2-BLOCKERS
Depletion Rating = **Insignificant Depletion** A supplement is not needed for most patients.

H2-blockers might modestly reduce iron absorption.
Details

PANCREATIC ENZYMES
Depletion Rating = **Moderate Depletion** Monitor for depletion; a supplement is needed in some patients.
Pancreatic enzymes reduce iron absorption and might decrease iron levels.
Details

PENICILLAMINE (Cuprimine, Depen)
Depletion Rating = **Insignificant Depletion** A supplement is not needed for most patients.
Penicillamine might modestly reduce iron absorption and reduce iron levels.
Details

PROTON PUMP INHIBITORS (PPIs)
Depletion Rating = **Insignificant Depletion** A supplement is not needed for most patients.
Proton pump inhibitors might modestly reduce iron absorption.
Details

QUINOLONE ANTIBIOTICS
Depletion Rating = **Insignificant Depletion** A supplement is not needed for most patients.
When taken together, iron and quinolone antibiotics can bind together, reducing absorption. When taken separately, this effect is unlikely to be clinically significant.
Details

TETRACYCLINE ANTIBIOTICS
Depletion Rating = **Insignificant Depletion** A supplement is not needed for most patients.
When taken together, iron and tetracycline antibiotics can bind together, reducing absorption. When taken separately, this effect is unlikely to be clinically significant.
Details

Overdose

Presentation

Acute overdosage, 60 mg/kg and more, can cause hematemesis and diarrhea, followed by cardiovascular, liver, or metabolic toxicity, and death (7135,20097,56582). Long-term use of high doses of iron can cause hemosiderosis that clinically resembles hemochromatosis (15).

Iron overdose during pregnancy in individuals with peak iron levels over 400 mcg/dL have been associated with organ failure, spontaneous abortion, preterm delivery, and maternal death (20109).

Iron supplementation appears to be associated with greater adverse events in children. For example, in a clinical trial of 24,076 children, there was a 12% increase in risk of hospitalization due to severe illness in children taking iron (50163).

Treatment

There is insufficient reliable information available about the treatment of overdose with iron.

Commercial Products Containing: Iron

View All

View Health Canada Licensed Products

View Certified Products

Pharmacokinetics

Absorption: The rate of iron absorption from food and supplements is variable. Heme iron is absorbed at a rate of 23% compared to 2% to 20% for non-heme iron. Non-heme iron is found in all foods containing iron. However, iron from plant sources is only in the non-heme form. Ascorbic acid and ferri-reductase in the duodenum aid in the absorption of dietary non-heme iron. Iron bioavailability from a vegetarian diet is estimated to be 5% to 10%. Meats and fish seem to enhance the absorption of non-heme iron (7135). Supplemental iron reduces non-heme iron absorption from food (56493).

Boiling, stir-frying, or hot air drying appears to enhance the bioavailability of iron contained in some vegetables including asparagus, broccoli, cabbage, cauliflower, and corn; however, cold storage of cooked vegetables might greatly reduce the increases in iron bioavailability gained from cooking (5044). Overall, dietary iron absorption is only 10% to 15%. However, this varies significantly depending on the person and the iron demand of the body (403).

Vegetarians and people who engage in intense physical exercise, particularly female athletes, may have increased iron requirements (7135). Blood loss and rapid growth also increase gastrointestinal absorption (1101). Iron is stored as ferritin or hemosiderin (7135).

Certain iron formulations are better absorbed than others. For example when ferrous fumarate is given as microencapsulated sprinkles in a maize-based porridge, it appears to be absorbed better (56592). Iron from purified soybean ferritin and also from recombinant human lactoferrin appears to be absorbed as well as ferrous sulfate (56622,56625). Iron bisglycinate seems to increase iron status more than iron polymaltose or lactoferrin (110189). The frequency of iron administration also seems to impact absorption. A small clinical study shows that taking ferrous sulfate 60 mg on alternate days in single doses appears to improve iron absorption when compared with taking 60 mg daily. However, dividing a daily dose of ferrous sulfate 120 mg twice daily does not improve absorption when compared with taking 120 mg once daily (96630).

Distribution: Most of the iron in the human body is incorporated into hemoglobin. The remaining iron is stored in the bone marrow, liver, spleen, or muscle (myoglobin) as ferritin or hemosiderin (7135).

Metabolism: Iron moves in the body by binding reversibly to the transport protein, transferrin. Two atoms of iron bind to one transferrin and then bind to the transferrin receptor complex. Iron that is transferred into cells can be incorporated into hemoglobin and myoglobin, stored as ferritin, or used to regulate cellular iron metabolism (7135).

Excretion: Body iron is highly conserved. In the absence of bleeding (including menstruation) or pregnancy, the body loses only a small quantity of iron each day, mostly through the feces (7135).

Mechanism of Action

General: Iron is a trace mineral found in two ionic forms in the body. It exists in a reduced state as ferrous iron and in an oxidized state as ferric iron. Most of the iron in the body is found in the hemoglobin of red blood cells and in the myoglobin of muscle cells where it is required for oxygen and carbon dioxide transport (1093). Iron also functions in the electron transport chain as an electron carrier in cytochromes. It is also found in the functional groups of most enzymes in the Krebs cycle (945). Iron is an essential cofactor in the synthesis of neurotransmitters such as dopamine, norepinephrine, and serotonin.

Meats, such as red meat, poultry, and fish provide iron in heme and non-heme forms. Meats contain about 40% heme iron and 60% non-heme iron. Heme iron is absorbed at a rate of 23% compared to 2% to 20% for non-heme iron. Iron from plant sources is only in the non-heme form. Ascorbic acid and ferri-reductase in the duodenum aid in the absorption of non-heme iron. Iron bioavailability from a vegetarian diet is estimated to be 5% to 10%. Meats and fish seem to enhance the absorption of non-heme iron (7135).

The absorption of iron supplements may be increased by intermittent administration (1-3 doses/week) compared with daily administration. Intermittent administration is thought to align better with intestinal cell turnover, increasing absorption efficiency via increased exposure to new cells. This dosing strategy may also decrease oxidative stress and reduce adverse effects (103806).

Iron deficiency anemia in early life seems to negatively affect behavioral and neural development (1093,9962). Signs and symptoms of deficiency include microcytic and hypochromic anemia, lethargy, cognitive impairment, developmental delay, amenorrhea, hair loss, enlarged liver, and others (7135). Iron deficiency in pregnancy has been associated with adverse pregnancy outcomes and increased perinatal maternal mortality (7135).

Neurological effects: There is interest in using iron to treat attention deficit-hyperactivity disorder (ADHD). Research suggests that children with ADHD are more likely to be iron deficient. The level of iron deficiency seems to be positively correlated with the severity of ADHD symptoms. ADHD symptoms are related to dopamine dysfunction where iron seems to plays a role. Iron affects dopamine synthesis and appears to play a role in dopamine receptors density (10700).

Respiratory effects: The cough induced by angiotensin converting enzyme (ACE) inhibitors may be linked to accumulation of nitric oxide. Since iron seems to reduce nitric oxide production, this effect might be clinically useful in the suppression of cough induced by ACE inhibitors (7307).

Classifications

Ergogenic Aids, Energy Boosters

References

See Monograph References

Monographs are reviewed on a regular schedule. See our Editorial Principles and Process for details. The literature evaluated in this monograph is current through 2/22/2023. This monograph was last modified on 3/20/2023. If you have comments or suggestions, please tell the editors.

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