

## **Herbal Supplements (Haematanics) and their Interactions with Medications: An Overview**

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### **ABSTRACT**

Herbal supplements, if taken at the same time as prescription medicines, can create potential problems for the user. Unfortunately, there is very little scientific information available about the way herbs and drugs interact. The present paper deals with various herbal supplements and their interactions with medications.

**Key- Words:** Herbals, Interactions, Iron.

### **INTRODUCTION**

Iron is an essential mineral and an important component of proteins involved in oxygen transport and metabolism. Iron is also an essential cofactor in the synthesis of neurotransmitters such as dopamine, norepinephrine, and serotonin. About 15 percent of the body's iron is stored for future needs and mobilized when dietary intake is inadequate. The body usually maintains normal iron status by controlling the amount of iron absorbed from food. There are two forms of dietary iron: heme and non-heme. Sources of heme iron include meat fish and poultry. Sources of non-heme iron, which is not absorbed as well as heme iron, include beans, lentils, flours, cereals, and grain products. Other sources of iron include dried fruit, peas, asparagus, leafy greens, strawberries, and nuts. The World Health Organization considers iron deficiency to be the largest international nutritional disorder. Although much of the ethnic disparity in iron deficiency anemia remains unexplained, socioeconomic factors may be involved. Iron deficiency can be determined by measurement of iron levels within the body, mainly serum ferritin levels, which can also help distinguish between iron deficiency anemia and anemia associated with chronic disease. Herbal preparations such as yellow dock root may be used in iron deficiency, although scientific evidence may be lacking.

### **Adults (18 years and older):**

The Recommended Dietary Allowance (RDA) for males (19- 50 years) is 8 milligrams per day; females (19- 50 years) 18 milligrams per day; adults (51 years and older) 8 milligrams per day; pregnant women (all ages) 27 milligrams per day; breastfeeding women (19 years and older) 9 milligrams per day.

The Tolerable Upper Intake Level (UL) for adults (19 years and older) is 45 milligrams per day.

The RDA for iron from a completely vegetarian diet should be adjusted as follows: 14 milligrams per day for adult men and postmenopausal women, 33 milligrams per day for premenopausal women, and 26 milligrams per day for adolescent girls.

Doses ranging from 60 to 180mg of elemental iron have been used for iron deficiency/anemia. Dextran-iron (INFeD®) is given by healthcare providers to replenish depleted iron stores in the bone marrow where it is incorporated into hemoglobin. The usual adult dose is 2 milliliters per day (100 milligrams iron).

### **Children (younger than 18 years):**

The Recommended Dietary Allowance (RDA) is 11 milligrams for 7-12 months; 7 milligrams for 1-3 years; 10 milligrams for 4-8 years; 8 milligrams for 9-13 years (male and female); 11 milligrams for males 14-18 years; 15 milligrams for females 14-18 years; 27 milligrams for pregnant females 14-18 years; 10 milligrams for breastfeeding females 14-18 years. For infants 0-6 months 0.27 milligrams is recommended as the adequate intake level (AI), which is used when RDA cannot be determined.

The Tolerable Upper Intake Level (UL) for infants (1-12 months) is not possible to establish; children (1-13 years) 40 milligrams per day; adolescents (14-18 years) 45 milligrams per day.

Dextran-iron (INFeD®) is an intravenous preparation given by qualified healthcare provider to replenish depleted iron stores in the bone marrow where it is incorporated into hemoglobin. Doses of 50 milligrams iron (1 milliliter) (5-10 kilograms) and 100 milligrams iron (2 milliliters) (10-50 kilograms) have been used.

### **Side Effects and Warnings**

In general, people with a history of kidney disease, intestinal disease, peptic ulcer disease, enteritis, colitis, pancreatitis, hepatitis, who consume excessive alcohol, plan to become pregnant, or are over age 55 and have a family history of heart disease, should consult a doctor and pharmacist before taking iron.

Liquid oral iron preparations can possibly blacken teeth.

Acute overdosage or iron accumulation symptoms may include arthritis, signs of gonadal failure (amenorrhea, early menopause, loss of libido, impotence), and shortness of breath/dyspnea. High doses may cause vomiting and diarrhea, followed by cardiovascular or metabolic toxicity, and death. It is unclear whether high levels are associated with cancer, coronary heart disease or myocardial infarction (MI).

Gastrointestinal upset including nausea, vomiting, constipation, diarrhea, and dark stools have been reported. Gastrointestinal side effects are relatively common and corrective bowel regimens such as increasing dietary fiber or over the counter medication might be recommended to balance these side effects. Supervision by a qualified healthcare provider is recommended.

Individuals with blood disorders who require frequent blood transfusions are also at risk of iron overload and should not take iron supplements without direction by a qualified healthcare provider. Long-term use of high doses of iron can cause hemosiderosis that clinically resembles hemochromatosis.

HCV infection and iron loading may aggravate oxidative stress in dialysis patients.

Iron overload is associated with several genetic diseases including hemochromatosis (a defect in iron metabolism with build up of iron in the body). The most commonly associated early hemochromatosis symptoms include fatigue, weakness, weight loss, abdominal pain, and arthralgia.

A case of hypsiderosis (uncontrollable sweating) has been reported with long-term iron supplementation in

uremic patients treated with periodic dialysis.

Accumulation of excess iron is being investigated as a potential contributor to neurodegenerative diseases such as Alzheimer's and Parkinson's disease.

Iron overload is possible in very low birth weight infants after multiple blood transfusions due to increase liver iron concentration. Prenatal iron-overload might contribute to the pathogenesis of the disease, but further studies are needed to confirm the assumption.

One study indicates that higher consumption of total red meat, especially various processed meats, may increase risk of developing type 2 diabetes in women.

### **Pregnancy and Breastfeeding**

Pregnant or breastfeeding women should seek guidance from a qualified healthcare provider before taking dietary supplements. Iron status of the pregnant woman should be measured early (before the 15th week of gestation) and iron supplements should be given as selective prophylaxis based on the serum ferritin level.

FDA Pregnancy Category B: Usually safe but benefits must outweigh the risks.

FDA Pregnancy Category C: Safety for use during pregnancy has not been established for replenishing depleted iron stores in the bone marrow where it is incorporated into hemoglobin.

### **INTERACTIONS**

Most herbs and supplements have not been thoroughly tested for interactions with other herbs, supplements, drugs, or foods. The interactions listed below are based on reports in scientific publications, laboratory experiments, or traditional use. You should always read product labels. If you have a medical condition, or are taking other drugs, herbs, or supplements, you should speak with a qualified healthcare provider before starting a new therapy.

#### **Interactions with Drugs**

Acetohydroxamic acid (AHA, Lithostat®) is prescribed to decrease urinary ammonia, and may help with antibiotics to work or help with other kidney stone treatment. Use with iron supplements may cause either medicine to be less effective.

Allopurinol (Zyloprim®), a medication used to treat gout, may increase iron storage in the liver and should not be used in combination with iron supplements.

Aminosalicylic acid (para-aminosalicylic acid, PAS, Paser) may cause a malabsorption syndrome (weight loss, iron and vitamin depletion, excessive fat in the stools (steatorrhea). A qualified healthcare provider should be contacted immediately if any of these symptoms are experienced.

Antacids may reduce iron absorption, and reduced efficacy has occurred occasionally. Clinically significant effects are unlikely with adequate dietary iron intake. However, it is recommended to avoid antacids or separate the doses of antacids and iron.

Aspirin and nonsteroidal anti-inflammatory drugs (NSAIDs) can cause mucosal damage and bleeding throughout the gastrointestinal tract. Chronic blood loss associated with long-term use of these agents may contribute to iron deficiency anemia. Since iron supplements may also irritate the gastrointestinal tract, patients should not use them concurrently with NSAIDs unless recommended by a physician. Iron rich food intake may be advised as an alternative.

Iron can decrease absorption of prescription drug bisphosphonates by forming insoluble complexes.

Bisphosphonates include alendronate (Fosamax®), etidronate (Didronel®), risedronate (Actonel®), and tiludronate (Skelid®). Doses of bisphosphonates should be separated by at least two hours from doses of all other medications, including supplements such as iron.

Chloramphenicol (Chloromycetin®) can reduce the response to iron therapy in iron deficiency anemia.

Cholestyramine (Questran®) and colestipol (Colestid®) may bind iron in the gut, reducing its absorption. Clinically significant iron deficiency induced by these drugs has not been reported, and supplements are not likely to be needed. If taking iron supplements for other causes of deficiency, it is recommended that the iron and cholestyramine or colestipol doses be separated by at least four hours.

Desferrioxamine (DFO) is an iron-chelating drug that lowers iron levels.

Iron supplements and dimercaprol may combine in the body to form a harmful chemical.

Bone marrow iron deposits have been shown to decrease significantly in patients on EPO-R.

Iron decreases the absorption of fluoroquinolone antibiotics. Fluoroquinolones include ciprofloxacin (Cipro®), levofloxacin (Levaquin®), ofloxacin (Floxin®), and others. It is recommended to take these antibiotics at least two hours before or two hours after iron-containing supplements.

Gastric acid is important for the absorption of iron, particularly dietary non-heme (plant-derived) iron. Adequate dietary iron intake is recommended when taking H<sub>2</sub> blockers like cimetidine (Tagamet®), ranitidine (Zantac®), famotidine (Pepcid®), or nizatidine (Axid®). Iron supplements are not usually required unless they are being used for another indication.

There is some evidence in healthy people that iron forms chelates with levodopa (Sinemet®), reducing the amount of levodopa absorbed by around 50%. Until further research is available, separate doses of levodopa and iron as much as possible.

Iron can decrease the absorption and efficacy of levothyroxine (Levoxyl®, Synthroid®) by forming insoluble complexes in the gastrointestinal tract. It is recommended that levothyroxine and iron doses be separated by at least two hours.

Iron can decrease absorption of methyldopa (Aldomet®), resulting in increases in blood pressure. It is recommended that methyldopa and iron doses be separated by at least two hours.

Oral iron supplements markedly reduce absorption of mycophenolate mofetil (CellCept®). It is recommended that iron be taken four to six hours before, or two hours after mycophenolate mofetil.

There is some evidence that pancreatic enzyme supplements (such as Cotazym®, Creon®, Pancrease®, Ultrase®, Viokase®), can reduce iron absorption, possibly by binding iron or altering pH. Clinical significance is unlikely, except in people with cystic fibrosis who need pancreatic enzyme supplements for prolonged periods, and have other factors contributing to iron deficiency. Iron status should be monitored by a qualified healthcare provider.

Oral iron supplements can reduce absorption of penicillamine (Cuprimine®, Depen®) by 30% to 70%, probably due to chelate formation. Efficacy of penicillamine is reduced in Wilson's disease; the clinical significance in people with rheumatoid arthritis (RA) has not been determined. Patients should be advised to take penicillamine at least two hours before or after iron-containing supplements.

Gastric acid is important for the absorption of iron. However, long-term treatment, up to 12.5 years, with proton pump inhibitors (such as esomeprazole (Nexium®), lansoprazole (Prevacid®), omeprazole (Prilosec®), rabeprazole (Aciphex®), pantoprazole (Protonix®, Pantoloc®) has not been associated with iron depletion or anemia in people with normal iron stores. Maintaining adequate dietary iron intake is recommended.

Concomitant use can decrease absorption of tetracycline antibiotics by 50% to 90%. Patients should be advised to take tetracyclines at least two hours before or after iron-containing supplements. Some of these drugs include doxycycline (Vibramycin®), minocycline (Minocin®), tetracycline (Achromycin®), and others.

### **Interactions with Herbs and Dietary Supplements**

Acacia forms an insoluble gel with ferric iron. Clinical significance is unknown.

Calcium supplements have been shown to inhibit absorption of iron supplements when taken with food. However, in people with adequate iron stores, this does not appear to be clinically significant. If at risk for iron deficiency, it is recommended to take calcium supplements at bedtime, instead of with meals, to avoid inhibiting dietary iron absorption.

Copper metabolism may be altered by iron supplements, but the clinical importance of this observation is unknown.

Citric, malic, tartaric, and lactic acids have some enhancing effects on nonheme iron absorption.

Phytic acid is present in legumes, grains, and rice and is an inhibitor of nonheme iron absorption. Small amounts of phytic acid can reduce nonheme iron absorption by 50%. The absorption of iron from legumes, such as soybeans, black beans, lentils, mung beans, and split peas, has been shown to be as low as 2%.

Polyphenols, found in some fruits, vegetables, coffee, tea, wines, and spices, can markedly inhibit the absorption of nonheme iron. This effect is reduced by the presence of vitamin C.

Riboflavin (vitamin B2) supplements may improve the hematological response to iron supplements in some people with anemia.

Based on preliminary data, iron may decrease selenium levels. Further research is needed to confirm these results.

Soy protein reduces absorption of dietary non-heme (plant-derived) iron, probably due to binding of iron by phytate and calcium present in soy. Fermented soy products seem to inhibit iron absorption less.

Vitamin A appears to be involved in mobilizing iron from tissue stores for delivery to developing red blood cells in the bone marrow. Vitamin A may also be involved in the differentiation and proliferation of blood stem cells in the bone marrow, and in the synthesis of erythropoietin. Preliminary evidence also suggests that vitamin A and beta-carotene may enhance non-heme iron absorption from iron-fortified wheat and corn flour, and rice. It is unlikely that vitamin A supplements would have significant effects on iron status in people without vitamin A deficiency.

The amount of vitamin C in the diet is a factor in dietary iron absorption and iron status. Vitamin C can counteract the effects of substances, which inhibit iron absorption. Supplemental or dietary vitamin C improves absorption of supplemental or dietary non-heme (plant-derived) iron ingested at the same time. Taking a vitamin C supplement to improve absorption of dietary or supplemental iron probably is not necessary for most people, especially if their diet contains adequate amounts of vitamin C.

Use of oral iron preparations in premature infants with low serum vitamin E levels may cause hemolysis and hemolytic anemia. Vitamin E deficiency should be corrected before administering supplemental iron.

Iron may decrease zinc absorption but there does not seem to be a clinically significant interaction between dietary iron and zinc, or between supplemental iron and zinc dietary sources.

<b>Herbal Supplement</b>	<b>Common Uses</b>	<b>Possible Problems</b>	<b>May Interact With</b>

<b>Dong Quai (Angelica)</b>	To treat menopausal symptoms, PMS, irregular menstruation cycles.	Enhances bleeding.	Drugs that hinder the clotting of blood.
<b>Echinacea</b>	To treat colds, flu, and mild infections, especially upper respiratory infections (chest colds).	May cause injury to the liver; may cause intestinal/ stomach upset.	Drugs that may cause injury to the liver; synthetic hormones; some anti-cancer drugs.
<b>Ephedra (Ma Huang, Ephedrine, Pseudo-ephedrine)</b>	To treat asthma and coughs; to stimulate weight loss.	May cause seizures; may cause adverse cardiac events, such as irregular heartbeat, high blood pressure, stroke, or heart attack.	Some heart medications; general anesthesia; some antidepressants; medicines that increase blood pressure; decongestants; stimulants.
<b>Garlic</b>	To decrease cholesterol and blood clot formation.	Enhances bleeding.	Drugs that hinder the clotting of blood.
<b>Ginger</b>	To relieve nausea.	Enhances bleeding; may affect the central nervous system; may lower blood pressure; may cause irregular heartbeat; may lower blood glucose levels.	Drugs that hinder the clotting of blood; medicines that increase blood pressure; cardiac drugs; drugs that lower blood sugar level; may increase the effects of sedatives.
<b>Ginkgo Biloba</b>	To improve circulation, especially to brain; also for memory loss, dizziness, and headache.	Enhances bleeding; may cause cramps and/or muscle spasms.	Drugs that hinder the clotting of blood.
<b>Ginseng</b>	To increase energy and reduce stress.	Enhances bleeding; may cause irregular heartbeat and/or increase blood pressure; may cause mania.	Drugs that hinder the clotting of blood; stimulants; medicines that lower blood pressure; some antidepressants; digoxin (a heart drug); may increase the effects of steroids and estrogens.
<b>Goldenseal</b>	Used as a mild antibiotic to treat sore throats and upper respiratory infections.	Increases fluid retention; may increase blood pressure; may cause nausea or nervousness.	Drugs that increase urination; medicines that lower blood pressure.
<b>Kava Kava</b>	To treat anxiety, nervousness, and insomnia.	May cause upset stomach; may cause liver damage and/or stimulate an allergic skin reaction that causes a yellow discoloration of skin.	May increase the effects of sedatives, muscle relaxants, anesthetics, and antidepressants.
<b>Licorice</b>	To treat hepatitis and peptic ulcers.	May increase blood pressure; may lower levels of potassium in the blood; may cause swelling.	Medicines that lower blood pressure; may increase the effects of steroids.
<b>SAM-e (S-adenosyl-L-methionine)</b>	To treat depression or osteoarthritis.	May induce drowsiness; may cause nausea and/or upset stomach.	May increase the effects of some antidepressants.
<b>St. John's</b>	To treat mild	Enhances bleeding.	May increase the effects of anti-

<b>Wort</b>	depression, anxiety, or seasonal affective disorder.		depressants; decreases the effectiveness of medications given to organ-transplant patients.
<b>Valerian</b>	To treat insomnia or anxiety.	May induce drowsiness; may cause digestion problems.	Enhances the effects of sedatives.

## CONCLUSIONS

Herbs are the vital sources in treating any diseases specially the disorders related to that of iron. The present paper review a comprehensive details on the herbal haematronics and their interaction with that of various available drugs. The table presented above indicates the uses of several herbs and the possible interaction's they caused. Hence, the present work will enlightens all the aspects of herbal haematronics and their interactions during the medications.

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