Iron (II) sulfate

CAS: 7720-78-7
MF: $FeSO_4$
MW: 151.91
Soluble in water [1].

Fe^{2+}
MW: 55.85

Major use
Iron (II) sulfate is used in manufacture of iron, iron compounds, other sulfates; in iron electroplating baths; in fertilizer; as food and feed supplement; in radiation dosimeters; as reducing agent in chemical processes; as wood preservative; as weed killer; in prevention of chlorosis in plants; in other pesticides; in writing ink; in process engraving and lithography; as dye for leather; in etching aluminum; in water treatment; in qualitative analysis ("brown ring" test for nitrates); as polymerization catalyst. Used in medication as hematinic (a drug that increases the amount of hemoglobin in the blood) [1].

Human toxicity
Major clinical findings are stupor, shock, acidosis, hematemesis, bloody diarrhea or coma. Minor clinical findings are vomiting, diarrhea, mild lethargy. Leukocytosis (WBC greater than 15,000) and hyperglycemia are sometimes observed but are not characteristic for an acute iron poisoning [2].

Lethal symptoms: haematemesis (the vomiting of blood from the stomach), gastrointestinal tract (GIT) perforation, pulmonary oedema, the central nervous system (CNS) excitation/depression, circulatory failure, liver and kidney failure [3].

The clinical course of poisoning includes the following:
PHASE I (0.5 to 2 h) includes vomiting, hematemesis, abdominal pain, diarrhea, hematochezia, lethargy, shock, acidosis, and coagulopathy. Necrosis to the GIT occurs from the direct effect of iron on gastrointestinal mucosa. Severe gastrointestinal hemorrhagic necrosis with large losses of fluid and blood contribute to shock. Free iron and ferritin produce vasodilatation that may also contribute to shock.
PHASE II (after phase I) includes apparent recovery and may contribute to a false sense of security.
PHASE III (2 to 12 hours after phase I) includes profound shock, severe acidosis, cyanosis and fever. Increased total peripheral resistance, decreased plasma volume, hemoconcentration, decrease in total blood volume, hypotension, CNS depression, and metabolic acidosis have been demonstrated.
PHASE IV (2 to 4 days) includes possible hepatotoxicity. Thought to be a direct action of iron on mitochondria. Acute lung injury may also occur.
PHASE V (days to weeks) includes GI scarring and strictures. GI obstruction secondary to gastric or pyloric scarring may occur due to corrosive effects of iron [2].

The phases of iron poisoning may not occur in all patients. After massive overdose, patients may present in shock. With less serious overdoses, the initial gastrointestinal

symptoms may be the only findings to develop even without treatment. Although serious iron poisoning in adults is rare, deaths have been reported [2].

The usual oral dose of iron is 2 to 3 mg/kg/day of elemental iron in divided doses [2]. Many authors believe ingestion of 60 mg/kg of elemental iron is the minimum for toxicity, however, 20 to 60 mg/kg may be potentially toxic [2]. The mean lethal dose (LD) of iron was 14 g; and the minimal lethal dose (MLD) of iron was 2.3 g [3].

The therapeutic plasma/serum blood levels for iron are 0.65-1.75 mg/l; toxic level is 6 mg/l; lethal levels are 20-50 mg/l [4]. According to Kaye [5], lethal blood level is 8 mg/l for iron salt.

Working place standards: TLV-TWA: 1 mg/m^3 [2]

Kinetic data

Absorption: About 5 to 15 percent of iron in food is absorbed from the GIT, but the uptake increases in the case of iron deficiency or depleted iron stores. Iron absorption is a capacity-limited active process. Following therapeutic dosing, 10-35% of iron is absorbed, but in conditions of iron deficiency it can increase to 80-95% [2]. At an overdose up to 90% is absorbed [3]. Complete absorption of iron preparations may not occur before 2 to 6 hours post-ingestion [2].

Kinetics is biphasic [3].

Volume of distribution: Since iron is transported throughout the body by numerous complex carrier proteins, it is difficult, if not impossible, to ascribe meaning to any volume of distribution referred to in the literature [2].

Distribution: Liver is a major storage site for iron; about 27% of the total body iron is in the liver. Iron is stored as ferritin or hemosiderin (in a pathological condition) [2]. Iron has biphasic kinetics. The passage of iron over the blood-brain barrier is restricted [3].

The plasma half-life: unknown.

Time to peak: Peak serum concentrations occur in approximately 2 to 3 hours after dosing. After overdose peak serum concentrations occur in 4 to 6 hours following ingestion [2].

Lethal blood concentration: Mean post-mortem acute lethal blood concentration in humans was reported to be 22 mg/l and mean clinically measured acute lethal blood concentration was reported to be 8 mg/l.[3].

Protein binding: 100% [3].

Passage of blood-brain barrier: restricted [3].

Metabolism and excretion

About two-thirds is bound to hemoglobin, 10% in myoglobin and iron-containing enzymes, and the remainder is bound to the iron storage proteins ferritin and hemosiderin.

Excretion: Iron elimination is slow. The main routes of excretion are desquamation of the mucosal cells in the gastrointestinal tract and loss of blood. About 0.2 to 0.5 mg is excreted in the feces and 0.2 to 0.3 mg in the urine [2].

Metabolites more toxic than iron sulfate: None

Pharmacological mechanisms
Iron is an essential constituent of the body, necessary for hemoglobin formation and for the oxidative processes of living tissues. The body contains approximately 3.5 g of iron, two thirds as hemoglobin and the remainder as stored iron in the reticuloendothelial system [6].

Toxicological mechanisms
Iron is a general cell poison, which inhibits oxidative phosphorylation and ATP. In acute iron poisoning, gastrointestinal injury appears within a few hours of ingestion and plays an important role in the pathogenesis. Subsequent clinical stages include: relative stability, shock and acidosis, hepatotoxicity, and gastrointestinal scarring. Once absorbed, iron is a potent catalyst of free radical formation and subsequent lipid peroxidation causing cellular injury. Significant concentrations of these toxins are required to overwhelm local detoxification pathways if actual tissue damage is to occur [2].

Target organs: vasculitis (inflammation of the walls of the blood vessels) and haemorrhages in GIT, liver, and lung; kidney, CNS, cardiovascular system [3].

References

1. HSDB, TOXNET (2005).
2. Poisindex, Thomson Micromedex (2005).
3. Ekwall, B., Clemedson, C., Crafoord, B., Ekwall, B., Hallander, S., Walum, E. & Bondesson, I. (1998) MEIC Evaluation of Acute Systemic Toxicity: Part V. Rodent and Human Toxicity Data for the 50 Reference Chemicals, ATLA 26, 571-616.
4. Winek, C.L. (1994) Drug and chemical blood-level data. Winek's Toxicological Annual, Pittsburgh. Allegheny County Department Laboratories.
5. Kaye, S. (1980) Handbook of Emergency Toxicology: A Guide for the Identification, Diagnosis and Treatment of Poisoning, 4th edn.Springfield, IL, USA.
6. *Casarett and Doull's Toxicology (The Basis Science of Poisons)* (1986) Klaassen, C.D., Amdur, M.O., Doull, J., eds., Macmillan Publishing Company.

Written by Cecilia Clemedson, December 2005, revised March 2007
Cecilia@Stifud.se