

Rethinking Iron Supplementation: A Shift Toward Next-Generation Solutions

Alok S Shah*

College of Medicine, University of Chicago, Chicago, IL, United States

***Corresponding Author:** Alok S Shah, College of Medicine, University of Chicago, Chicago, IL, United States.

Received: July 14, 2025; **Published:** August 06, 2025

Iron deficiency anemia (IDA) remains a pervasive global health issue, with India bearing a disproportionate share of the burden. Anemia is a frequent comorbidity in individuals with COPD, with reported prevalence ranging from 7.5% to 33%. It significantly affects quality of life, increases healthcare resource utilization and costs, and is associated with higher mortality rates. According to the National Family Health Survey (2019-2021), anemia affects nearly 57% of pregnant women and over 67% of children under five figures that highlight an urgent public health crisis. Despite national initiatives like Anemia Mukht Bharat, anemia rates have shown minimal improvement and, in some regions, have even worsened. These numbers reflect not just the scale of the problem but the shortcomings of current intervention strategies.

At the physiological level particularly concerning pulmonary health the impact of IDA extends far beyond general fatigue and weakness. It directly impairs oxygen transport throughout the body, a function that is critical for respiratory efficiency. Iron is a key component of hemoglobin, the oxygen-carrying protein in red blood cells that transports oxygen from the lungs to peripheral tissues. When iron stores are depleted, hemoglobin synthesis is compromised, leading to reduced oxygen-carrying capacity.

This deficiency manifests in respiratory symptoms such as breathlessness (dyspnea), low exercise tolerance, and an increased respiratory rate. In vulnerable populations, this impaired oxygen transport may worsen overall pulmonary function and contribute to greater physical limitations, with potential long-term consequences on health and quality of life.

Limitations of traditional iron therapies

Conventional iron salts like ferrous sulfate, ferrous ascorbate, ferrous fumarate, ferrous gluconate remained the mainstay of treatment for IDA. However, their effectiveness is frequently compromised by gastrointestinal (GI) side effects and poor bioavailability. Common complaints include nausea, constipation, abdominal discomfort, and metallic taste. These symptoms are largely attributed to unabsorbed iron lingering in the GI tract. Iron absorption is also limited by its dependence on Divalent Metal Transporter 1 (DMT-1), a rate-limiting pathway that leaves a large portion of oral iron unabsorbed, further aggravating GI discomfort and reducing compliance. Moreover, dietary components like phytates, calcium, and polyphenols inhibit non-heme iron absorption, making it difficult to maintain consistent iron levels through traditional supplements alone.

Chelated iron

Preventive and protective measures have helped minimize oxidative damage by chelating reactive metal ions like Fe^{2+} and binding them to stabilizing agents to reduce their reactivity. Chelated iron, for instance, is more stable and less likely to catalyze harmful oxidative reactions. Additional steps like shielding from light and air further reduce degradation. However, these methods are not always fully

effective, as various factors such as formulation stability, environmental conditions, or the presence of other reactive compounds can still compromise product integrity over time.

The push for innovative iron delivery systems

In light of these limitations, the need for advanced iron formulations is more critical than ever. Emerging technologies are reshaping the landscape of iron supplementation, with a focus on improving absorption, minimizing side effects, and enhancing compliance. Novel delivery systems such as nanoparticle-based iron, sustained-release formulations, liposomal carriers, and polysaccharide-iron complexes offer significant improvements over conventional salts. These systems help protect iron from gastric degradation, facilitate targeted release, and promote absorption across the intestinal barrier without causing oxidative damage or mucosal irritation.

Among these innovations, liposomal and sucrosomial iron supplements have garnered attention for their improved bioavailability and reduced side-effect profile. However, it is important to note that not all liposomal formulations are created equal. The composition and chemical properties of liposomes primarily made of lipids and phospholipids are key to their performance as drug delivery systems. Variations in lipid type and structure can significantly influence critical factors such as size, zeta potential, encapsulation efficiency, stability, drug release, intracellular uptake, and overall bioactivity. Phospholipid selection affects not only encapsulation and toxicity but also biodistribution, membrane permeability, and clearance. While chemical modifications can optimize these properties, they may also lead to drawbacks like reduced stability or inconsistent absorption. Therefore, not all liposomal formulations are equally effective.

Microencapsulation and ferric pyrophosphate: A game-changer

Microencapsulation has emerged as a promising technology to further enhance the tolerability and bioavailability of iron supplements. By coating iron particles in protective layers, microencapsulation reduces direct interaction with the gastrointestinal mucosa and potentially the gut microbiota. This not only improves absorption but also significantly reduces the gastrointestinal side effects associated with unabsorbed iron.

One of the most promising forms of microencapsulated iron is ferric pyrophosphate, a compound with a high affinity for transferrin, making it highly efficient for systemic delivery.

Compared to other Iron salts, it is postulated that ferric pyrophosphate should show a lot more efficacy if its poor absorption can be bypassed, as it has the highest affinity for Transferrin compared to all iron salts. This is the rationale used by all the encapsulated iron preparations that contain ferric pyrophosphate.

A micronized form of ferric pyrophosphate featuring a particle size as small as 0.3 - 0.5 microns has demonstrated better absorption compared to standard ferric pyrophosphate (8 microns).

SunActive™ Fe: A breakthrough in iron supplementation

At the forefront of next-generation iron supplements is SunActive™ Fe, a patented, micronized, and microencapsulated form of ferric pyrophosphate. Engineered with the smallest particle size among iron salts, SunActive™ Fe leverages a unique absorption mechanism via M cells in the intestinal lining bypassing traditional DMT-1 transport and enabling more efficient uptake. Its technology eliminates gastrointestinal irritation while delivering superior absorption and compliance. Notably, it is recognized and recommended by the World Health Organization (WHO) and UN for its safety and application in public health nutrition.

SunActive™ Fe offers a combination of high efficacy, excellent stability, and consumer acceptability with no metallic aftertaste or adverse GI effects. It represents a transformative step forward in iron therapy particularly for populations where adherence and absorption are persistent challenges.

Being the only encapsulated iron with the highest M-cell transport, it also shows the highest efficacy for increasing hemoglobin in many human clinical trials. Of the all iron salts and preparations examined this iron supplement appears at this time to be the safest and most efficacious in a variety of conditions - in IDA, during pregnancy, chronic kidney disease, cardiac conditions, gastrointestinal diseases or in cancer cases.

Conclusion

As we continue to grapple with the high burden of iron deficiency anemia, especially in low- and middle-income countries like India, the limitations of traditional therapies must be addressed through innovation. Next-generation iron formulations such as SunActive™ Fe, offer new hope in the fight against IDA delivering better absorption, minimal side effects, and improved patient outcomes. Iron supplementation should serve not only as a therapeutic strategy but also as a routine prophylactic/preventive approach for overall well-being. The future of iron supplementation lies not just in correcting deficiency, but in doing so with precision, efficiency, and safety [1-4].

Bibliography

1. Mariné-Casadó R., *et al.* "Comparative study of the effects of different iron sources on bioavailability and gastrointestinal tolerability in iron-deficient rats". *Scientific Reports* 15.1 (2025): 21033.
2. Maherani, B., *et al.* "Liposomes: A review of manufacturing techniques and targeting strategies". *Current Nanoscience* 7.3 (2011): 436-452.
3. Biniwale Parag., *et al.* "Liposomal iron for iron deficiency anemia in women of reproductive age: review of current evidence". *Open Journal of Obstetrics and Gynecology* 8.11 (2018): 993-1005.
4. Zečkanović A., *et al.* "Micronized, microencapsulated ferric iron supplementation in the form of >your< iron syrup improves hemoglobin and ferritin levels in iron-deficient children: double-blind, randomized clinical study of efficacy and safety". *Nutrients* 13.4 (2021): 1087.

Volume 14 Issue 9 September 2025
©All rights reserved by Alok S Shah.