EURASIAN EXPERIMENT JOURNAL OF BIOLOGICAL SCIENCES (EEJBS)
ISSN: 2992-4138 ©EEJBS Publications
Volume 6 Issue 2 2025

Emerging Therapeutic Strategies for Iron-Deficiency Anemia: A Review of Novel Iron Formulations and Delivery Systems

Mukamana Sandra Gisele

School of Applied Health Sciences Kampala International University Uganda

ABSTRACT

Iron-deficiency anemia (IDA) remains the most prevalent form of anemia worldwide, affecting over two billion people, particularly women and children in low- and middle-income countries. While conventional oral iron salts like ferrous sulfate have been the cornerstone of treatment, they are often limited by poor absorption, gastrointestinal side effects, and non-compliance. This review explores recent advancements in iron therapy aimed at improving efficacy, tolerability, and patient adherence. Novel formulations such as liposomal iron, heme iron polypeptides, and ferric maltol offer enhanced bioavailability with fewer side effects. Advances in intravenous (IV) iron therapy, including ferric carboxymaltose and iron isomaltoside, provide rapid replenishment for patients unresponsive to oral formulations. Additionally, innovative delivery systems such as nano-encapsulation, transdermal patches, and iron-fortified bioactive food matrices are being developed to address limitations in conventional treatments. This article synthesizes recent clinical findings and evaluates the safety, pharmacokinetics, and therapeutic potential of emerging iron therapies. Addressing the global burden of IDA requires a shift toward patient-centered, context-sensitive, and technologically advanced approaches to iron supplementation.

Keywords: Iron-deficiency anemia, oral iron therapy, intravenous iron, liposomal iron, nano-delivery systems

INTRODUCTION

Iron-deficiency anemia (IDA) is a widespread hematological condition marked by a decrease in red blood cell count or hemoglobin concentration due to insufficient iron availability [1]. Iron is an essential micronutrient required for hemoglobin synthesis and effective oxygen transport in the body [2]. An iron deficiency impairs cellular metabolism and leads to symptoms such as fatigue, weakness, cognitive impairment, reduced work capacity, and compromised immune function [3]. Vulnerable populations include children, pregnant women, and individuals with chronic illnesses or poor dietary intake. Despite the existence of effective diagnostic and therapeutic approaches, IDA continues to pose a significant global health challenge. It accounts for the majority of anemia cases worldwide, with over two billion people affected, particularly in low- and middle-income regions [4]. The persistence of IDA is largely attributed to socioeconomic disparities, inadequate nutrition, chronic infections, parasitic infestations, and limited access to advanced healthcare. Traditional treatment of IDA focuses primarily on oral iron supplementation using iron salts such as ferrous sulfate [5]. While these therapies are affordable and widely available, they are often associated with poor gastrointestinal tolerability, low adherence, and suboptimal absorption. Side effects like nausea, constipation, metallic taste, and abdominal discomfort frequently result in poor patient compliance. Moreover, conventional iron formulations face challenges related to bioavailability, especially in individuals with chronic inflammation or intestinal disorders. In recent years, considerable research efforts have been directed toward developing alternative iron formulations and innovative delivery methods to improve therapeutic outcomes. These novel strategies aim to enhance iron bioavailability, reduce gastrointestinal side effects, and provide flexible administration routes tailored to individual patient needs [6]. This review explores emerging therapies, including next-generation oral supplements, improved intravenous iron preparations, and cutting-edge delivery systems designed to address the limitations of conventional treatments and meet the diverse needs of patients with IDA.

2. Conventional Iron Therapies and Their Limitations

For decades, oral iron salts such as ferrous sulfate, ferrous gluconate, and ferrous fumarate have been the first-line treatment for IDA. These compounds deliver non-heme iron, which is primarily absorbed in the duodenum and proximal jejunum through active transport mechanisms [7]. They are inexpensive and accessible, making them a practical choice for many healthcare systems, especially in resource-limited settings. However, their clinical utility is hindered by several drawbacks. Gastrointestinal side effects are the most common reason for non-compliance. These include constipation, epigastric pain, nausea, vomiting, and diarrhea [8]. Additionally, iron salts can cause oxidative stress in the gastrointestinal mucosa, further exacerbating discomfort and inflammation in susceptible individuals [9]. Another major limitation is the inconsistent absorption of non-heme iron. Factors such as dietary inhibitors (phytates in grains and legumes, calcium, tannins in tea), concurrent medications, and the presence of systemic inflammation or gastrointestinal disorders can significantly reduce iron uptake [10]. In inflammatory states, elevated hepcidin levels downregulate iron absorption and mobilization, making oral iron ineffective [11]. Due to these issues, many patients fail to achieve adequate replenishment of iron stores, leading to persistent or recurrent anemia. These challenges underscore the need for more bioavailable, better-tolerated alternatives that can support long-term management of IDA.

3. Novel Oral Iron Formulations

Recent advancements in oral iron therapy have focused on improving absorption, minimizing side effects, and enhancing patient compliance. Several novel formulations have emerged as promising alternatives to conventional iron salts.

3.1 Liposomal Iron

Liposomal iron encapsulates iron within lipid-based vesicles, which shield it from direct contact with the gastrointestinal mucosa and digestive enzymes [12]. This protects the iron from premature degradation and reduces oxidative stress on the gut lining. The result is enhanced absorption through lymphatic transport and significantly fewer gastrointestinal side effects. Clinical studies have shown that liposomal iron effectively increases hemoglobin levels and replenishes iron stores with improved tolerability, making it suitable for long-term use [13].

3.2 Heme Iron Polypeptides

Heme iron is derived from hemoglobin and is absorbed through a distinct mechanism that does not rely on the same regulatory pathways as non-heme iron [14]. Heme iron polypeptides offer superior bioavailability and are less influenced by dietary factors. They are particularly beneficial for patients with absorption issues, such as those with celiac disease, inflammatory bowel disease, or post-bariatric surgery [15]. Their use, however, may be limited by cost and availability.

3.3 Ferric Maltol and Ferric Citrate

These are newer iron complexes that offer improved gastrointestinal tolerability and efficient absorption. Ferric maltol, approved for use in conditions like inflammatory bowel disease, provides a stable ferric iron compound bound to a sugar-derived ligand that enhances solubility and uptake in the intestine [16]. Ferric citrate also serves dual roles by managing hyperphosphatemia in chronic kidney disease while correcting anemia [17]. Both formulations demonstrate favorable safety profiles and represent significant progress in oral iron therapy.

4. Advances in Intravenous Iron Therapy

Intravenous (IV) iron therapy provides a crucial alternative for individuals who are intolerant to oral iron or who require rapid replenishment of iron stores. This is especially relevant in cases of severe anemia, chronic kidney disease (CKD), inflammatory bowel disease (IBD), or ongoing blood loss [18]. Traditional IV iron formulations, such as iron dextran, were associated with high rates of adverse reactions, particularly anaphylaxis, which limited their use [19]. However, advancements in pharmaceutical technology have led to the development of safer and more efficient IV iron preparations that offer higher doses with fewer side effects and more convenient administration schedules. IV iron bypasses the gastrointestinal tract, eliminating issues of poor absorption and dietary interference. This makes it ideal for patients with malabsorption syndromes, gastrointestinal inflammation, or those undergoing dialysis [20]. Modern formulations have been engineered with carbohydrate shells that stabilize the iron core and control its release, reducing the risk of free iron toxicity and hypersensitivity [21].

4.1 Ferric Carboxymaltose

Ferric carboxymaltose is a widely used next-generation IV iron formulation that allows for high single-dose administration, often up to 1,000 mg in a single infusion over 15–30 minutes [22]. Its safety and efficacy have been well-documented in various clinical settings, including anemia associated with heart failure, CKD, and IBD. The advantage of fewer infusions reduces hospital visits, enhances patient adherence, and facilitates rapid correction of anemia. Ferric carboxymaltose also improves functional outcomes in patients with chronic illnesses and has been incorporated into several treatment guidelines worldwide [23].

4.2 Iron Isomaltoside and Ferumoxytol

Iron isomaltoside is another high-dose IV formulation designed for flexible dosing with minimal risk of adverse reactions. It can be administered as a single large infusion or split into smaller doses based on individual patient needs [24]. It has demonstrated effectiveness in treating anemia in CKD, cancer, and postpartum populations [24]. Ferumoxytol is a unique IV iron compound with a carbohydrate shell that allows for controlled iron release. It is approved for use in patients with CKD and has shown a lower incidence of allergic reactions compared to older iron formulations [25]. Notably, ferumoxytol also functions as a contrast agent in magnetic resonance imaging (MRI), providing both diagnostic and therapeutic applications [26]. Its dual utility is particularly valuable in settings where imaging and anemia management are concurrent clinical priorities [26].

5. Innovative Iron Delivery Systems

Emerging technologies in iron supplementation aim to improve iron delivery, reduce side effects, and offer alternative routes of administration for patients with specific needs [26]. These innovations are still largely in the experimental or early clinical phases but show promise for the future of anemia management.

5.1 Nano-encapsulation

Nano-encapsulation involves the use of nanoparticles to encase iron molecules, enabling controlled and targeted delivery. This method improves iron stability, reduces oxidative stress on the gastrointestinal mucosa, and enhances absorption at specific intestinal sites [27]. Nanocarriers can also be engineered to release iron in response to pH or enzymatic triggers, increasing efficiency [28]. Although most research is still preclinical, these systems could offer significant benefits for patients with inflammation or absorption disorders.

5.2 Transdermal and Buccal Delivery

Transdermal iron patches and buccal films represent non-invasive alternatives to oral and intravenous routes. These systems are designed to bypass the gastrointestinal tract entirely, avoiding issues of absorption and irritation [29,30]. They offer a more user-friendly option, particularly for pediatric and geriatric populations or those with swallowing difficulties. While still under investigation, early studies suggest that these delivery methods can maintain therapeutic iron levels with acceptable bioavailability [31].

5.3 Fortified Bioactive Food Matrices

Food-based iron delivery is a long-standing public health strategy, particularly effective in addressing iron deficiency at the population level [32]. Recent innovations have focused on bioactive food matrices such as iron-fortified cereals, dairy products, and probiotic-enriched foods [33]. These formulations aim to improve iron solubility and absorption while integrating into daily diets to promote adherence. This approach is especially beneficial in low-income settings where pill compliance is low and dietary iron intake is insufficient.

6. Clinical Implications and Future Directions

The evolving landscape of iron therapy offers exciting possibilities for individualized treatment. Clinicians are increasingly moving toward tailoring iron supplementation based on etiology, severity, and patient-specific factors such as comorbid conditions, age, pregnancy status, and socioeconomic background. Point-of-care testing for iron biomarkers, including ferritin, transferrin saturation, and hepcidin, can support more precise treatment decisions.

Personalized dosing algorithms, along with the strategic combination of iron with erythropoiesis-stimulating agents, are being evaluated in clinical trials. The integration of novel iron delivery systems into public health frameworks could help reduce the global burden of anemia, especially in vulnerable populations. Future research should prioritize long-term safety, cost-effectiveness, and comparative effectiveness studies to guide widespread adoption of these emerging therapies.

As the science of iron supplementation advances, the ultimate goal remains the same: to offer safe, effective, and accessible treatments that restore health and quality of life for individuals affected by iron-deficiency anemia.

CONCLUSION

Tackling the global issue of iron-deficiency anemia involves more than just increasing iron intake; it requires rethinking how iron is delivered, absorbed, and tolerated by the body. New formulations and advanced delivery methods provide fresh hope for better treatment adherence, effectiveness, and quality of life for patients in various clinical and demographic settings. Ongoing research, along with fair access to these innovations, is crucial for achieving lasting control of IDA worldwide.

REFERENCES

1. Turner J, Parsi M, Badireddy M. Anemia. StatPearls – NCBI Bookshelf. 2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK499994/
2. Abbaspour N, Hurrell R, Kelishadi R. Review on iron and its importance for human health. 2014. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC3999603/

3. Obeagu EI. Iron homeostasis and health: understanding its role beyond blood health – a narrative review. Annals of Medicine and Surgery. 2025;87(6):3362–71. doi:10.1097/MS9.0000000000003100
4. Kumar SB, Arnipalli SR, Mehta P, Carrau S, Ziouzenkova O. Iron deficiency anemia: efficacy and limitations of nutritional and comprehensive mitigation strategies. Nutrients. 2022;14(14):2976. doi:10.3390/nu14142976
5. Ebea-Ugwuanyi PO, Vidyasagar S, Connor JR, Frazer DM, Knutson MD, Collins JF. Oral iron therapy: current concepts and future prospects for improving efficacy and outcomes. British Journal of Haematology. 2024;204(3):759–73. doi:10.1111/BJH.19268
6. Pantopoulos K. Oral iron supplementation: new formulations, old questions. Haematologica. 2024. doi:10.3324/haematol.2024.284967
7. Kumar A, Sharma E, Marley A, Samaan MA, Brookes MJ. Iron deficiency anaemia: pathophysiology, assessment, practical management. BMJ Open Gastroenterology. 2022;9(1):e000759. doi:10.1136/BMJGAST-2021-000759
8. Bharucha AE, Chakraborty S, Sletten CD. Common functional gastroenterological disorders associated with abdominal pain. Mayo Clinic Proceedings. 2016;91(8):1118–32. doi:10.1016/j.mayocp.2016.06.003
9. Bhattacharyya A, Chattopadhyay R, Mitra S, Crowe SE. Oxidative stress: an essential factor in the pathogenesis of gastrointestinal mucosal diseases. Physiological Reviews. 2014;94(2):329–54. doi:10.1152/physrev.00040.2012
10. Piskin E, Cianciosi D, Gulec S, Tomas M, Capanoglu E. Iron absorption: factors, limitations, and improvement methods. ACS Omega. 2022;7(24):20441–56. doi:10.1021/ACSOMEGA.2C01833
11. Nemeth E, Ganz T. Hepcidin and iron in health and disease. Annual Review of Medicine. 2022;74(1):261–77. doi:10.1146/annurev-med-043021-032816
12. Cesarano D, Borrelli S, Campilongo G, D'Ambra A, Papadia F, Garofalo C, et al. Efficacy and safety of oral supplementation with liposomal iron in non-dialysis chronic kidney disease patients with iron deficiency. Nutrients. 2024;16(9):1255. doi:10.3390/NU16091255
13. Zahr SB, Allata Y, Mansoury ME, Chouhani BA, Kabbali N, Bardai GE, et al. Oral liposomal iron versus injectable iron sucrose for anemia treatment in non-dialysis chronic kidney disease patients: a non-inferiority study. Cureus. 2024. doi:10.7759/CUREUS.70114
14. Ems T, St Lucia K, Huecker MR. Biochemistry, iron absorption. StatPearls – NCBI Bookshelf. 2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK448204/
15. Kalman D, Hewlings S, Madelyn-Adjei A, Ebersole B. Dietary heme iron: a review of efficacy, safety and tolerability. Nutrients. 2025;17(13):2132. doi:10.3390/NU17132132
16. Gasche C, Ahmad T, Tulassay Z, Baumgart DC, Bokemeyer B, Büning C, et al. Ferric maltol is effective in correcting iron deficiency anemia in patients with inflammatory bowel disease. Inflammatory Bowel Diseases. 2015;21(3):579–88. doi:10.1097/MIB.0000000000000314
17. Ding X, Sun S, Zhang J, Zhao H, Lun F, Liu X, et al. Ferric citrate for the treatment of hyperphosphatemia and iron deficiency anaemia in patients with NDD-CKD: a systematic review and meta-analysis. Frontiers in Pharmacology. 2024;15. doi:10.3389/FPHAR.2024.1285012
18. Koch TA, Myers J, Goodnough LT. Intravenous iron therapy in patients with iron deficiency anemia: dosing considerations. Anemia. 2015;2015:1–10. doi:10.1155/2015/763576
19. Arastu AH, Elstrott BK, Martens KL, Cohen JL, Oakes MH, Rub ZT, et al. Analysis of adverse events and intravenous iron infusion formulations in adults with and without prior infusion reactions. JAMA Network Open. 2022;5(3):e224488. doi:10.1001/JAMANETWORKOPEN.2022.4488
20. Cançado RD, Muñoz M. Intravenous iron therapy. Revista Brasileira de Hematologia e Hemoterapia. 2011;33(6):461–9. doi:10.5581/1516-8484.20110123
21. Van Doren L, Auerbach M. IV iron formulations and use in adults. Hematology. 2023;2023(1):622–9. doi:10.1182/HEMATOLOGY.2023000495
22. Friedrisch JR, Cançado RD. Intravenous ferric carboxymaltose for the treatment of iron deficiency anemia. Revista Brasileira de Hematologia e Hemoterapia. 2015;37(6):400–5. doi:10.1016/J.BJHH.2015.08.012
23. Rangwala BS, Zuhair V, Mustafa MS, Mussarat A, Khan AW, Danish F, et al. Ferric carboxymaltose for iron deficiency in patients with heart failure: a systematic review and meta-analysis. Future Science OA. 2024;10(1). doi:10.1080/20565623.2024.2367956

24. Kalra P, Bhandari S. Efficacy and safety of iron isomaltoside (Monofer®) in the management of patients with iron deficiency anemia. International Journal of Nephrology and Renovascular Disease. 2016;53. doi:10.2147/IJNRD.S89704
25. Derman R, Roman E, Modiano MR, Achebe MM, Thomsen LL, Auerbach M. A randomized trial of iron isomaltoside versus iron sucrose in patients with iron deficiency anemia. American Journal of Hematology. 2017;92(3):286–91. doi:10.1002/AJH.24633
26. Emmanuel Ifeanyi Obeagu, Getrude Uzoma Obeagu, Simeon Ikechukwu Egba and Obioma Raluchukwu Emeka Obi. Combatting Anaemia in Paediatric Malaria: Effective management strategies Int. J. Curr. Res. Med. Sci. 2023. 9(11): 1-7
27. Garbati P, Picco C, Magrassi R, Signorello P, Cacopardo L, Serra MD, et al. Targeting the gut: a systematic review of specific drug nanocarriers. Pharmaceutics. 2024;16(3):431. doi:10.3390/PHARMACEUTICS16030431
28. Karimi M, Eslami M, Sahandi-Zangabad P, Mirab F, Farajisafiloo N, Shafaei Z, et al. pH-sensitive stimulus-responsive nanocarriers for targeted delivery of therapeutic agents. Wiley Interdisciplinary Reviews: Nanomedicine and Nanobiotechnology. 2016;8(5):696–716. doi:10.1002/WNAN.1389
29. Khan S, Sharman T. Transdermal medications. StatPearls – NCBI Bookshelf. 2024. Available from: https://www.ncbi.nlm.nih.gov/books/NBK556035/
30. Ritu Mg, Mohd I, Sunny S, Neeraj G. A clinical perspective on mucoadhesive buccal drug delivery systems. Journal of Biomedical Research. 2014;28(2):81. doi:10.7555/JBR.27.20120136
31. Surekha B, Misra P, Thippaiah AC, Shamanna BR, Madathil A, Rajadurai M. A microneedle transdermal patch loaded with iron(II) nanoparticles for non-invasive sustained delivery to combat anemia. Materials Advances. 2024;5(8):3247–56. doi:10.1039/D3MA01166F
32. Kaur N, Agarwal A, Sabharwal M. Food fortification strategies to deliver nutrients for the management of iron deficiency anaemia. Current Research in Food Science. 2022;5:2094–107. doi:10.1016/J.CRFS.2022.10.020
33. Kouamé KJEP, Bora AFM, Li X, Liu L, Coulibaly I, Sun Y, et al. New insights into functional cereal foods as an alternative for dairy products: a review. Food Bioscience. 2023;55:102840. doi:10.1016/J.FBIO.2023.102840

Mukamana Sandra Gisele. Emerging Therapeutic Strategies for Iron-Deficiency Anemia: A Review of Novel Iron Formulations and Delivery Systems. EURASIAN EXPERIMENT JOURNAL OF BIOLOGICAL SCIENCES, 6(2):106-110.