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Nanoparticles in the Treatment of Anemia: A Narrative Review

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ABSTRACT

Background: Anemia is a common haematological disorder characterised by reduced haemoglobin concentration and impaired oxygen transport. Although conventional iron supplementation remains a standard therapeutic approach, its effectiveness may be limited by poor absorption and gastrointestinal adverse effects. Nanoparticle-based systems have therefore emerged as potential platforms for improving iron delivery and therapeutic efficacy.

Methods: A narrative review was conducted using PubMed, Scopus, and Web of Science to identify relevant publications published between 2010 and 2026. The search included terms related to anemia, nanoparticles, iron supplementation, targeted drug delivery, and haematological therapies. Preclinical, animal, in vitro, and relevant review studies were considered, and findings were synthesised qualitatively.

Results: Preclinical and experimental evidence suggests that several nanoparticle-based systems, particularly iron-containing nanocarriers and iron oxide nanoparticles, may improve iron delivery, bioavailability, sustained release, and treatment tolerability. Some animal and in vitro studies have also reported improvements in haemoglobin and other haematological parameters, together with potential antioxidant and anti-inflammatory effects. However, these findings are largely derived from experimental models, and evidence from human clinical studies remains limited. In addition, certain nanomaterials have demonstrated potential oxidative, genotoxic, or systemic toxicities, highlighting the importance of safety evaluation.

Conclusion: Nanoparticle-based technologies show promising preclinical potential for improving iron delivery and addressing selected mechanisms associated with anemia . However, current evidence is insufficient to establish their clinical efficacy or long-term safety. Well-designed clinical studies are required to determine whether the benefits observed in experimental models can be translated into effective and safe therapies for patients with anemia.

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INTRODUCTION

Chronic diseases, including cancer, iron-deficiency anaemia, and other long-term health conditions, represent major public health challenges, causing significant physical and psychological suffering, impairing quality of life, and placing a substantial burden on patients, their families, and healthcare systems (1, 2). Anemia is one of the most common haematological disorders worldwide and is characterised by a reduction in haemoglobin concentration, a decreased

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red blood cell (RBC) count, or impaired oxygen-carrying capacity of the blood (3). It affects hundreds of millions of individuals globally, particularly young children, pregnant women, older adults, and patients with chronic illnesses, making it a major public health concern (3). The condition is associated with fatigue, generalised weakness, impaired cognitive performance, delayed growth and development, reduced physical productivity, and an increased risk of morbidity and mortality (3). Anemia arises from a wide range of underlying causes, including iron deficiency, vitamin B12 and folate deficiencies, chronic inflammatory disorders, inherited haematological diseases, chronic kidney disease, malnutrition, and infectious diseases (4). Given its high prevalence and substantial clinical burden, the development of safe, effective, and targeted therapeutic strategies remains an important priority in modern medicine (3, 4).

The pathophysiological mechanisms underlying anemia vary according to its aetiology and generally involve impaired erythrocyte production, accelerated destruction of circulating red blood cells, or excessive blood loss (4). Iron deficiency anemia develops when depleted iron stores compromise haemoglobin biosynthesis, thereby reducing tissue oxygenation (5). In anemia associated with chronic inflammation, increased production of pro-inflammatory cytokines, particularly interleukin-6 (IL-6) and tumour necrosis factor-α (TNF-α), stimulates hepcidin expression, resulting in reduced intestinal iron absorption and impaired mobilisation of stored iron (6). Furthermore, excessive oxidative stress and the accumulation of reactive oxygen species (ROS) can damage erythrocyte membranes, disrupt erythropoiesis, and shorten red blood cell lifespan (5). In hereditary disorders such as thalassaemia and sickle cell disease, genetic abnormalities alter the structure or function of haemoglobin, further contributing to disease pathogenesis (6). The multifactorial nature of these mechanisms highlights the need for therapeutic approaches capable of addressing multiple pathological pathways simultaneously.

Current therapeutic options for anemia include oral and intravenous iron supplementation, erythropoiesis-stimulating agents, blood transfusion, vitamin replacement therapy, and, in selected cases, haematopoietic stem cell transplantation (7). Although these interventions have substantially improved patient outcomes, each possesses important limitations. Oral iron preparations often exhibit poor bioavailability, limited intestinal absorption, gastrointestinal intolerance, and poor patient adherence, whereas parenteral iron administration may be associated with iron overload, infusion-related reactions, and the need for repeated clinical visits (8). Common gastrointestinal adverse effects including nausea, constipation, abdominal discomfort, and dyspepsia remain major barriers to long-term compliance with oral iron therapy (9). Moreover, patients with chronic inflammatory disorders frequently demonstrate suboptimal responses to conventional iron supplementation because inflammatory pathways interfere with iron metabolism. These limitations have stimulated considerable interest in developing advanced drug delivery systems capable of improving iron absorption while reducing systemic toxicity and treatment-related adverse effects (8, 9).

Recent advances in nanotechnology have opened new avenues for the diagnosis and treatment of haematological disorders. Owing to their nanoscale dimensions, large surface-area-to-volume ratio, tunable physicochemical properties, and versatile surface functionalisation, nanoparticles have emerged as highly promising drug delivery platforms (10, 11). These nanocarriers can enhance pharmaceutical stability, improve intestinal absorption, provide sustained and controlled drug release, and facilitate targeted delivery to specific tissues or cell populations (10, 11). Furthermore, nanoparticle-based formulations protect therapeutic agents from premature degradation, thereby improving the bioavailability of iron, vitamins, erythropoiesis-stimulating agents, and other bioactive molecules involved in erythropoietic regulation (10, 11).

A broad range of nanoparticle systems including iron nanoparticles, polymeric nanoparticles, lipid nanoparticles, liposomes, nanoemulsions, dendrimers, and nanocomposite materials has been investigated for the treatment of anemia (12). Iron-based nanoparticles have attracted particular attention because they demonstrate superior bioavailability, enhanced gastrointestinal absorption, and fewer gastrointestinal adverse effects than conventional iron supplements (13). Experimental studies have shown that these nanocarriers facilitate more efficient intestinal iron uptake while providing sustained and controlled iron release (12, 13). In addition, several nanoparticle platforms have been engineered to deliver erythropoietin, antioxidants, and anti-inflammatory agents directly to target tissues, thereby enhancing erythropoiesis through attenuation of oxidative stress and inflammatory responses (13, 14).

Nanotechnology also offers promising therapeutic opportunities for complex forms of anemia, including thalassaemia, sickle cell disease, and anemia of chronic disease (15). Nanoparticle-mediated delivery systems have been explored for gene therapy applications, including the transport of small RNA molecules and genome-editing components designed to correct inherited haemoglobin disorders (16). Beyond therapeutic delivery, multifunctional nanoplatforms have demonstrated considerable potential as theranostic systems by integrating diagnostic imaging with targeted treatment within a single platform (16). Magnetic

nanoparticles have likewise shown considerable value in blood cell separation, targeted drug delivery, and the enhancement of diagnostic procedures, further expanding the clinical applications of nanomedicine in haematology (15, 16).

Despite these encouraging advances, several important challenges continue to limit the clinical translation of nanoparticle-based therapies (17). Potential cytotoxicity, long-term tissue accumulation, nanoparticle-induced oxidative stress, unintended immune activation, and uncertainties regarding long-term biosafety remain major concerns (17). Additional obstacles include the lack of standardised manufacturing protocols, high production costs, formulation stability issues, and the limited availability of robust clinical evidence supporting routine therapeutic use (18). Consequently, comprehensive evaluation of nanoparticle biocompatibility, toxicological profiles, pharmacokinetics, and long-term safety remains essential before widespread clinical implementation can be considered (19).

Given the rapid expansion of research in nanomedicine and haematology, a comprehensive synthesis of the available evidence is both timely and necessary. Although numerous studies have investigated nanoparticle-based approaches for the treatment of anemia, current evidence remains fragmented, particularly regarding their mechanisms of action, therapeutic efficacy, safety profiles, existing limitations, and future clinical prospects. Therefore, this review aims to critically evaluate the current evidence on the therapeutic applications of nanoparticles in the treatment and management of anemia, with particular emphasis on their underlying biological mechanisms, clinical potential, safety considerations, and future directions for research and clinical translation.

METHODS

This study was conducted as a narrative review of the therapeutic applications of nanoparticles in anemia. A literature search was performed in PubMed, Scopus, Web of Science, SID, and ISC for publications published from January 2010 to 2025.

The search combined keywords related to anemia, iron deficiency anemia, nanoparticles, nanomedicine, nanocarriers, iron supplementation, drug delivery, targeted therapy, and erythropoiesis using the Boolean operators AND and OR. A representative search strategy was: (Anemia OR Iron Deficiency Anemia) AND (Nanoparticles OR Nanomedicine OR Nanocarriers) AND (Iron Supplementation OR Drug Delivery OR Targeted Therapy).

Relevant original studies, preclinical and in vitro investigations, animal studies, and pertinent narrative or systematic reviews were considered. Publications were excluded if they were duplicates, lacked sufficient relevant information, were unavailable in full text, or focused exclusively on nanoparticle toxicity without therapeutic relevance to anemia.

Relevant publications were screened for their relevance to the objectives of the review, and key information was extracted regarding nanoparticle type, experimental model, therapeutic target, delivery strategy, mechanism of action, efficacy, safety, and study limitations. Because this was a narrative review, no formal meta-analysis or quantitative statistical synthesis was performed. Findings were qualitatively synthesised according to nanoparticle type, iron delivery, erythropoiesis, antioxidant and anti-inflammatory mechanisms, iron deficiency anemia, chronic disease-associated anemia, and emerging nanomedicine approaches.

The literature selection and synthesis were intended to provide a critical overview of the current evidence rather than a systematic estimation of treatment effects.

RESULTS

The included studies evaluated several nanoparticle-based approaches for anemia , predominantly in animal and other preclinical models. Iron-based nanoparticles and nanoformulations, including Fe_3O_4, ferric pyrophosphate, ferrihydrite, and solid lipid nanoparticles, were mainly investigated for improving iron delivery, absorption, bioavailability, and controlled release. Several studies reported improvements in haemoglobin concentration, red blood cell indices, and other haematological parameters in experimental models.

Other nanoparticle systems, including gold, tin, and gadofullerene nanoparticles, were investigated for their effects on oxidative stress, inflammation, and erythropoiesis. Reported findings included reduced reactive oxygen species and oxidative damage, modulation of antioxidant and inflammatory pathways, and improved erythropoietic responses. Advanced platforms such as albumin-based nanoparticles and folate-targeted systems were also investigated for targeted or enhanced delivery of iron and other therapeutic agents.

The evidence was predominantly preclinical, while clinical evidence was limited. Some studies also reported formulation-dependent toxicity, oxidative stress, or genotoxic effects, indicating variability in the biological effects of different nanomaterials. Overall, the findings were heterogeneous with respect to nanoparticle type, experimental model, therapeutic target, and measured outcomes.

A detailed summary of the characteristics and principal findings of the studies included in this review is presented in Table 1 and 2.

A total of 25 publications were initially identified through the literature search. Following assessment of

Table 1. Representative animal and experimental studies investigating nanoparticle-based approaches for anemia.

Author	Nanoparticle / Delivery System	Active Agent	Animal/Experimental Model	Main Mechanism	Main Findings
Goorani et al. (2020)(20)	Biogenic gold nanoparticles (AuNPs)	Plant extract	In vivo/in vitro; mouse	Antioxidant and anti-inflammatory effects; ROS reduction	Improved haematological parameters in experimental models
Jia et al. (2020)(22)	Gadofullerene nanoparticles (GFNPs)	Gadofullerene	Mouse model of aplastic anemia	ROS scavenging; erythrocyte maturation	Enhanced erythropoiesis and red blood cell maturation
Ahmeda et al. (2020)(23)	Green tin nanoparticles (SnNPs)	Plant extract	Mouse model of haemolytic anemia	Antioxidant and anti-inflammatory effects	Reduced oxidative damage and improved haematological indices
Fathy et al. (2019)(25)	Lipid matrix nanoparticles (LMNPs)	$FeSO_4$	Mouse model of IDA	Enhanced iron bioavailability	Improved iron absorption compared with conventional formulations
Hashem et al. (2018)(26)	Fe_3O_4 nanoparticles	Iron	Mouse model of IDA	Folate-mediated targeting	Improved targeted iron delivery and correction of iron deficiency
Elsayed et al. (2014)(27)	Magnetite nanoparticles	Iron	Mouse model of IDA	Controlled iron release	Improved therapeutic efficiency through sustained iron delivery
Hosny et al. (2015)(28)	Iron-loaded solid lipid nanoparticles (Fe-SLNs)	Iron	In vivo pharmacokinetic model	Enhanced intestinal absorption	Improved pharmacokinetic profile and treatment tolerability
Shafie et al. (2016)(29)	Iron nanoparticles	Iron	Mouse model of haemolytic anemia	Anti-inflammatory activity	Reduced inflammation and improved haematological parameters
Szudzik (2021)(31)	Sucrosomial® iron	Iron	Guinea pig model	Sustained gastrointestinal absorption	Efficient iron uptake with prolonged absorption
Bahal et al. (2016)(32)	γPNA nanoparticles	Gene-editing construct	Mouse model of β-thalassaemia	Targeted β-globin gene correction	Demonstrated gene-editing and therapeutic potential
Wang et al. (2019)(34)	Fe_3O_4@APS nanoparticles	Iron with polysaccharide coating	Mouse model	Haematopoietic stimulation	Demonstrated therapeutic and potential theranostic functions
El-Bahr et al. (2021)(35)	Plant-derived iron oxide nanoparticles	Iron	Mouse model	Antioxidant activity	Reduced oxidative stress and improved blood parameters
Darwish et al. (2021)(36)	BSA–Fe nanoparticles	Iron + folic acid	Mouse model of IDA	Albumin-based nanoencapsulation	Improved iron delivery and therapeutic effectiveness
Srinivasu et al. (2015)(37)	Ferric pyrophosphate nanoparticles (FePP NPs)	Iron	Mouse model of IDA	Increased bioavailability	Enhanced iron absorption compared with conventional preparations
Powell et al. (2014)(38)	Ferrihydrite nanoparticles	Iron	Mouse model	Ferritin-mimetic iron storage	Efficient physiological iron delivery and favourable bioavailability

relevance and eligibility, 7 publications were excluded. Consequently, 18 publications were included in the final narrative synthesis. The characteristics and principal findings of the included studies are summarised in Tables 1 and 2

Based on the studies summarized above, no single nanoparticle can be considered universally the most effective, as the investigated anemia models and therapeutic mechanisms differ substantially. Nevertheless, gadolinium-based fullerene nanoparticles (GFNPs) have shown notable efficacy in a murine model of chemotherapy-induced aplastic anemia, primarily through ROS scavenging and enhanced erythrocyte maturation, whereas in iron-

Table 2. Representative review studies and secondary evidence on nanoparticle-based approaches to anemia.

Author	Nanoparticle / Approach	Evidence Type	Main Focus	Principal Conclusions
Alphandéry (2019)(21)	Iron oxide nanoparticles (IONPs)	Narrative review	Iron delivery and magnetic targeting	Discussed the potential of IONPs for targeted iron delivery and therapeutic applications
Kumari & Chauhan (2022)(24)	Iron nanoparticles	Narrative review	Iron bioavailability and absorption	Summarised evidence regarding nanoparticle-based iron delivery and improved absorption
Pai & Garba (2012)(39)	Ferumoxytol	Clinical	Intravenous	Reported clinical evidence supporting intravenous

deficiency anemia (IDA), formulations such as FePP, Fe_3O_4, and iron-loaded solid lipid nanoparticles (Fe-SLNs) have mainly improved hematological outcomes by enhancing iron absorption and bioavailability. A major limitation of these studies is their predominantly preclinical nature, together with differences between animal models and human disease, limited information on the long-term safety and tissue accumulation of nanoparticles, and interspecies differences in dosage and pharmacokinetics. Therefore, findings from animal studies cannot be directly extrapolated to humans. Among the approaches reviewed, ferumoxytol is distinct in that it is an iron-based nanoparticle formulation supported by clinical evidence, particularly in patients with chronic kidney disease and iron deficiency, although safety considerations, including hypersensitivity reactions, remain important.

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DISCUSSION

Anemia remains one of the most prevalent nutritional and haematological disorders worldwide and continues to impose a substantial clinical and socioeconomic burden through its adverse effects on physical development, cognitive performance, work productivity, and overall quality of life (41). Although oral and intravenous iron preparations remain the cornerstone of treatment, particularly for iron deficiency anemia, their therapeutic effectiveness is frequently compromised by limited gastrointestinal absorption, poor bioavailability, treatment-related adverse effects, prolonged administration, and suboptimal patient adherence (41). The findings synthesised in this review indicate that nanoparticle-based drug delivery systems have the potential to overcome many of these limitations by improving iron transport, optimising pharmacological delivery, and enhancing therapeutic efficacy.

One of the most consistently reported advantages of iron-containing nanoplatforms is their ability to improve iron bioavailability and gastrointestinal uptake. The reviewed studies demonstrated that iron oxide nanoparticles, iron-loaded nanocapsules, and other engineered nanostructures can protect iron from premature degradation or precipitation within the gastrointestinal tract while facilitating its transport across intestinal epithelial cells (42). Consequently, a greater proportion of administered iron becomes available for systemic circulation and erythropoiesis. These improvements have been reflected by significant increases in haemoglobin concentration, red blood cell counts, and serum ferritin levels across numerous experimental models (42). Such findings suggest that nanotechnology may substantially enhance the therapeutic efficiency of iron replacement therapy compared with conventional formulations.

Controlled drug release and tissue-specific targeting represent additional strengths of nanoparticle-based therapeutic systems. Several advanced nanocarriers have been designed to deliver iron or erythropoiesis-stimulating agents in a sustained manner, thereby maintaining more stable circulating iron concentrations and reducing fluctuations associated with conventional supplementation (42). This controlled-release profile may improve therapeutic efficiency while potentially reducing transient exposure to high levels of iron and, consequently, the risk of iron-related oxidative stress (43). Furthermore, the physicochemical properties of some nanoparticle-based delivery systems may offer opportunities for preferential iron delivery to hematopoietic tissues; however, direct targeting of the bone marrow or erythroid progenitor cells has not been sufficiently established and requires further validation in appropriate in vivo models (43). Such approaches may therefore have potential to enhance erythropoietic support while limiting unnecessary systemic exposure, although their targeting efficiency, biodistribution, and long-term safety remain to be determined.

Beyond serving as delivery vehicles, numerous

nanoparticle formulations possess intrinsic biological activities that may further contribute to anemia management. Chronic inflammation and oxidative stress play pivotal roles in the pathogenesis of several forms of anemia, particularly anemia associated with chronic disease. Evidence reviewed in this study indicates that certain nanoplatforms exhibit antioxidant and anti-inflammatory properties capable of reducing reactive oxygen species, suppressing inflammatory mediators such as C-reactive protein (CRP), and protecting haematopoietic stem and progenitor cells from oxidative injury. These complementary mechanisms may create a more favourable microenvironment for erythropoiesis and could be particularly advantageous in patients whose anemia is driven by persistent inflammatory processes.

Another important observation emerging from the current literature is the rapid development of multifunctional nanoplatforms that integrate therapeutic and diagnostic capabilities within a single system. Iron oxide-based magnetic nanoparticles, for example, have demonstrated considerable promise not only as iron delivery vehicles but also as contrast agents for medical imaging and treatment monitoring. In parallel, advances in nanoparticle-mediated gene delivery have expanded opportunities for transporting therapeutic genes, regulatory nucleic acids, and genome-editing components aimed at correcting inherited disorders of haemoglobin synthesis. Although these approaches remain largely experimental, they represent promising directions for the future treatment of genetically determined and treatment-resistant forms of anemia.

Despite these encouraging advances, important safety concerns continue to limit the clinical translation of nanoparticle-based therapies. Several studies have reported that certain nanoparticles, particularly when administered at high doses or following prolonged tissue accumulation, may induce oxidative stress, disrupt cellular membrane integrity, impair mitochondrial function, and produce genotoxic effects. Titanium dioxide nanoparticles and selected iron oxide formulations have been identified among the materials associated with such adverse biological responses under specific experimental conditions. These findings emphasise that therapeutic efficacy must always be balanced against potential toxicological risks through comprehensive preclinical safety assessment and rigorous optimisation of nanoparticle design.

In addition to toxicological considerations, several practical challenges remain before nanoparticle-based therapies can be routinely incorporated into clinical practice. Most available evidence has been generated from in vitro experiments and animal models, whereas high-quality clinical data evaluating long-term safety, pharmacokinetics, biodistribution, and therapeutic efficacy in humans remain limited. Moreover, substantial variability in nanoparticle composition, synthesis methods, particle size, surface modification, dosing strategies, and outcome measures complicates direct comparisons across studies. Establishing standardised manufacturing protocols and conducting well-designed multicentre clinical trials will therefore be essential for translating these promising technologies into evidence-based therapeutic options for patients with anemia.

CONCLUSION

The evidence reviewed in this study indicates that nanoparticle-based drug delivery systems represent a highly promising strategy for improving the management of anemia. By enhancing iron absorption and bioavailability, promoting erythropoiesis, reducing oxidative stress and inflammatory responses, and enabling sustained, targeted drug delivery, nanotherapeutic platforms have the potential to address several limitations associated with conventional treatment modalities. Nevertheless, successful clinical implementation will require a more comprehensive understanding of nanoparticle–host interactions, optimisation of biocompatible and safe nanocarriers, and robust evidence from large-scale, well-controlled clinical trials. Continued advances in nanomedicine, precision drug delivery, and biomaterial engineering are expected to accelerate the development of safer, more effective, and increasingly personalised therapeutic approaches for patients with anemia.

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Author Contributions

Saeed Razavi-Dizaji was responsible for the conceptualization, methodology, investigation, data collection, analysis, interpretation of results, and preparation of the manuscript. The author read and approved the final version of the manuscript.

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Availability of Data and Materials

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Ethics Approval and Consent to Participate

Ethical approval was obtained from the Ethics Committee of Urmia University of Medical Sciences (Ethics approval code: [insert code, if applicable]). All

procedures were conducted in accordance with relevant ethical guidelines.

Consent to Publication

Not applicable.

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