

# Anaemia and Oxidative Stress: Toxicological Perspectives and Herbal Therapeutics

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## ABSTRACT

Anaemia remains a major global health burden with multifactorial aetiologies including nutritional deficiency, chronic disease, genetic disorders, and toxic exposures. Oxidative stress—an imbalance between pro-oxidant species and antioxidant defenses—plays a central and underappreciated role in the pathogenesis of many anaemia types. Reactive oxygen and nitrogen species damage erythrocyte membranes and haem proteins, precipitating hemolysis; they impair bone marrow erythropoiesis via oxidative injury to progenitors; and they dysregulate iron metabolism through ferritin/ferroportin modulation and hepcidin-driven sequestration. Exogenous toxicants (heavy metals, organic solvents, certain pharmaceuticals) amplify oxidative insults and may precipitate or worsen anaemia. Conversely, a growing body of experimental and clinical research suggests that selected herbal therapeutics—rich in polyphenols, flavonoids, alkaloids, and micronutrients—can mitigate oxidative damage, modulate iron homeostasis, and support erythropoiesis. This review synthesizes mechanistic links between oxidative stress and anaemia, surveys relevant toxicological drivers, evaluates evidence for herbal interventions, and highlights safety concerns and research priorities. We argue that phytomedicines, when standardized and deployed with attention to interactions and patient vulnerability (for example G6PD deficiency or iron-overload disorders), may serve as valuable adjuncts to conventional therapy, especially in resource-limited settings. Robust clinical trials with mechanistic endpoints, quality-assured formulations, and integrated safety monitoring are necessary to translate promise into practice.

**Keywords:** anaemia, oxidative stress, hemolysis, herbal therapeutics, toxicology

## INTRODUCTION

Anaemia, a condition defined by a reduction in haemoglobin concentration or total red blood cell mass, remains one of the most prevalent public health challenges worldwide [1]. It compromises oxygen delivery to tissues, resulting in fatigue, reduced work capacity, impaired cognitive development in children, and increased morbidity and mortality across all age groups [1]. The World Health Organization estimates that nearly two billion people suffer from anaemia globally, with a disproportionate burden in low- and middle-income countries [1]. The condition arises from a wide array of causes, including iron and micronutrient deficiencies, chronic infectious or inflammatory diseases, genetic disorders such as sickle cell disease and thalassaemia, toxic exposures, and bone marrow suppression [2]. While iron deficiency has traditionally been highlighted as the dominant cause, it is increasingly recognized that oxidative stress is a common denominator linking many different aetiologies of anaemia [3]. Oxidative mechanisms affect both the lifespan of circulating erythrocytes and the efficiency of red blood cell production in the bone marrow [4]. Reactive oxygen and nitrogen species compromise cell membranes, alter haemoglobin structure, and disrupt iron metabolism, thereby precipitating haemolysis and ineffective erythropoiesis [5]. Toxicological factors such as heavy metals, pesticides, and oxidant drugs further aggravate this imbalance, creating a vicious cycle of oxidative injury and anaemia.

Herbal medicines, long used in traditional medical systems, are gaining renewed attention in this context. Rich in phytochemicals with antioxidant, anti-inflammatory, and iron-regulating properties, these remedies are used both for prevention and treatment of anaemia in diverse cultural settings. For example, polyphenol-rich extracts can scavenge free radicals, while nutrient-dense plants provide bioavailable iron and vitamins essential for erythropoiesis [6]. However, their safety, efficacy, and interaction with conventional therapies require critical evaluation. Understanding the interplay between oxidative stress, toxicological drivers, and herbal therapeutics is therefore essential for developing integrative strategies against anaemia that are evidence-based, safe, and accessible.

## 2. Oxidative stress: a central mediator in anaemia

Oxidative stress arises when the generation of reactive oxygen species (ROS) and reactive nitrogen species (RNS) exceeds the capacity of endogenous antioxidant defenses such as glutathione, catalase, and superoxide dismutase [7]. Erythrocytes are particularly vulnerable to oxidative damage because they transport high oxygen loads and contain haem iron that can catalyze free radical reactions [8]. Their membranes are also rich in polyunsaturated fatty acids, which are prone to lipid peroxidation [9].

One major mechanism involves direct damage to haem and haemoglobin. Oxidation of haem iron from ferrous ( $Fe^{2+}$ ) to ferric ( $Fe^{3+}$ ) forms methaemoglobin, incapable of oxygen transport and rapidly targeted for removal [10]. Persistent oxidative stress promotes denaturation of haemoglobin, Heinz body formation, and premature erythrocyte clearance by the spleen [11]. Lipid peroxidation further compromises membrane integrity, decreasing red cell deformability and increasing fragility, which accelerates intravascular hemolysis [12]. In parallel, oxidative modification of structural proteins such as spectrin and ankyrin disrupts cytoskeletal stability, impairing red cell survival [13]. Beyond circulating erythrocytes, oxidative stress also impairs bone marrow function. Hematopoietic stem and progenitor cells are highly sensitive to ROS, and excess oxidative signals lead to apoptosis, defective differentiation, and reduced responsiveness to erythropoietin [14]. The bone marrow microenvironment suffers collateral damage, further compromising erythropoiesis.

Iron metabolism is tightly regulated by oxidative pathways. ROS influence hepcidin expression and ferroportin function, leading to sequestration of iron in storage sites and limiting availability for haem synthesis [15]. Meanwhile, labile iron pools catalyze Fenton reactions, generating additional radicals and perpetuating redox imbalance [16]. Finally, oxidative stress amplifies inflammatory cascades through activation of NF- $\kappa$ B and inflammasomes [17]. The resulting cytokine storm suppresses erythroid activity and exacerbates functional iron deficiency, as seen in anaemia of chronic disease.

## 3. Toxicological drivers of oxidative anaemia

A range of exogenous agents promote oxidative injury and anaemia:

**Heavy metals.** Lead, cadmium, arsenic, and mercury generate ROS directly or disrupt antioxidant enzymes. Lead inhibits  $\delta$ -aminolevulinic acid dehydratase and ferrochelatase, impairing haem synthesis and producing microcytic anaemia [18]. Cadmium and arsenic induce oxidative damage in erythrocytes and bone marrow [19]. Organic solvents and industrial chemicals. Benzene and related compounds produce marrow toxicity and oxidative metabolites that suppress erythropoiesis and provoke aplastic or hypoplastic anaemia [20].

**Pharmaceutical agents.** Certain antimicrobials (dapsone, primaquine), sulfonamides, and nitrofurantoin provoke oxidative haemolysis, particularly in individuals with glucose-6-phosphate dehydrogenase (G6PD) deficiency [21]. Chemotherapeutic agents and high-dose NSAIDs can impair marrow function [22].

**Pesticides and herbicides.** Organophosphates and paraquat produce systemic oxidative stress; paraquat in particular causes widespread ROS generation with multi-organ injury and can contribute to haemolytic processes [23]. Mycotoxins and natural plant toxins. Some plant-derived toxins induce oxidative hemolysis or bone marrow suppression [24]. Environmental and lifestyle factors. Chronic alcohol, smoking, and pollutants augment oxidative burden and expedite red cell turnover [25].

**Recognizing these toxicants is vital in both prevention and management.** Exposure reduction, chelation for metal toxicity, and targeted supportive care (transfusion, erythropoietic agents) remain mainstays; adjunctive antioxidant strategies are under investigation.

## 4. Herbal therapeutics: mechanisms relevant to anaemia and oxidative stress

Herbal medicines may mitigate oxidative anaemia through several mechanisms: Direct antioxidant activity. Polyphenols, flavonoids, and tannins scavenge free radicals and reduce lipid peroxidation in erythrocytes, preserving membrane integrity [26]. Enhancement of endogenous defenses. Activation of transcription factors such as Nrf2 upregulates glutathione synthesis and antioxidant enzymes, improving cellular resilience [27].

Iron modulation. Some herbs facilitate iron absorption or mobilize stores; others chelate labile iron and reduce Fenton-driven ROS [28]. The net effect depends on constituent chemistry and dosing. Support of erythropoiesis. Certain botanicals stimulate erythroid progenitors or enhance erythropoietin signaling indirectly via anti-inflammatory actions or improved nutritional status. Anti-inflammatory effects [29]. By suppressing cytokine-mediated erythropoiesis inhibition, herbs may counteract anaemia of chronic disease. Mitochondrial protection. Phytochemicals that preserve mitochondrial function support the energy needs of erythroid precursors and red cell maintenance [30].

### Representative classes and agents:

**Circuminoids.** Curcumin exhibits radical-scavenging activity, upregulates Nrf2-dependent genes, and reduces inflammatory cytokines that suppress erythropoiesis [31]. Experimental models show reduced hemolysis and improved marrow parameters. **Flavonoids.** Quercetin and rutin protect erythrocytes from oxidative damage and have been shown to stabilize membranes and reduce lipid peroxidation [32]. **Silymarin.** Silymarin's antioxidant and

membrane-stabilizing effects support red cell survival in toxin-induced hemolysis; it also improves hepatic function, indirectly benefiting iron metabolism [33]. Polysaccharide-rich herbs. Certain seaweeds and mushrooms provide micronutrients and prebiotic effects that enhance iron bioavailability and general nutritional status [34]. Iron-containing botanicals. *Moringa oleifera* and other greens supply bioavailable iron and vitamin C, which together facilitate absorption; however, quantification is essential to avoid iron overload [35]. Erythropoiesis-supporting mixtures. Traditional multi-herb formulas often combine nutrient-rich plants with antioxidant species to address both deficiency and oxidative mechanisms.

## 6. Safety considerations and toxicological risks of herbal use

Herbal remedies are not inherently benign and may pose risks particularly relevant to anaemia and oxidative stress: Pro-oxidant effects at high doses. Some polyphenols exhibit pro-oxidant properties in the presence of transition metals, potentially worsening oxidative haemolysis if not dosed appropriately. Iron absorption interference [36]. Tea, green tea extracts, and certain polyphenol-rich herbs inhibit non-heme iron absorption and can exacerbate iron-deficiency anaemia if consumed with meals [37]. G6PD deficiency and hemolytic risk. Agents such as fava bean derivatives and other aromatic compounds may precipitate acute hemolysis in individuals with enzymatic deficiencies. Contamination and adulteration [38]. Heavy-metal contamination, misidentified plant species, or addition of pharmaceuticals (e.g., iron salts or erythropoiesis-stimulating agents) can cause harm or mask true efficacy. Herb-drug interactions [39]. Phytochemicals modulate cytochrome P450 enzymes and transporters, altering pharmacokinetics of drugs used in anaemia management (e.g., immunosuppressants after transplant) or other comorbid medications [40]. Allergic and idiosyncratic reactions. Immunoallergic hemolytic anaemia has been reported with certain botanicals in rare cases.

These safety signals motivate careful screening (including G6PD testing in at-risk populations), use of quality-assured products, counseling on timing relative to iron-rich meals, and active adverse-event monitoring.

## CONCLUSION

Oxidative stress is a pivotal mechanism linking diverse causes of anaemia through hemolysis, impaired erythropoiesis, and iron dysregulation. Toxicological exposures amplify these processes, necessitating prevention and targeted interventions. Herbal therapeutics offer multi-modal mechanisms-antioxidant action, enhancement of endogenous defenses, iron modulation, and support for erythropoiesis-that can complement conventional care, particularly in settings where access to standard therapies is limited. However, safety considerations, quality assurance, and rigorous clinical validation are essential before broad adoption. With methodical translational research and prudent clinical practice, phytomedicines may become valuable adjuncts in the integrated management of anaemia driven or complicated by oxidative stress.

## REFERENCES

1. Aja O. A., Egba S. I., Omoboyowa D. A., Odo C. E., Vining-Ogu I. C., Oko F. O (2020) Anti-anaemic and immunomodulatory potentials of aqueous, chloroform and methanol leaf extracts of *whitfieldia lateritia* on 2, 4-dinitrophenylhydrazine induced anaemia in rats. *World Journal of Pharmacy Research* 2020; 9(10): 44-58
2. Eberechukwu Laura Ikechukwu, Polycarp Nnacheta Okafor and Simeon Ikechukwu Egba. In vitro assessment of the anti-sickling properties of *Buchholzia coriacea* and *Mucuna pruriens* seed extracts. *In vitro Cellular and Development Biology-Animal*. 2020, <https://doi.org/10.1007/s11626-020-00512-y>
3. Alum, E. U., Ugwu, O. P. C., Aja, P. M., Obeagu, E. I., Inya, J. E., Onyeije, P. E., Agu, E. and Awuchi, C. G. Restorative effects of ethanolic leaf extract of *Datura stramonium* against methotrexate-induced hematological impairments, *Cogent Food & Agriculture*, 2023; 9:1, DOI: 10.1080/23311932.2023.2258774
4. Obeagu EI, Igwe MC, Obeagu GU. Oxidative stress's impact on red blood cells: Unveiling implications for health and disease. *Medicine*. 2024;103(9):e37360. doi:10.1097/MD.00000000000037360
5. Wang Q, Zennadi R. The role of RBC oxidative stress in sickle cell disease: From the molecular basis to pathologic implications. *Antioxidants*. 2021;10(10):1608. doi:10.3390/antiox10101608
6. Rudrapal M, Rakshit G, Singh RP, Garse S, Khan J, Chakraborty S. Dietary Polyphenols: Review on Chemistry/Sources, Bioavailability/Metabolism, antioxidant effects, and their role in disease management. *Antioxidants*. 2024;13(4):429. doi:10.3390/antiox13040429
7. Uti, D.E., Offor, C.E., & Alum, E.U. Redox Signaling Disruption and Antioxidants in Toxicology: From Precision Therapy to Potential Hazards. *Cell Biochem Biophys* (2025). <https://doi.org/10.1007/s12013-025-01846-8>
8. Comporti M, Signorini C, Buonocore G, Ciccoli L. Iron release, oxidative stress and erythrocyte ageing. *Free Radical Biology and Medicine*. 2002;32(7):568–76. doi:10.1016/S0891-5849(02)00759-1
9. Clemens MR, Waller HD. Lipid peroxidation in erythrocytes. *Chemistry and Physics of Lipids*. 1987;45(2–4):251–68. doi:10.1016/0009-3084(87)90068-5
10. Sandal S, Thakur R, Vats T, Jamwal V, Thakur S, Verma L, et al. From Remedy to risk: A contemporary case report of methemoglobinemia caused by unregulated intake of a herbal product. *Cureus*. 2025. doi:10.7759/cureus.92096

11. Herman TF, Killeen RB, Javaid MU. Heinz Body. StatPearls - NCBI Bookshelf. 2023. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK551622/>
12. Akwari, A.A., Okoroh, P.N., Aniokete, U.C., Abba, J.N., Uti, D.E. Phytochemicals as modulators of ferroptosis: a novel therapeutic avenue in cancer and neurodegeneration. *Mol Biol Rep* **52**, 636 (2025). <https://doi.org/10.1007/s11033-025-10752-4>
13. Spinelli S, Straface E, Gambardella L, Caruso D, Falliti G, Remigante A, et al. Aging injury impairs structural properties and cell signaling in human red blood cells; açaí berry is a keystone. *Antioxidants*. 2023;12(4):848. doi:10.3390/antiox12040848
14. Ugwu, OPC and Alum, EU. Exploring the Potential of Medicinal Plants in Bone Marrow Regeneration and Hematopoietic Stem Cell Therapy. *Int J Bone Marrow Res*. 2025; 8(1): 001-005. <https://dx.doi.org/10.29328/journal.ijbmr.1001019>. DOI: 10.29328/journal.ijbmr.1001019.
15. Roemhild K, Von Maltzahn F, Weiskirchen R, Knüchel R, Von Stillfried S, Lammers T. Iron metabolism: pathophysiology and pharmacology. *Trends in Pharmacological Sciences*. 2021;42(8):640–56. doi:10.1016/j.tips.2021.05.001
16. Abdulkarimov N, Kokabi K, Kunz J. Ferroptosis and iron homeostasis: molecular mechanisms and neurodegenerative disease implications. *Antioxidants*. 2025;14(5):527. doi:10.3390/antiox14050527
17. Sun X, Tang Y, Jiang C, Luo S, Jia H, Xu Q, et al. Oxidative stress, NF-κB signaling, NLRP3 inflammasome, and caspase apoptotic pathways are activated in mammary gland of ketotic Holstein cows. *Journal of Dairy Science*. 2020;104(1):849–61. doi:10.3168/jds.2020-18788
18. Essien E.B., Alum E.U., and Abbey E.W (2014). Heavy Metals Content of Food Crops Grown in Oil Exploration Areas of Rivers State. *International Journal of Science and Nature*, **5** (3):486-493.
19. Alum, E. U. Highlights of Heavy Metals: Molecular Toxicity Mechanisms, Exposure Dynamics, and Environmental Presence. *IAA Journal of Applied Sciences*. 2023; 10(3):8-19. <https://doi.org/10.59298/IAAJAS/2023/4.2.3222>
20. Agency for Toxic Substances and Disease Registry (US). HEALTH EFFECTS. Toxicological Profile for Benzene - NCBI Bookshelf. 2007. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK591289/>
21. Recht J, Chansamouth V, White NJ, Ashley EA. Nitrofurantoin and glucose-6-phosphate dehydrogenase deficiency: a safety review. *JAC-Antimicrobial Resistance*. 2022;4(3). doi:10.1093/jacamr/dlac045
22. Pountos I, Georgouli T, Calori GM, Giannoudis PV. Do Nonsteroidal Anti-Inflammatory Drugs affect bone healing? A critical analysis. *The Scientific World Journal*. 2012;2012:1–14. doi:10.1100/2012/606404
23. Mehta PP, Annam RS, Hadiyel IN. Catastrophic Outcomes: Rapid Multi-Organ Failure from Paraquat Poisoning- A Case Report. *PubMed*. 2025;66(2):811–7. Available from: <https://pubmed.ncbi.nlm.nih.gov/40703903/>
24. Malvandi AM, Shahba S, Mehrzad J, Lombardi G. Metabolic disruption by naturally occurring mycotoxins in circulation: a focus on vascular and bone homeostasis dysfunction. *Frontiers in Nutrition*. 2022;9. doi:10.3389/fnut.2022.915681
25. Al-Gubory KH. Environmental pollutants and lifestyle factors induce oxidative stress and poor prenatal development. *Reproductive BioMedicine Online*. 2014;29(1):17–31. doi:10.1016/j.rbmo.2014.03.002
26. Rudrapal M, Khairnar SJ, Khan J, Dukhyil AB, Ansari MA, Alomary MN, et al. Dietary Polyphenols and Their Role in Oxidative Stress-Induced Human Diseases: Insights Into Protective Effects, Antioxidant Potentials and Mechanism(s) of Action. *Frontiers in Pharmacology*. 2022;13. doi:10.3389/fphar.2022.806470
27. Bell KFS, Fowler JH, Al-Mubarak B, Horsburgh K, Hardingham GE. Activation of NRF2-Regulated glutathione pathway genes by ischemic preconditioning. *Oxidative Medicine and Cellular Longevity*. 2011;2011:1–7. doi:10.1155/2011/689524
28. Cotoraci C, Ciceu A, Sasu A, Hermenean A. Natural antioxidants in anemia treatment. *International Journal of Molecular Sciences*. 2021;22(4):1883. doi:10.3390/ijms22041883
29. Creangă EC, Stan R, Nicolae AC, Drăgoi CM, Dumitrescu IB. Personalized therapeutic advances in erythropoietin signaling: from anemia management to extensive clinical applications. *PubMed*. 2025;17(9). Available from: <https://pubmed.ncbi.nlm.nih.gov/41012526/>
30. Ramya RP, Megha KB, Reshma S, Krishnan MJA, Amir S, Sharma R, et al. Mitochondrial disease management through phytochemical interventions. *Molecular and Cellular Biochemistry*. 2025. doi:10.1007/s11010-025-05360-6
31. Rahban M, Habibi-Rezaei M, Mazaheri M, Saso L, Moosavi-Movahedi AA. Anti-Viral potential and modulation of NRF2 by curcumin: pharmacological implications. *Antioxidants*. 2020;9(12):1228. doi:10.3390/antiox9121228

32. Zbikowska HM, Antosik A, Szejk M, Bijak M, Olejnik AK, Saluk J, et al. Does quercetin protect human red blood cell membranes against  $\gamma$ -irradiation? *Redox Report.* 2013;19(2):65–71. doi:10.1179/1351000213Y.0000000074

33. Jaffar HM, Al-Asmari F, Khan FA, Rahim MA, Zongo E. Silymarin: Unveiling its pharmacological spectrum and therapeutic potential in liver diseases—A comprehensive narrative review. *Food Science & Nutrition.* 2024;12(5):3097–111. doi:10.1002/fsn3.4010

34. Mandal AK, Parida S, Behera AK, Adhikary SP, Lukatkin AA, Lukatkin AS, et al. Seaweed in the diet as a source of bioactive metabolites and a potential natural immunity booster: A comprehensive review. *Pharmaceuticals.* 2025;18(3):367. doi:10.3390/ph18030367

35. Palanisamy H, Manikandan M, Manoharan JP, Vidyalakshmi S. Enhancing the bioavailability of iron in *Moringa oleifera* for nutrient deficiency. *Nutrire.* 2022;47(2). doi:10.1186/s41110-022-00167-7

36. Scarano A, Laddomada B, Blando F, De Santis S, Verna G, Chieppa M, et al. The chelating ability of plant polyphenols can affect iron homeostasis and gut microbiota. *Antioxidants.* 2023;12(3):630. doi:10.3390/antiox12030630

37. He Y, Chen J. Severe iron-deficiency anemia after short-term moderate consumption of green tea in woman: a rare case report. *Heliyon.* 2024;10(17):e36666. doi:10.1016/j.heliyon.2024.e36666

38. Al-Dubai H, Al-Mashdali A, Hailan Y. Acute hemolysis and methemoglobinemia secondary to fava beans ingestion in a patient with G6PD deficiency. *Medicine.* 2021;100(47):e27904. doi:10.1097/MD.00000000000027904

39. Luo L, Wang B, Jiang J, Fitzgerald M, Huang Q, Yu Z, et al. Heavy metal Contaminations in Herbal Medicines: Determination, comprehensive risk assessments, and solutions. *Frontiers in Pharmacology.* 2021;11. doi:10.3389/fphar.2020.595335

40. Journal of Advances in Medical and Pharmaceutical Sciences. 2019. doi:10.9734/jamps

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