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**Review Article**

# Anemia of Chronic Inflammation: Hepcidin, Iron Sequestration and Erythropoietin Resistance through the Concept of *Pandu*

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**ABSTRACT:**

**Background:** Anemia of chronic inflammation develops when inflammatory activity restricts iron availability and impairs red-cell production. Hepcidin-mediated iron sequestration is central to this process, but reduced erythropoietin production, altered marrow responsiveness and shortened erythrocyte survival also contribute. These mechanisms complicate the common assumption that anemia necessarily reflects depleted iron stores.

**Objective:** To examine the interaction between hepcidin, iron sequestration and erythropoietin resistance, and to appraise the conceptual relevance of *Pandu* without assuming equivalence between Ayurvedic and biomedical categories.

**Methods:** A targeted narrative review considered primary mechanistic studies, human clinical investigations, intervention trials, authoritative guidance and verified classical Ayurvedic passages. Evidence concerning inflammatory anemia was distinguished from evidence concerning uncomplicated iron-deficiency anemia.

**Discussion:** Inflammation can reduce intestinal iron transfer and macrophage iron release through the hepcidin–ferroportin pathway. Iron restriction also influences erythropoietin receptor availability, linking inadequate substrate supply with altered cellular responsiveness. Consequently, ferritin, transferrin saturation and inflammatory findings require joint interpretation, particularly when absolute iron deficiency coexists. Classical descriptions of *Pandu* address altered complexion, weakness and disturbed tissue function. They provide a historical clinical framework but do not identify hepcidin excess or a specific erythropoietic defect. Ayurvedic studies conducted in iron-deficiency anemia cannot establish efficacy in inflammatory anemia or demonstrate reversal of erythropoietin resistance.

**Conclusion:** The useful relationship between inflammatory anemia and *Pandu* lies in formulating testable questions about clinical presentation, nutrition and functional recovery. Such investigation requires defined anemia phenotypes, reproducible

interventions and objective assessment of iron availability and erythropoiesis alongside appropriate treatment of the underlying disease.

**Keywords:** anemia of inflammation; hepcidin; ferroportin; iron sequestration; erythropoietin resistance; Ayurveda; *Pandu*.

## Introduction

Anemia accompanying chronic inflammatory illness presents a practical difficulty: circulating iron may be low even when storage iron has not been exhausted. Giving this pattern the same interpretation as uncomplicated nutritional iron deficiency overlooks how inflammation changes iron distribution. The demonstration that interleukin-6 (IL-6) induces hepcidin and lowers circulating iron provided an experimental explanation for this separation between stored iron and iron available for erythropoiesis.[1]

The discovery that hepcidin binds the cellular iron exporter ferroportin further clarified the mechanism. Inflammatory signalling can restrict iron release from cells, limiting delivery to developing erythrocytes.[2] However, this pathway does not explain every component of the anemia. A patient may also have an inadequate erythropoietin response, impaired marrow responsiveness, blood loss or another nutritional deficiency. The relative contribution of each determines whether an intervention is likely to help.

An Ayurvedic appraisal through *Pandu* is relevant because the classical account considers changes in complexion together with weakness and disturbances of bodily function. The central question is whether that account can inform clinical description and research without being treated as an earlier molecular explanation of inflammatory anemia. This review argues that a useful comparison must preserve the distinction between an observed syndrome, its proposed mechanism and demonstrated treatment benefit.

## Review approach

This narrative review drew on targeted searches of PubMed records, journal websites, accessible full-text repositories and official guidance available. Search concepts included anemia of inflammation, hepcidin, ferroportin, iron sequestration, erythropoietin resistance, erythroferrone, *Pandu* and Ayurvedic anemia trials. Primary studies were prioritised for mechanistic and clinical claims. Classical passages were checked for chapter and verse, with historical descriptions evaluated separately from modern explanatory commentary.

The review did not use a registered protocol, duplicate screening or a quantitative synthesis. It therefore offers a focused interpretation rather than an exhaustive assessment of all anemia interventions. Particular attention was given to whether a study examined inflammatory anemia, iron-deficiency anemia or a mixed population.

## Hepcidin and the restriction of iron availability

Hepcidin is a liver-derived peptide hormone that regulates the movement of iron into plasma. Ferroportin exports iron from intestinal enterocytes and from macrophages that recycle ageing erythrocytes. Hepcidin binding promotes ferroportin internalisation and degradation, reducing iron transfer from these sources.[2] The resulting limitation is especially consequential for the marrow, where sustained haemoglobin production requires a continuing iron supply. Stored iron can therefore coexist with inadequate iron delivery to erythroid precursors.

IL-6 provides a well-characterised link between inflammation and hepatic hepcidin production. Nemeth and colleagues demonstrated this relationship using cellular experiments, animal models and human IL-6 administration.[1] Wrighting and Andrews subsequently showed that signal transducer and activator of transcription 3 (STAT3) mediates IL-6-induced hepcidin transcription.[3] These findings explain how an inflammatory signal can change systemic iron handling. They do not imply that IL-6 alone determines hepcidin concentration in every chronic illness.

Iron regulation also responds to erythropoietic demand. Kautz and colleagues identified erythroferrone as an erythroid-derived regulator that suppresses hepcidin during increased

erythropoiesis.[4] This introduces a competing physiological signal: the marrow seeks greater iron availability while inflammation may favour its retention. The measured hepcidin concentration reflects the interaction of these influences, together with iron status and other clinical factors. A high value should therefore be interpreted within a defined disease context rather than treated as an isolated diagnosis.

Absolute iron deficiency can coexist with inflammatory iron restriction. Theurl and colleagues examined iron regulation in chronic-disease anemia, iron-deficiency anemia and combined states, demonstrating differences in hepcidin regulation and cellular iron handling.[5] This distinction has direct clinical relevance. A person with inflammatory bowel disease, for example, may have both inflammation-related restriction and depleted stores from blood loss. The presence of inflammation does not remove the need to investigate actual iron loss, and a low serum iron concentration cannot distinguish these mechanisms by itself.

**Erythropoietin resistance involves more than an inadequate iron supply**

Erythropoietin, produced predominantly by the kidneys, supports erythroid precursor survival and maturation in response to reduced oxygen availability. During inflammatory illness, its circulating concentration may be insufficient for the severity of the anemia. Baer and colleagues demonstrated a blunted erythropoietin response in rheumatoid arthritis.[6] This is relative insufficiency: a value within or above a laboratory reference interval may still be lower than expected for the haemoglobin concentration. It should be distinguished from reduced cellular responsiveness to an otherwise adequate hormonal signal.

Experimental work also shows why inflammatory cytokines should not be treated as interchangeable. In Hep3B cells, Faquin and colleagues found that several cytokines inhibited hypoxia-induced erythropoietin production, whereas IL-6 stimulated it under the tested conditions.[7] This was a hepatoma-cell experiment, not a direct measurement of renal hormone production in patients. Its relevance is that cytokine effects depend on the cellular setting; a general statement that all inflammatory mediators suppress erythropoietin would be inaccurate.

Inflammation can also affect erythroid development and red-cell survival. Libregts and colleagues showed that sustained interferon-γ production caused anemia in mice through reduced erythrocyte lifespan and impaired erythropoiesis, with an IRF-1/PU.1 transcriptional pathway implicated in erythroid precursors.[8] These findings support mechanisms beyond iron sequestration. They also explain why improving circulating iron may produce an incomplete response when inflammatory pressure on erythropoiesis persists. The extent to which a particular experimental pathway dominates in an individual patient remains uncertain.

Iron restriction itself can change responsiveness to erythropoietin. Khalil and colleagues identified a pathway involving transferrin receptor 2 and the receptor-trafficking protein Scribble. Iron deprivation reduced surface erythropoietin receptor availability and impaired proliferative and differentiation responses while preserving survival signalling.[9] Iron supply and hormone responsiveness are therefore mechanistically connected. Resistance need not mean complete loss of erythropoietin signalling, and it cannot always be overcome by increasing the hormone dose.

These observations favour a layered interpretation of a poor erythropoietic response. Reduced hormonal production, restricted iron delivery and altered precursor behaviour can coexist. Calling the whole process "erythropoietin resistance" may be convenient, but it can conceal different therapeutic problems. Research and clinical reports should specify whether they mean an inadequate endogenous hormone response, a high requirement for an erythropoiesis-stimulating agent (ESA), or experimentally demonstrated impairment of receptor signalling.

**Interpreting iron studies in an inflammatory setting**

Ferritin is useful because a low concentration supports depleted iron stores, but inflammation can raise its concentration independently of storage sufficiency. WHO guidance therefore requires attention to inflammation when ferritin is used to assess iron status.[10] C-reactive protein can help characterise that inflammatory context. A normal or raised ferritin concentration cannot, by itself, exclude coexisting deficiency or demonstrate adequate iron delivery to erythroid precursors. Interpretation must account for the underlying disease, recent treatment and the wider laboratory pattern.

Transferrin saturation estimates how much circulating transferrin carries iron and is commonly reduced in both absolute deficiency and inflammatory restriction. Transferrin or total iron-binding capacity often rises in uncomplicated deficiency but may fall with inflammation; combined disease can blur the distinction.[5] Reticulocyte and red-cell indices contribute to assessment of marrow output and iron delivery within the wider clinical evaluation.

**Table 1. Indicative patterns in absolute deficiency and inflammatory iron restriction**

| Measurement | Predominant absolute iron deficiency | Predominant inflammatory restriction | Coexisting deficiency and inflammation |
|---|---|---|---|
| Serum ferritin | Low | Often normal or raised | May be low, normal or raised |
| Transferrin saturation | Low | Low | Low |
| Transferrin or total iron-binding capacity | Often raised | Often low or normal | Variable |
| Mean corpuscular volume | Often reduced as deficiency advances | Frequently normal; may be reduced | Normal or reduced |
| Main interpretive issue | Establish the cause of iron depletion | Assess inflammation and restricted availability | Avoid excluding deficiency because ferritin is preserved |

Table note: These are qualitative patterns, not diagnostic cut-offs. Disease-specific criteria, treatment history and additional causes of anemia must be considered.[5,10]

Hepcidin measurement can strengthen mechanistic investigation, but analytical comparability matters. In an international harmonisation study, van der Vorm and colleagues demonstrated substantial differences in absolute hepcidin results across measurement procedures and evaluated a shared reference material.[11] That historical finding should not be used to dismiss subsequent analytical improvements. It does require investigators to report the assay and calibration approach and to justify any proposed threshold. A change measured within one laboratory is not automatically transferable to another platform.

**What intervention studies establish**

Treatment should address the condition sustaining inflammation while identifying additional causes of anemia. Chronic kidney disease requires particular care because reduced erythropoietin production and iron restriction may occur together. KDIGO guidance recommends systematic evaluation and treatment decisions based on the clinical setting, iron status and the benefits and risks of available therapies.[12] Its recommendations apply to kidney disease; they

should not be transferred unchanged to every patient with inflammatory anemia.

Evidence from rheumatoid arthritis illustrates the potential value of disease control. In an exploratory analysis of the randomised MEASURE study, Isaacs and colleagues found that tocilizumab treatment was associated with lower hepcidin and acute-phase markers, followed by improved haemoglobin and iron-binding capacity.[13] This supports a role for IL-6 signalling in rheumatoid-arthritis-associated anemia. Because several disease processes change during treatment, the analysis does not establish that every haemoglobin improvement was mediated solely through hepcidin reduction.

Iron treatment also requires a defined population and comparator. In PIVOTAL, a proactive higher-dose intravenous iron strategy improved the primary composite clinical outcome and reduced ESA requirements compared with a reactive lower-dose strategy in patients receiving maintenance haemodialysis.[14] The result supports that monitored strategy in the studied setting. It does not establish that all inflammatory anemia requires intravenous iron or that the same approach is appropriate during every active infection. Bypassing intestinal absorption does not remove the need to consider iron status and the underlying illness.

The consequences of increasing erythropoietic stimulation are similarly context dependent. In TREAT, darbepoetin targeting a higher haemoglobin concentration in patients with type 2 diabetes and chronic kidney disease did not improve the principal cardiovascular or renal outcomes and increased stroke risk.[15] Thus, a haemoglobin rise cannot be assumed to establish an overall clinical benefit. An inadequate response should prompt reassessment of reversible causes rather than automatic escalation. Current kidney guidance specifically addresses evaluation of ESA hyporesponsiveness.[12]

Direct hepcidin inhibition offers mechanistic proof of concept. Van Eijk and colleagues showed that lexaptepid, a hepcidin-binding agent, prevented the fall in serum iron during experimental human endotoxaemia.[16] This demonstrates that the pathway can be modified in humans. The participants and short experimental exposure differ substantially from patients with sustained inflammatory anemia. Maintaining circulating iron in that model does not establish durable haemoglobin improvement, reduced transfusion requirements or improved functional outcomes in chronic disease.

## Appraising *Pandu* without assuming molecular equivalence

### The classical clinical description

The *Charaka Samhita* describes *Pandu* through changes in complexion, strength and tissue condition. *Chikitsa Sthana* 16/4–6 presents a *Pitta*-predominant disturbance involving the *Dhatu* and describes diminished complexion and strength, together with reduced *Rakta* (*Alpa Rakta*). Verses 13–16 include weakness, impaired appetite, fatigue, dizziness, breathlessness and exertional difficulty.[17] These observations support comparison at the level of clinical presentation. They do not distinguish iron-deficiency anemia from inflammatory, renal or other haematological causes.

The resemblance is therefore clinically suggestive but diagnostically incomplete. Pallor and reduced exercise tolerance can direct attention towards anemia; laboratory evaluation establishes whether haemoglobin is reduced and helps determine why. A modern diagnosis should not be inferred from complexion alone. Equally, assigning every inflammatory anemia to a particular *Dosha* subtype because a cytokine has been associated with inflammation would require evidence that is currently absent from the studies considered here.

### Tissue nourishment and functional impairment

The classical account of nourishment provides a second point for appraisal. In *Charaka Samhita*, *Chikitsa Sthana* 15/27–28, *Rasa* is described as undergoing transformation into *Rakta* through the action associated with *Pitta*.[18] The passage belongs to a historical account of tissue formation. It should not be translated into a claim that *Rasa* denotes transferrin or that *Pitta* identifies hepatic hepcidin signalling. Its research relevance lies in asking how

nutritional intake, nutrient availability and bodily function relate within a defined clinical population.

Inflammatory iron restriction makes the distinction between intake and availability particularly useful. Adequate dietary iron does not guarantee adequate marrow delivery when iron export is restricted. This modern observation can guide a question framed through tissue nourishment, but the biochemical explanation comes from contemporary experimental evidence. The conceptual comparison is an interpretation proposed in this review, not a mechanism demonstrated in a classical text.

The description of reduced strength and disturbed tissue condition in *Pandu* also encourages assessment beyond haemoglobin alone.[17] Fatigue, appetite and physical capacity may remain relevant patient outcomes. However, they are influenced by the underlying inflammatory illness and may improve independently of erythropoiesis. A symptom response should therefore be reported alongside objective measures rather than used to infer release of sequestered iron or restored erythropoietin sensitivity.

**Table 2. Classical observations and questions suitable for investigation**

| Classical observation or concept | Potential research question | Suitable contemporary assessment | Interpretive boundary |
|---|---|---|---|
| Altered complexion and *Alpa Rakta* in *Pandu*[17] | How does the clinical assessment relate to objectively confirmed anemia? | Haemoglobin, blood count and evaluation of anemia cause | Neither observation identifies iron stores or hepcidin activity |
| Reduced strength and exertional difficulty[17] | Does treatment improve physical function alongside erythropoiesis? | Validated fatigue measures, functional assessment and haematological outcomes | Symptom improvement alone does not demonstrate a marrow mechanism |
| *Rasa–Rakta* transformation[18] | How do nutritional status and measured iron availability relate? | Dietary assessment, iron indices and clinical context | Classical tissue categories do not identify transport proteins or receptors |
| *Pitta*-predominant tissue disturbance[17] | Are prespecified Ayurvedic assessments reproducible within inflammatory anemia? | Assessor agreement and independently measured disease activity | A *Dosha* category is not a validated inflammatory biomarker |

**Ayurvedic clinical evidence and the problem of transferring findings**

Evidence labelled as *Pandu* research must be examined for the anemia phenotype actually studied. Prajapati and colleagues reported an open-label randomised trial enrolling 105 participants in a study designed for iron-deficiency anemia. It compared *Opuntia elatior* fruit juice with *Punarnava Mandura* and reported changes in haemoglobin and iron-related measurements.[19] It did not establish treatment effects in a population defined by inflammatory iron sequestration or assess erythropoietin resistance. Its findings cannot resolve the central mechanistic questions of the present review.

The distinction matters for iron-containing Ayurvedic preparations. A haemoglobin increase after such a preparation may result from iron provision, changes in diet, treatment of an accompanying condition or other influences. Establishing a separate effect on

inflammation or hepcidin requires an appropriate comparator and direct measurement. Describing an intervention as improving *Agni*, the classical digestive and transformative function, or supporting *Rakta* does not determine which pathway produced the observed response.

**A research framework for inflammatory anemia and *Pandu***

Future studies should first define the biological population. Participants with predominantly absolute deficiency should be distinguished from those with inflammatory restriction and from those with combined disease. The underlying inflammatory diagnosis, renal function, disease activity and recent treatments should be recorded. Recruiting a broad *Pandu* population without this classification would make an apparent treatment effect difficult to interpret: improvement in a deficient subgroup could conceal little or no effect in those with preserved stores.

The Ayurvedic assessment should be specified independently of the laboratory findings. Investigators need operational definitions, assessor training and an estimate of agreement before testing associations with hepcidin or erythropoietic measurements. If a classification is altered after investigators see the biological results, a supposedly informative correlation may simply reflect the way the groups were constructed. A reproducible clinical classification has value even if its eventual relationship with an inflammatory biomarker is weak or absent.

Interventions require equally clear description. For herbal products, reporting should include botanical identity, plant part, preparation, dose and quality characterisation, consistent with the elaborated CONSORT recommendations for herbal trials.[20] For *Lauha* or *Mandura* preparations, additional questions include the amount and form of iron delivered, batch consistency, dissolution characteristics and relevant contaminant testing. These measurements would help separate an effect of iron supplementation from any proposed effect on inflammatory signalling.

A controlled add-on trial could preserve appropriate care for the underlying disease in both groups. If the question concerns a specific effect beyond iron replacement, the comparator should account for the iron supplied rather than simply compare treatment with no treatment. Outcome assessment should be masked where feasible. Changes in immunomodulatory drugs, iron therapy, transfusion and ESA exposure need to be captured because each can affect the same outcomes attributed to the investigational treatment.

Clinical and mechanistic outcomes should be prespecified separately. Haemoglobin response, transfusion burden, ESA requirement and validated functional outcomes address treatment benefit. Hepcidin, transferrin saturation and reticulocyte measurements can examine the proposed pathway. Repeated measurements are preferable when the hypothesis involves sequence: a fall in hepcidin should precede improved iron delivery if it is claimed to mediate that improvement. A correlation between two changes alone would still be insufficient to establish mediation.

Safety evaluation should reflect the enrolled population and the intervention. Relevant outcomes include intolerance, discontinuation, hepatic and renal findings and iron accumulation when iron-containing products are used. A study involving chronic inflammatory disease must also record changes in the underlying illness. Completion rates and reasons for withdrawal should remain visible in the analysis, so that apparent improvement among completers is not mistaken for the experience of everyone assigned to treatment.

**Discussion**

The evidence supports a connected account of iron restriction and erythropoietic dysfunction. Hepcidin limits iron export, while iron deprivation can alter erythropoietin receptor availability. Cytokine effects and shortened red-cell survival add further mechanisms. This explains why neither an iron measurement nor an erythropoietin concentration can summarise the entire disorder. It also explains the

variable response to interventions aimed at only one component.

An appraisal through *Pandu* is most productive when it preserves that clinical diversity. The classical syndrome can inform the description of complexion, appetite, strength and exertional symptoms, while modern investigations determine the anemia phenotype. The relationship becomes scientifically useful if a reproducible Ayurvedic assessment helps characterise symptoms, treatment tolerance or functional recovery. Its value should be assessed through those outcomes rather than assumed from similarities in terminology.

This review is limited by selective narrative retrieval, heterogeneous study populations and dependence on accessible classical editions and translations. Cellular and animal findings identify plausible mechanisms but do not quantify their contribution in every human illness. Trials in haemodialysis or rheumatoid arthritis cannot establish a uniform treatment strategy across all inflammatory conditions. The Ayurvedic evidence considered does not directly establish reversal of hepcidin-mediated sequestration or erythropoietin resistance. These limitations define the questions that future studies need to answer.

## Conclusion

Anemia of chronic inflammation reflects restricted iron availability together with variable impairment of erythropoietin production, marrow responsiveness and erythrocyte survival. Hepcidin connects inflammation with iron sequestration, while cellular iron sensing helps explain why iron restriction and hormonal resistance can occur together. *Pandu* offers a historical clinical framework for describing impaired complexion and function, but it does not identify a specific molecular anemia phenotype. Meaningful integration requires accurate diagnosis, treatment of the underlying disease and controlled investigation of reproducible interventions using both clinical and mechanistic outcomes.

## References


1. Nemeth E, Rivera S, Gabayan V, Keller C, Taudorf S, Pedersen BK, et al. IL-6 mediates hypoferremia of inflammation by inducing the synthesis of the iron regulatory hormone hepcidin. J Clin Invest. 2004;113(9):1271–1276. doi:10.1172/JCI20945.

2. Nemeth E, Tuttle MS, Powelson J, Vaughn MB, Donovan A, Ward DM, et al. Hepcidin regulates cellular iron efflux by binding to ferroportin and inducing its internalization. Science. 2004;306(5704):2090–2093. doi:10.1126/science.1104742.

3. Wrighting DM, Andrews NC. Interleukin-6 induces hepcidin expression through STAT3. Blood. 2006;108(9):3204–3209. doi:10.1182/blood-2006-06-027631.

4. Kautz L, Jung G, Valore EV, Rivella S, Nemeth E, Ganz T. Identification of erythroferrone as an erythroid regulator of iron metabolism. Nat Genet. 2014;46(7):678–684. doi:10.1038/ng.2996.

5. Theurl I, Aigner E, Theurl M, Nairz M, Seifert M, Schroll A, et al. Regulation of iron homeostasis in anemia of chronic disease and iron deficiency anemia: diagnostic and therapeutic implications. Blood. 2009;113(21):5277–5286. doi:10.1182/blood-2008-12-195651.

6. Baer AN, Dessypris EN, Goldwasser E, Krantz SB. Blunted erythropoietin response to anemia in rheumatoid arthritis. Br J Haematol. 1987;66(4):559–564. doi:10.1111/j.1365-2141.1987.tb01344.x.

7. Faquin WC, Schneider TJ, Goldberg MA. Effect of inflammatory cytokines on hypoxia-induced erythropoietin production. Blood. 1992;79(8):1987–1994. doi:10.1182/blood.V79.8.1987.bloodjournal7981987.

8. Libregts SF, Gutiérrez L, de Bruin AM, Wensveen FM, Papadopoulos P, van Ijcken W, et al. Chronic IFN-γ production in mice induces anemia by reducing erythrocyte life span and inhibiting erythropoiesis through an IRF-1/PU.1 axis. Blood. 2011;118(9):2578–2588. doi:10.1182/blood-2010-10-315218.

9. Khalil S, Delehanty L, Grado S, Holy M, White Z 3rd, Freeman K, et al. Iron modulation of erythropoiesis is associated with Scribble-mediated control of the erythropoietin receptor. J Exp Med. 2018;215(2):661–679. doi:10.1084/jem.20170396.

10. World Health Organization. WHO guideline on use of ferritin concentrations to assess iron status in individuals and populations [Internet]. Geneva: World Health Organization; 2020 [cited 2026 Oct 27]. Available from: https://www.who.int/publications/i/item/9789240000124

11. van der Vorm LN, Hendriks JCM, Laarakkers CM, Klaver S, Armitage AE, Bamberg A, et al. Toward worldwide hepcidin assay harmonization: identification of a commutable secondary reference material. Clin Chem. 2016;62(7):993–1001. doi:10.1373/clinchem.2016.256768.

12. Kidney Disease: Improving Global Outcomes (KDIGO) Anemia Work Group. KDIGO 2026 Clinical Practice Guideline for the Management of Anemia in Chronic Kidney Disease (CKD). Kidney Int. 2026;109(1S):S1–S99. doi:10.1016/j.kint.2025.06.006.

13. Isaacs JD, Harari O, Kobold U, Lee JS, Bernasconi C. Effect of tocilizumab on haematological markers implicates interleukin-6 signalling in the anemia of rheumatoid arthritis. Arthritis Res Ther. 2013;15:R204. doi:10.1186/ar4397.

14. Macdougall IC, White C, Anker SD, Bhandari S, Farrington K, Kalra PA, et al. Intravenous iron in patients undergoing maintenance hemodialysis. N Engl J Med. 2019;380(5):447–458. doi:10.1056/NEJMoa1810742.

15. Pfeffer MA, Burdmann EA, Chen CY, Cooper ME, de Zeeuw D, Eckardt KU, et al. A trial of darbepoetin alfa in type 2 diabetes and chronic kidney disease. N Engl J Med. 2009;361(21):2019–2032. doi:10.1056/NEJMoa0907845.

16. van Eijk LT, John ASE, Schwoebel F, Summo L, Vauléon S, Zöllner S, et al. Effect of the antihepcidin Spiegelmer lexaptepid on inflammation-induced decrease in serum iron in humans. Blood. 2014;124(17):2643–2646. doi:10.1182/blood-2014-03-559484.

17. Agnivesha. *Charaka Samhita*: *Pandu Chikitsa*, *Chikitsa Sthana*, chapter 16, verses 4–6 and 13–16 [Internet]. Charak Samhita Research, Training and Skill Development Centre; 2020 [cited 2026 Oct 27]. doi:10.47468/CSNE.2020.e01.s06.017. Available from: https://carakasamhitaonline.com/index.php?title=Pandu_Chikitsa_Adhyaya

18. Agnivesha. *Charaka Samhita*: *Grahani Chikitsa*, *Chikitsa Sthana*, chapter 15, verses 27–28 [Internet]. Charak Samhita Research, Training and Skill Development Centre; 2020 [cited 2026 Oct 27]. doi:10.47468/CSNE.2020.e01.s06.016. Available from: https://carakasamhitaonline.com/index.php?title=Grahani_Chikitsa_Adhyaya

19. Prajapati SM, Anand S, Acharya R, Goyal M. Effect of *Opuntia elatior* Mill. (Nagaphani) in the management of *Pandu Roga* w. s. r to iron deficiency anemia; an open labeled randomized standard controlled clinical trial. Ayu. 2020;41(2):87–97. doi:10.4103/ayu.AYU_31_18.

20. Gagnier JJ, Boon H, Rochon P, Moher D, Barnes J, Bombardier C; CONSORT Group. Reporting randomized, controlled trials of herbal interventions: an elaborated CONSORT statement. Ann Intern Med. 2006;144(5):364–367. doi:10.7326/0003-4819-144-5-200603070-00013.