RESEARCH PAPER

Enhancing Haematological Health in Children: Role of *Dwigun Pippali Yog* in *Bal Pandu*

Dr. Anamika Banjare[1*], Dr. Neeraj Agrawal[2*], Dr. Lowkesh Chandravanshi[3*], Dr. Satyawati Rathiya[4*], Dr. Chudamani Sinha[5*], Dr. Deeplata Bunker[6*], Dr. Rahul Yadav[7*]

[1].MD Scholar, Dept. of kaumarabhritya, GAC, Raipur, C.G, Email ID: anamikabanjare26@gmail.com
[2].MD, PhD, Professor and HOD, Dept of kaumarabhritya, GAC, Raipur, C.G Email ID: dr. neeraj2001in@yahoo.co.in
[3].M.D. Associate Professor, Dept of kaumarabhritya, GAC, Raipur, C.G. Email ID: lowkeshc@gmail.com
[4].M.D. PhD, Lecturer, Dept of kaumarabhritya, GAC, Raipur, C.G Email ID: satirathiya@gmail.com
[5].MD Scholar, Dept of kaumarabhritya, GAC, Raipur, C.G, Email ID: lsinha207@gmail.com
[6].MD Scholar, Dept of kaumarabhritya, GAC, Raipur, C.G, Email ID: deepa91bunker@gmail.com
[7].MD Scholar, Dept of kaumarabhritya, GAC, Raipur, C.G., Email ID: rahulyadav123.ry86@gmail.com

Corresponding Author-Dr. Anamika Banjare
Email ID: anamikabanjare26@gmail.com

ABSTRACT

Childhood anaemia is still a major public health problem especially in developing countries where nutritional deficits and recurrent infections contribute considerably to morbidity. Iron deficiency anaemia severely affects physical growth, cognitive development, immunological competence and academic performance. In Ayurveda, paediatric anaemia is associated with the *Pandu.* It is characterised by the *Pandu varnata* (pallor), *Daurbalya* (weakness), *Agnimandya* (bad digestion), *Aruchi* (lack of appetite) and reduced vitality. Classical Ayurvedic management involves rectification of deficient *Agni*, nutrition of Rasa and *Rakta Dhatu* and restoration of systemic vigour. *Dwigun Pippali Yog*, a classical formulation containing Jaggery (*Guda*), Ginger (*Shunthi*), *Mandura Bhasma*, Sesame (*Tila*), and Long Pepper (*Pippali*) in double proportion is a rational therapeutic approach. A detailed review of classical Ayurvedic literature including *Charaka Samhita, Sushruta Samhita, Ashtanga Hridaya, Bhavaprakasha*, and authoritative *Rasashastra* texts was done. The current day biomedical literature on childhood anaemia and pharmacology of individual ingredients was also reviewed. The formulation possesses multi-dimensional therapeutic utility such as *Deepana-Pachana* (digestive stimulation), correction of *Agnimandya*, enhancement of nutrient absorption, haematinic activity, antioxidant protection, immunomodulation and tissue restorative effects. *Mandura Bhasma* is a source of bioavailable iron, *Pippali* helps in absorption through Yogvahi action, Shunthi supports gastrointestinal function, *Tila* is a nutritional support and *Guda* is an iron supplement with anabolic nourishment. These measures in totality support Rasa-Rakta *Dhatu Poshana* and correction of *Pandu Samprapti*. *Dwigun Pippali Yog* seems to be a clinically relevant classical formulation for the management of Bal Pandu especially in cases of iron deficiency with impaired digestion and undernutrition. Its holistic pharmacodynamic profile advocates its potential as a safe and sensible ayurvedic strategy in paediatric anaemia. More well-designed clinical studies are needed to evaluate its efficacy and safety.

Objective: To review the role of *Dwiguna Pippali Yoga* in *Bal Pandu* using Ayurvedic principles and current pharmacological evidences.

Methods: Review of classical Ayurvedic classics including *Charaka Samhita, Sushruta Samhita, Ashtanga Hridaya, Bhavaprakasha* and *Rasashastra* texts along with recent literature on anaemia and ingredient pharmacology was done.

Results: The formulation has shown multi-dimensional utility via haematinic, digestive stimulant, bioavailability enhancer, nutritional, antioxidant and tissue restorative activities.

Conclusion: *Dwiguna Pippali Yoga* seems to be therapeutically important classical formulation for paediatric anaemia particularly in case of coexisting poor digestion, under nutrition and iron deficiency.

Keywords: *Pandu, Childhood Anaemia, Dwigun Pippali Yog, Mandura Bhasma, Pippali, Ayurveda, Iron Deficiency Anaemia*

How to cite this article: Banjare A, Agrawal N, Chandravanshi L, Rathiya S, Sinha C, Bunker D, Yadav R. Enhancing Haematological Health in Children: Role of Dwigun Pippali Yog in Bal Pandu. Int J Drug Deliv Technol. 2026;16(62s): 443-450. DOI: 10.25258/ijddt.16.62s.51

Source of support: Nil.

Conflict of interest: None.

1. INTRODUCTION

Iron deficiency anaemia (IDA) is the most common micronutrient deficiency in the world, affecting more than 1.62 billion people, which accounts for about 24.8% of the world population.[1] The highest disease burden of IDA is in children under five years and pregnant women as IDA has direct impact on cognitive development, immune function, physical growth and school performance.

The problem is worrisome in India with 67.1% of Indian children in the age group of 6–59 months being anaemic according to NFHS-5 (2019–2021) data. In Chhattisgarh, the prevalence increased from 59% (NFHS-4) to 67% (NFHS-5) in the same age group with 36.3% moderate and 2.2% severe anaemia cases.[2,3]

The standard of management is oral ferrous sulphate, although poor tolerability in paediatric patients, including nausea, vomiting, stomach irritation and constipation, considerably interferes with compliance. This means we need to look for better tolerated and bioavailable iron formulations.

The classical Ayurvedic formulation *Dwigun Pippali Yog* described in *Ashtanga Hridayam*, Chikitsasthana (Ch. 16/15) by Acharya Vagbhata4 is a sophisticated multi-ingredient approach.[4] This review critically evaluates the pharmacological basis of the formulation using contemporary molecular and clinical evidence.

2. MATERIAL AND METHODS

A systematic literature review was conducted using the following databases and sources:

- PubMed/MEDLINE — clinical trials, pharmacokinetic studies, in vitro/in vivo studies
- Google Scholar — pharmacology reviews and herbal medicine research
- AYUSH Research Portal — traditional medicine evidence
- Classical Ayurvedic texts: Charaka Samhita, Ashtanga Hridayam, Bhavaprakasha, Rasaratna Samuccaya
- Inclusion criteria: Studies on IDA, *Mandura Bhasma*, Piperine, Zingiber officinale**,** Sesamum indicum, jaggery published 1990–2024

3. FORMULATION: DWIGUN PIPPALI YOG

The name *Dwigun Pippali Yog* originates from its formation in *Ashtanga Hridayam*, *Chikitsasthana*, Chapter 16, verse 15.[4] The name means double proportion (*Dwigun*) of *Pippali* with respect to other ingredients — a planned formulation technique to maximise the bioavailability increase.

3.1 Composition table

Ingredient	Botanical/ Source	Active Constituents	Classical Role	Modern Category
Mandura Bhasma	Ferric oxide (Fe_2O_3) — incinerated with *Triphala* decoctions	Fe_2O_3 nanoparticles, phytoconstituents from processing herbs	*Rakta Vardhaka, Pandu nashana*	Hematinic, Iron supplement
Pippali (×2)	*Piper longum* L. (Long pepper)	Piperine (5–10%), Piperlongumine, Pellitorine, Pipernonaline	*Yogvahi, Deepana, Pachana*	Bioavailability Enhancer, Digestive stimulant
Shunthi	Zingiber officinale Roscoe (Dried ginger)	6-Gingerol, 8-Gingerol, Shogaols, Zingerone, Zingiberene	*Amapachaka, Vatanulomana*	Prokinetic, Anti-emetic, Anti-inflammatory

Guda (Jaggery)	Saccharum officinarum — unrefined sugarcane product	Natural iron (11 mg/100g), sucrose, minerals, antioxidants	*Vata-Pittahara, Anupana*	Natural iron source, Prebiotic, Vehicle
Tila (Sesame)	*Sesamum indicum* L. (Black sesame seeds)	Sesamin, Sesamolin, Sesamol, Calcium, Fe, Zinc, Vitamin E	*Asthi-Majja Poshana, Balya*	Antioxidant, Bone marrow support, Mineral supplement

4. DETAILED PHARMACOLOGICAL ANALYSIS OF INDIVIDUAL COMPONENTS

4.1 *Mandura Bhasma* (Calcined Ferric Oxide)

4.1.1 Pharmaceutical Characterization

Mandura Bhasma is prepared by repeated incineration (*Marana*) of raw iron with decoctions of *Triphala (Amalaki, Bibhitaka, Haritaki)*.[5] This Ayurvedic processing results in nano-crystalline Fe2O3 particles (50–200 nm) coated with phytoconstituents, which is fundamentally different from conventional ferrous sulfate.[6,7]

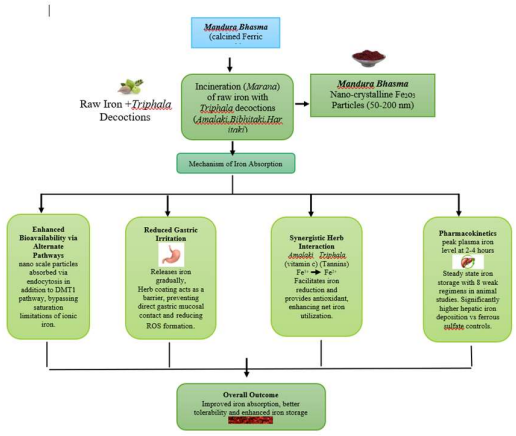
4.1.2 Iron Absorption Mechanism

1.Increased Bioavailability via Alternative Pathways: The nano-scale size of the particles allows absorption via endocytosis as well as the traditional DMT1 (Divalent Metal Transporter-1) pathway, avoiding saturation constraints of ionic iron.[8]

2. Reduced Gastric Irritation: Unlike ferrous sulphate, which releases significant amounts of free Fe 2+ that generate reactive oxygen species (ROS), *Mandura Bhasma* releases iron slowly. Organic herb-coating functions as a physical barrier against direct contact with gastric mucosa.[9]

3. Synergistic Herb Interaction: Phytoconstituents of *Triphala* (ascorbic acid from *Amalaki*, tannins) help in the reduction of iron ($Fe^{3+} \rightarrow Fe^{2+}$) and also give antioxidant protection throughout absorption process, improving net iron utilisation.[10]

4. Pharmacokinetics: Peak plasma iron levels occur at 2–4 hours post-administration. Steady state iron storage is observed with 8-week regimens in animal experiments with considerably greater hepatic iron deposition vs. ferrous sulphate controls.[11]



4.2 *Pippali* (Piper longum) – Enhancer of Bioavailability

4.2.1 Principle of Activity: Piperine

Piperine (1-piperoylpiperidine), which constitutes about 5–10% of Piper longum, is the principal bioactive alkaloid responsible for the bioavailability increasing action of the formulation. The Dwigun (double) fraction of *Pippali* is specially formulated to maximise this effect.[12]

4.2.2 Molecular Bases

P-glycoprotein (P-gp) Inhibition: Piperine inhibits the P-gp efflux pump (MDR1/ABCB1) in the intestinal epithelium, therefore inhibiting efflux of iron and co-administered medication molecules back into the gut lumen. This considerably improves net absorption in the intestine.

4.2.3. CYP3A4 Inhibition:

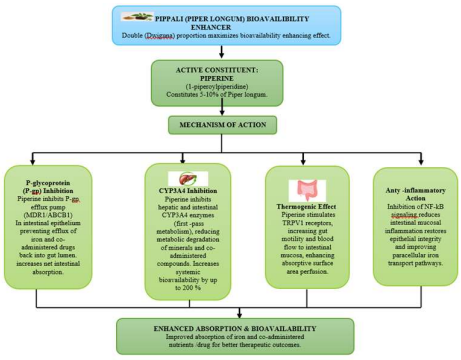
Piperine inhibits hepatic and intestinal CYP3A4 enzymes responsible for first-pass metabolism and lowers the metabolic degradation of minerals and co-administered drugs, improving systemic bioavailability to 200%. [13]

4.2.4. Thermogenic Effect:

Piperine stimulates TRPV1 (Transient Receptor Potential Vanilloid 1) receptors, boosting gastrointestinal motility and blood flow to intestinal mucosa, improving perfusion of absorptive surface area.[14]

4.2.5. Anti-inflammatory Effect:

Blocking NF-κB signalling lowers inflammation in the intestinal mucosa, helps restore the integrity of the epithelium and improves paracellular iron transport pathways.[15]



4.3 Shunthi — Zingiber officinale (Dry Ginger)

4.3.1 Active ingredients

Bioactives like 6-Gingerol, 8-Gingerol, 6-Shogaol, Zingerone, α/β-Zingiberene. These chemicals work synergistically at many targets.

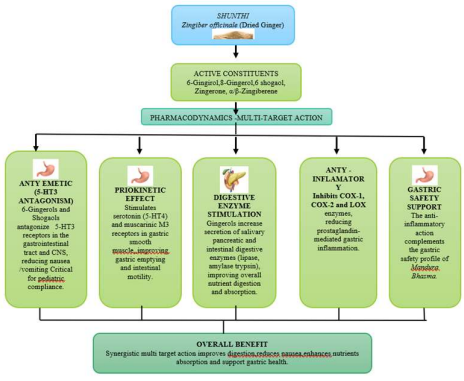
4.3.2 Pharmacodynamics

4.3.2.1 Anti-emetic (5-HT3 Antagonism): 6-Gingerol and Shogaols have been shown to antagonise 5-hydroxytryptamine type 3 (5-HT3) receptors in the gastrointestinal tract and CNS and reduce nausea/vomiting – crucial for paediatric compliance.[16]

4.3.2.2 Prokinetic effect: Activates serotonin (5-HT4) and muscarinic M3 receptors located in the stomach smooth muscle, leading to enhanced gastric emptying and intestinal motility. [17]

4.3.2.3 Stimulation of Digestive Enzymes: The gingerols boost the production of digestive enzymes (lipase, amylase, trypsin) from the salivary, pancreatic and intestinal glands, hence enhancing the total digestion and absorption of nutrients.[18]

4.3.2.4 Anti-inflammatory: Inhibits COX-1, COX-2 and LOX enzymes and thereby reduces prostaglandin driven gastric inflammation -- complements the gastric safety profile of *Mandura Bhasma*.[19]



4.4 *Guda* (Jaggery) -- Natural Iron Carrier

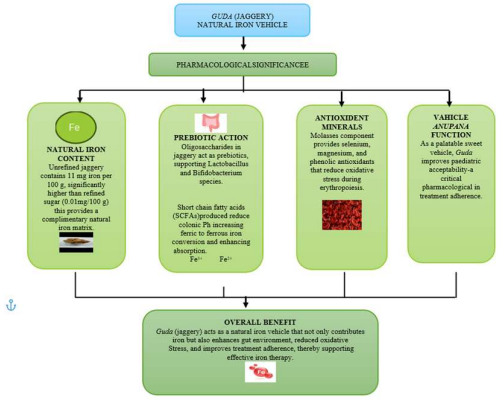
4.4.1 Pharmacological Importance

4.4.1.1 Natural Iron Content: Unrefined jaggery contains around 11 mg of iron per 100 g. Refined sugar contains a mere 0.01 mg/100 g. It gives an additional natural iron matrix.[20]

4.4.1.2 Prebiotic Action: The oligosaccharides in Jaggery function as prebiotics that help the Lactobacillus and Bifidobacterium species. Short-chain fatty acids (SCFAs) decrease intestinal pH, which increases ferric-to-ferrous iron conversion and absorption.[21]

4.4.1.3 Antioxidant Minerals: The molasses component includes selenium, magnesium and phenolic antioxidants which decrease oxidative stress in erythropoiesis.

4.1.1.4 Vehicle (*Anupana*) Function: *Guda* being a tasty sweet vehicle, increases paediatric acceptance, an important pharmacological aspect in adherence to therapy.



4.5 *Tila* (Sesamum indicum) – Bone and Antioxidant Support

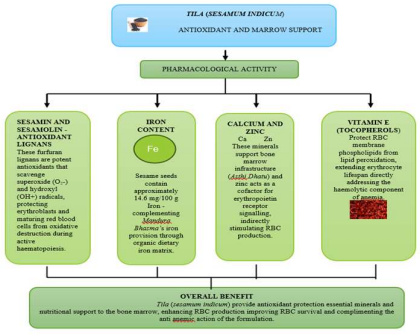
4.5.1 Pharmacological action

4.5.1.1 Sesamin and Sesamolin — Antioxidant Lignans Sesamin and sesamolin are furofuran lignans with high antioxidant activity. They scavenge superoxide (O 2-) and hydroxyl (OH•) radicals, protecting erythroblasts and mature red blood cells from oxidative damage during active hematopoiesis.[22,23]

4.5.1.2 Iron Content: Sesame seeds provide approximately 14.6 mg/100 g of iron – supplementing *Mandura Bhasma*'s iron supply through an organic dietary iron matrix.[24]

4.5.1.3 Calcium and Zinc: Calcium and zinc are involved in building the infrastructure of bone marrow (*Asthi Dhatu*), and zinc is a cofactor for erythropoietin receptor signalling, indirectly increasing RBC synthesis.

4.5.1.4 Vitamin E (Tocopherols): Prevents lipid peroxidation of RBC membrane phospholipids, hence increasing erythrocyte life span — thereby counteracting the haemolytic component of anaemia.



5. KEY CLINICAL STUDY –

The following table summarizes key clinical trials, in vivo, and in vitro studies on individual components of *Dwigun Pippali Yog*, providing the modern scientific foundation for this formulation

S. No.	Author / Year	Study Type	Ingredient / Drug	Key Findings	Conclusion / Relevance
1	Bhardwaj RK et al., 2002	In vitro, human intestinal cells	Piperine (*Piper longum*)	Piperine inhibited P-gp efflux and CYP3A4 activity in Caco-2 cells; enhanced bioavailability of co-administered compounds by 60–200%	Validates *Pippali* as *Yogvahi*; molecular mechanism of bioavailability enhancement confirmed
2	Kulkarni S et al., 2020	In vivo (Wistar rats)	*Mandura Bhasma* vs. Ferrous Sulfate	*Mandura Bhasma* showed higher Hb, serum ferritin, and lower gastric toxicity (ROS, mucosal damage) than ferrous sulfate	Supports superiority of *Mandura Bhasma* in safety and efficacy over conventional iron salt therapy
3	Rathore B et al., 2020	Pharmaceutical and clinical review	*Mandura Bhasma*	Nano-crystalline Fe_2O_3 structure confirmed by XRD and TEM; therapeutic efficacy in anaemia validated in clinical settings	Establishes pharmaceutical standardization and hematinic efficacy of *Mandura Bhasma*
4	Beaudry C et al., 2023	Systematic review	Herbo-mineral	Herbo-mineral	Strongly supports use

			formulations / *Mandura Bhasma*	formulations demonstrate significantly better GI tolerability than ionic iron supplements; phytoconstituent coating reduces mucosal oxidative stress	of *Mandura Bhasma* as a pediatric-friendly iron formulation
5	Balsubramani SP et al., 2015	Pharmacological review	*Triphala* + Iron formulations	Vitamin C (from *Amalaki*) reduces Fe^{3+} to Fe^{2+}, enhancing intestinal iron absorption; tannins modulate iron chelation and transport	Explains the role of *Triphala* in *Mandura Bhasma* processing — enhances iron bioavailability biochemically
6	Solanki R et al., 2011	Pharmacokinetic study	Piperine — multiple	*Trikatu* combination (including pepper combination (*Piper longum*)	ding *Piper longum*) increased bioavailability of co-administered drugs by enhancing GI absorption and reducing first-pass hepatic metabolism	ration ale for *Pippali*'s *Yogvahi* role and justifies *Dwigun* (double) proportion in the formulation

6. DISCUSSION

The pharmacological investigation of *Dwigun Pippali Yog* indicates a comprehensive multi-mechanistic approach to paediatric iron deficient anaemia that tackles the main limitations of standard iron therapy.

Superiority over Ferrous sulphate: Standard ferrous sulphate therapy is effective but produces high concentrations of free Fe^{2+} in the gastric environment. These are responsible for the production of reactive oxygen species which cause mucosal damage, nausea, vomiting and constipation resulting in poor compliance especially in children. The nano-crystalline structure of *Mandura Bhasma* with herbal coating releases irons gradually and is absorbed through several channels (DMT1 and endocytosis) that demonstrably reduce stomach toxicity.[25,26]

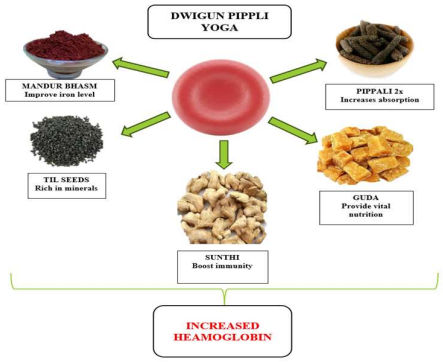
The *Dwigun* (Double) *Pippali* Principle : The Pharmacological Validation of the Deliberate Doubling of *Pippali* Proportion Piperine, a clinically validated method for bioavailability augmentation, works via dual inhibition of both the P-glycoprotein efflux pump and the CYP3A4 enzyme system. Bhardwaj et al. (2002) observed up to 200% enhancement in bioavailability of co-administered

substances — explaining why classical Ayurvedic practitioners expressly advised double-proportion *Pippali* with mineral preparations. **Complementary Iron Sources :** *Mandura Bhasma* (inorganic Fe2O3 nanoparticles), Guda (organic dietary iron matrix, ~11 mg/100g) and Tila (sesame iron, ~14.6 mg/100g) offer iron in three different chemical forms and absorption pathways that decrease reliance on any one absorption mechanism and thus enhance overall iron delivery even in children with partial absorptive dysfunction **Paediatric Compliance Optimisation:** *Shunthi*'s 5-HT3 antagonism (anti-emetic), *Guda*'s palatability, and *Mandura Bhasma*'s low GI irritation, combined, address the single greatest hurdle to paediatric iron therapy — treatment compliance. This pharmacological complementarity could be an explanation for the classical Ayurvedic physicians' combination of these particular substances.

Research Limitations: The review is constrained by the absence of dedicated randomised clinical studies on *Dwigun Pippali Yog* as a whole formulation. Pharmacological evidence is drawn from examinations of specific ingredients. Dose standardisation, pharmacokinetic profile of the whole formulation and paediatric safety studies are still important areas for future research.

7. CONCLUSION

1. ***Dwigun Pippali Yog*** represents a pharmacologically sophisticated classical Ayurvedic formulation for Childhood Iron Deficiency Anaemia (*Bal Pandu*). Each of its five components contributes distinct, molecularly validated mechanisms:
2. ***Mandura Bhas*ma:** Nano-crystalline hematinic with superior bioavailability and gastric safety
3. ***Pippali* (*Dwigun*):** First-in-class plant-derived bioavailability enhancer via P-gp/CYP3A4 inhibition
4. ***Shunthi*:** Prokinetic and anti-emetic ensuring formulation tolerability and gut readiness
5. ***Guda*:** Natural iron matrix with prebiotic activity and pediatric acceptability
6. ***Tila***: Antioxidant protection of erythropoiesis and bone marrow mineral support



Modern pharmacological evidence strongly corroborates the classical prescription rationale. Future priorities must include prospective RCTs in pediatric IDA populations, pharmacokinetic profiling of the complete formulation, and GMP standardization protocols.

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