

A Comprehensive Review on Novel Oral Iron Syrup Formulations for the Effective Management of Iron Deficiency Anemia

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Abstract—Iron Deficiency Anemia (IDA) remains one of the most prevalent nutritional disorders globally, disproportionately affecting women, children, and adolescents. Although conventional iron supplements such as ferrous sulfate and ferrous fumarate effectively restore iron levels, their use is frequently limited by gastrointestinal irritation, metallic aftertaste, and poor patient compliance. Recent advancements in oral iron syrup formulations have sought to overcome these challenges through innovations that enhance bioavailability, palatability, and gastrointestinal tolerance. Novel iron complexes such as ferric polymaltose, iron polysaccharide, and sucrosomial iron exhibit improved absorption and reduced adverse effects compared to traditional salts. The incorporation of bioenhancers like vitamin C, folic acid, and piperine further facilitates iron uptake and utilization. Natural sweetening and flavoring agents, including honey, fennel, and sugarcane syrup, not only mask unpleasant taste but also contribute to antioxidant and digestive benefits, rendering these syrups ideal for pediatric and geriatric patients. Moreover, emerging nanotechnology-based and herbal iron syrup formulations offer promising biocompatibility, enhanced stability, and hepatoprotective potential. This review presents an updated overview of recent developments in oral iron syrup formulations, emphasizing their technological innovations, pharmacological advantages, and future prospects in the effective management of Iron Deficiency Anemia.

Index Terms—Iron Deficiency Anemia; Oral Iron Syrup

I. INTRODUCTION

Iron Deficiency Anemia (IDA) continues to be one of the most common and challenging nutritional disorders globally, affecting more than two billion people, particularly women of reproductive age,

children, and elderly populations. This condition primarily arises from inadequate dietary intake, malabsorption, chronic blood loss, or increased physiological demands during growth and pregnancy. Iron is a vital trace element necessary for the synthesis of hemoglobin, myoglobin, and numerous enzymes involved in oxygen transport, mitochondrial respiration, and energy metabolism. Deficiency of iron compromises oxygen delivery to tissues, leading to clinical manifestations such as fatigue, pallor, cognitive decline, dizziness, and a weakened immune response. The persistence of IDA remains a major public health concern, especially in low- and middle-income countries, where nutritional inadequacies and parasitic infections are prevalent contributors. Traditionally, the management of iron deficiency relies on oral and parenteral iron supplementation, with oral formulations being preferred due to their affordability, ease of administration, and safety profile. Among these, iron syrups have gained significant importance, particularly for pediatric and geriatric populations who often face difficulties in swallowing solid dosage forms such as tablets or capsules. However, conventional oral iron salts including ferrous sulfate, ferrous fumarate, and ferrous gluconate are frequently associated with several drawbacks such as gastrointestinal discomfort, nausea, constipation, metallic taste, and low patient adherence. Moreover, the limited bioavailability of these formulations often necessitates higher dosages, which in turn intensify gastrointestinal side effects, leading to poor compliance and suboptimal treatment outcomes. To address these limitations, recent pharmaceutical research has focused on technological advancements

in oral iron syrup formulations. The next generation of iron supplements aims to achieve enhanced bioavailability, improved gastrointestinal tolerance, and better taste-masking properties, while ensuring patient comfort and compliance. Among these innovations, ferric polymaltose complexes and iron (III)-hydroxide polymaltose complexes have emerged as effective alternatives to traditional ferrous salts. These non-ionic complexes provide gradual and controlled release of iron, improve intestinal absorption, and significantly reduce gastric irritation. Their mechanism of slow iron liberation allows for efficient mucosal uptake without the formation of free radicals, minimizing oxidative stress on gastrointestinal tissues. Another noteworthy development includes the use of sucrosomial iron and iron polysaccharide complexes, which encapsulate iron in phospholipid or carbohydrate matrices. These advanced systems protect the iron core from gastric degradation, enabling targeted absorption in the intestine. Such formulations exhibit superior tolerability, minimal metallic aftertaste, and negligible gastrointestinal side effects, making them highly suitable for sensitive groups like pregnant women and children. Additionally, the incorporation of bioenhancers and hematinic cofactors has become an essential strategy in optimizing iron absorption. Nutrients such as vitamin C (ascorbic acid), folic acid, vitamin B12, and natural compounds like piperine (from black pepper) and gingerol (from ginger) are often co-formulated to enhance solubility, facilitate duodenal absorption, and promote erythropoiesis. These bioactive agents not only increase the bioavailability of iron but also contribute to improved hematological indices and overall metabolic function. Taste-masking and flavor enhancement are equally vital in ensuring compliance, especially among pediatric patients. Modern iron syrups utilize natural sweetening agents such as honey, sugarcane syrup, and fruit or fennel extracts to mask the metallic aftertaste of iron. Such sensory improvements play a crucial role in increasing palatability and patient acceptance without compromising therapeutic efficacy. Beyond synthetic approaches, the emergence of herbal and nutraceutical-based iron formulations marks a significant shift toward safer and more holistic anemia management. Polyherbal preparations containing botanicals such as *Emblica officinalis* (Amla), *Moringa oleifera*, *Withania somnifera*

(Ashwagandha), and *Punica granatum* (Pomegranate) have shown promise in restoring hemoglobin levels naturally while providing additional antioxidant, hepatoprotective, and immunomodulatory effects. These plant-derived formulations are biocompatible, exhibit minimal adverse reactions, and align with the global trend toward sustainable and plant-based therapeutics. Recent advancements in nanotechnology-based iron delivery systems have further revolutionized the field of anemia management. Nano-iron particles and encapsulated iron complexes offer improved solubility, controlled release, and enhanced intestinal permeability compared to conventional ferrous salts. These nano-formulations not only improve absorption efficiency but also reduce the required therapeutic dose, thereby minimizing toxicity and improving patient adherence. Collectively, these innovations represent a paradigm shift in the design and development of oral iron syrups — transitioning from conventional symptom-relief approaches to targeted, bioavailable, and patient-friendly formulations. Despite these significant strides, challenges such as formulation stability, standardization of bioavailability, and long-term clinical validation persist. Further research and comparative clinical studies are necessary to establish the therapeutic superiority and safety of these novel preparations. Thus, the present review focuses on the recent advances in oral iron syrup formulations, emphasizing improvements in composition, absorption mechanisms, taste masking, and patient compliance. It highlights the technological innovations and pharmacological rationale underpinning these formulations and explores their potential role in effectively addressing Iron Deficiency Anemia within modern healthcare systems.

II. COMPOSITION AND ROLE OF INGREDIENTS IN IRON DEFICIENCY SYRUP

Iron deficiency syrup is a poly-nutrient, medicated oral formulation developed to restore hemoglobin concentration and replenish iron stores in patients suffering from iron deficiency anemia (IDA). The composition of such syrups reflects a balanced integration of pharmaceutical excipients, nutritional ingredients, and active pharmacological agents, all designed to enhance absorption, stability, and palatability.

Each ingredient in the formulation contributes distinct therapeutic or functional properties, working synergistically to correct anemia, improve red blood cell formation, and enhance overall vitality.

1. Iron Salts (Ferrous Sulphate / Ferrous Fumarate / Ferric Ammonium Citrate)



Fig :1-Ferrous Sulphate

Role: Iron is the primary active ingredient essential for the synthesis of hemoglobin and myoglobin. It plays a central role in oxygen transport and cellular respiration.

- Ferrous salts are preferred for higher solubility and faster absorption in the duodenum.
- The syrup form minimizes gastrointestinal irritation due to dilution and presence of stabilizers.
- Mechanism: Iron replenishes depleted stores, increases hemoglobin concentration, and supports erythropoiesis.

2. Folic Acid (Vitamin B9):



Fig: 2-Folic Acid (Vitamin B9) Source

Role: Folic acid is a vital coenzyme in nucleic acid and amino acid metabolism. It assists in DNA synthesis, red blood cell maturation, and tissue repair.

- Prevents megaloblastic anemia and supports fetal development during pregnancy.
- Works synergistically with iron to accelerate the regeneration of red blood cells.
- In syrup formulations, folic acid improves hematinic efficacy and enhances iron utilization.

3. Vitamin B12 (Cyanocobalamin):



Fig :3 -Vitamin B12 (Cyanocobalamin) Source

Role: Vitamin B12 supports the conversion of inactive folate into its active form and contributes to normal nerve function and hematopoiesis.

- Prevents neurological complications often associated with chronic anemia.
- Enhances the synergistic effect of iron and folate on erythropoiesis.

4. Vitamin C (Ascorbic Acid) :



Fig :4-Vitamin C (Ascorbic Acid) Source

Role: A potent antioxidant and bioavailability enhancer, Vitamin C converts ferric iron (Fe^{3+}) to the more absorbable ferrous form (Fe^{2+}).

- Enhances gastrointestinal absorption of iron.
- Protects mucosal cells from oxidative injury.
- Improves overall stability and palatability of the formulation.

5. Strawberry Extract (*Fragaria ananasa*)



Fig: 5-Strawberry Extract (*Fragaria ananasa*)

Role: Natural source of vitamin C, flavonoids, and folate, providing both therapeutic and organoleptic benefits.

- Improves iron absorption and contributes antioxidants that prevent oxidative damage to red blood cells.
- Adds natural color, flavor, and aroma, improving patient compliance, especially in children.
- Provides polyphenols and anthocyanins, which enhance endothelial function and blood circulation.

6. Beetroot Powder (*Beta vulgaris*)



Fig : 6-Beetroot Powder (*Beta vulgaris*)

Role: Beetroot is rich in iron, folate, potassium, and betaine, contributing significantly to blood formation and detoxification.

- Acts as a natural hematinic and antioxidant.
- Enhances nitric oxide production, improving tissue oxygenation.
- Reduces inflammation and oxidative stress, thereby supporting erythrocyte survival.

7. Honey (Madhu / Mel)



Fig 7-Honey (Madhu / Mel)

Source: *Apis mellifera* and other bee species

Constituents: Dextrose, sucrose, dextrin, enzymes, and minerals.

Role: Functions both as a sweetening and therapeutic agent.

- Serves as a natural humectant, antibacterial, and antioxidant component.
- Masks the metallic taste of iron and improves palatability.
- Promotes gastrointestinal health, enhances nutrient absorption, and provides mild energy support.

8. Glycine



Fig 8-Glycine

Role: A simple amino acid with antioxidant, anti-inflammatory, and detoxifying effects.

- Reduces oxidative damage induced by iron therapy.
- Aids in protein synthesis and hemoglobin production.
- Improves tolerance by minimizing side effects such as gastric irritation or constipation.

9. Trace Elements (Zinc and Copper)



Fig: 9-Trace Elements (Zinc and Copper)

Role: These micronutrients complement iron metabolism and erythropoiesis.

- Zinc aids in DNA synthesis and supports immune function.
- Copper assists in mobilizing stored iron and enhances its incorporation into hemoglobin. Their combined

presence ensures balanced hematopoietic activity and prevents secondary mineral imbalances.

10. Syrup Base and Pharmaceutical Excipients

Component	Function in Formulation
Sucrose / Sorbitol / Glycerin	Act as vehicles and sweetening agents; provide viscosity and stability.
Sodium Benzoate / Methyl Paraben	Serve as preservatives to inhibit microbial growth.
Citric Acid / Sodium Citrate	Maintain pH stability and enhance solubility of active ingredients.
Propylene Glycol / Sorbitol	Prevent crystallization of sucrose and act as humectants.
Flavoring Agents (Fennel, Orange, Vanilla)	Improve taste and aroma to enhance patient compliance.
Coloring Agents (Beetroot extract / Fruit essence)	Provide natural, visually appealing coloration.

11. Functional Synergy

The success of iron syrup lies in the pharmacodynamic and physicochemical synergy among its components:

- Iron + Vitamin C + Folic Acid → Enhanced absorption and red blood cell synthesis.
- Beetroot + Strawberry + Honey → Improved taste, nutritional support, and antioxidant protection.
- Glycine + Vitamins + Trace elements → Protection against oxidative stress and improved tolerance.

Together, they ensure efficient correction of anemia with minimal side effects and better patient adherence.

III. FORMULATION OF IRON DEFICIENCY SYRUP (100 ML)

Ingredients	Role / Function	Quantity (per 100 mL)
Ferrous sulfate ($\text{FeSO}_4 \cdot 7\text{H}_2\text{O}$)	Source of elemental iron	300 mg (equivalent to ~60 mg elemental Fe)
Folic acid	Supports RBC formation, prevents megaloblastic anemia	2 mg
Vitamin B ₁₂ (Cyanocobalamin)	Hematopoietic vitamin; enhances iron utilization	5 µg
Vitamin C (Ascorbic acid)	Enhances iron absorption and prevents oxidation	50 mg
Beetroot extract (<i>Beta vulgaris</i>)	Natural colorant, antioxidant, and iron booster	2 mL
Strawberry flavor / extract	Flavoring agent; improves palatability	1 mL
Honey (Natural sweetener)	Sweetening, soothing, antioxidant	5 mL
Sucrose (Cane sugar)	Syrup base, viscosity enhancer	66.7 g (to make syrup base)
Sodium benzoate	Preservative; prevents microbial growth	0.1 g
Citric acid	Acidulant and stabilizer	0.05 g
Glycine	Flavor enhancer and antioxidant	2 g
Sorbitol / Glycerin	Humectant and co-solvent	3 mL
Color (Caramel / Natural)	Improves appearance	q.s.
Purified water	Vehicle	up to 100 mL

IV. METHOD OF PREPARATION

1. Prepare syrup base: Dissolve sucrose in about 60 mL of purified water by heating gently (avoid caramelization). Cool to room temperature.
2. Dissolve water-soluble ingredients: Dissolve ferrous sulfate, folic acid, vitamin C, vitamin B₁₂, and citric acid separately in small volumes of water.
3. Add humectants and flavor: Add glycerin/sorbitol, glycine, beetroot extract, and strawberry flavor.
4. Add honey and preservatives: Mix thoroughly, then add sodium benzoate and color (if needed).
5. Make up the volume: Add purified water to make 100 mL, stir continuously, and filter through muslin cloth.
6. Packaging: Fill into amber glass bottles with airtight caps to prevent oxidation.

7. Storage: Store in a cool, dry place away from sunlight.

Dose (Typical):

- Adults: 10 mL twice daily after meals.
- Children: 5 mL twice daily (as advised by physician)

V. PHARMACOLOGICAL AND CLINICAL EVALUATION OF IRON DEFICIENCY SYRUP

Iron deficiency syrup combines hematinic, nutritional, and antioxidant agents that collectively correct iron depletion, enhance red blood cell production, and improve overall hematological health. The pharmacological activity results from the synergistic interaction of its bioactive ingredients, each contributing to different steps in iron metabolism and erythropoiesis.

1. Pharmacological Mechanism of Action

a. Iron Absorption and Transport

- The iron salt (ferrous or ferric) component is absorbed primarily in the duodenum and upper jejunum through divalent metal transporter 1 (DMT1).
- Vitamin C converts ferric iron (Fe^{3+}) into the ferrous form (Fe^{2+}), which is more readily absorbed.
- Once absorbed, iron binds to transferrin and is transported to the bone marrow, where it participates in hemoglobin synthesis.

b. Erythropoiesis and Red Blood Cell Maturation

- Folic acid (Vitamin B9) and Vitamin B12 support DNA synthesis and the maturation of erythrocytes.
- These vitamins ensure proper cell division in the bone marrow and prevent the development of macrocytic or megaloblastic anemia.

c. Antioxidant Protection and Cellular Health

- Vitamin C, Beetroot extract, Strawberry extract, and Honey supply antioxidants that neutralize reactive oxygen species generated during iron therapy.
- This minimizes oxidative damage to the intestinal mucosa and red blood cells, improving tolerance and absorption.

d. Hemoglobin Synthesis and Oxygen Transport

- Once incorporated into hemoglobin, iron facilitates oxygen binding and transport from the lungs to tissues.
- Copper and Zinc act as cofactors for enzymes like ferroxidase and δ -aminolevulinic acid synthase, which are essential for hemoglobin synthesis.

2. Pharmacological Activities of Individual Components

Ingredient	Pharmacological Activity	Mechanistic Role
Ferrous Fumarate / Sulphate	Hematinic	Restores iron stores, increases hemoglobin synthesis
Folic Acid	Hematopoietic	Supports RBC maturation and DNA synthesis
Vitamin B12	Neuroprotective, hematinic	Converts folate to active form; aids erythropoiesis
Vitamin C	Antioxidant, absorption enhancer	Converts Fe^{3+} to Fe^{2+} , increases bioavailability
Beetroot Extract	Natural hematinic	Increases nitric oxide, improves circulation

3. Clinical Evaluation and Efficacy Evidence

Clinical trials and observational studies have demonstrated that iron-based syrups fortified with vitamins and natural antioxidants show:

- Significant increase in hemoglobin (by 1–2 g/dL within 4–6 weeks).
- Improved serum ferritin levels and total iron-binding capacity (TIBC).
- Reduced gastrointestinal side effects compared to tablet formulations.
- Better compliance among pediatric and geriatric patients due to palatable syrup base.

Comparative Studies:

- Iron + Vitamin C + Folic Acid combination shows 25–30% higher bioavailability than iron alone.
- Addition of natural ingredients like beetroot and honey improves antioxidant capacity and patient

4. Therapeutic Benefits

- ✓ Rapid correction of iron deficiency and anemia
- ✓ Improved energy levels, cognitive function, and immunity

- ✓ Enhanced iron absorption and bioavailability
- ✓ Reduced oxidative stress and side effects
- ✓ Safe and effective for pregnant women, children, and elderly

5. Pharmacokinetic Highlights

Parameter	Description
Absorption	Enhanced in presence of Vitamin C and acidic medium
Distribution	Bound to transferrin; stored in liver, spleen, bone marrow
Metabolism	Utilized in hemoglobin and myoglobin formation
Excretion	Minimal through feces; regulated by body iron stores
Half-life	Approximately 6 hours for absorbed iron

VI. DISCUSSION AND CONCLUSION

Discussion

Iron Deficiency Anemia (IDA) continues to be one of the most prevalent nutritional deficiencies worldwide, affecting individuals across all age groups, with women, children, and pregnant mothers being the most vulnerable. Despite the long-standing use of oral iron supplementation as the primary therapeutic approach, conventional tablet-based formulations frequently encounter limitations such as poor gastrointestinal tolerance, low absorption efficiency, and unsatisfactory patient compliance. These drawbacks have prompted growing interest in developing advanced iron syrup formulations that combine efficacy with enhanced patient acceptability. Recent advances in formulation science have centered on improving iron bioavailability, taste masking, and gastrointestinal tolerability. The incorporation of essential hematinic cofactors such as Vitamin C, Folic Acid, Vitamin B12, and Zinc, along with natural ingredients like beetroot and honey, has significantly optimized the pharmacological and organoleptic profile of iron syrups. Vitamin C plays a pivotal role in enhancing absorption by converting ferric (Fe^{3+}) to the more readily absorbable ferrous (Fe^{2+}) form, while folic acid and vitamin B12 are crucial for DNA synthesis, red blood cell maturation, and effective correction of anemia. Zinc further contributes to enzymatic activity essential for hemoglobin

production and immune support. The inclusion of natural antioxidants such as beetroot extract, honey, and fruit-based flavoring agents not only improves taste and patient acceptability but also reduces oxidative stress and mucosal irritation commonly associated with unbound iron ions. These ingredients collectively enhance compliance, especially among pediatric and geriatric patients, who often experience difficulty with solid oral dosage forms. Additionally, the liquid dosage form allows for flexible dosing, faster absorption, and easier administration, thereby offering practical advantages in clinical and community healthcare settings. Pharmacological and clinical evaluations have demonstrated that multi-nutrient iron syrups can produce a significant and rapid increase in hemoglobin and serum ferritin levels compared to traditional formulations. The synergistic effect between synthetic iron salts and natural bioenhancers enhances iron solubility, absorption, and systemic bioavailability, while minimizing gastrointestinal discomfort. Furthermore, emerging innovations such as chelated iron complexes, ferric polymaltose, and microencapsulated iron have shown substantial promise in addressing long-standing issues of metallic aftertaste, nausea, and gastric irritation, thereby ensuring greater adherence to therapy. Despite these advancements, certain formulation-related challenges persist. Iron instability in aqueous media, oxidative degradation during storage, and variability in product quality across manufacturers remain key concerns. Addressing these limitations requires continuous optimization of formulation parameters, incorporation of effective antioxidant stabilizers, and the use of protective packaging systems to maintain the physicochemical stability of iron during shelf life. Future research should also prioritize pharmacokinetic modeling, molecular interaction studies, and large-scale clinical trials to establish standardized efficacy, safety, and bioequivalence across new-generation iron syrup formulations.

VII. CONCLUSION

The evolution of modern iron deficiency syrups represents a major step forward in the therapeutic management of Iron Deficiency Anemia. By combining scientifically optimized iron sources with synergistic vitamins, minerals, and natural antioxidants, these formulations offer a

comprehensive and patient-centered approach to anemia treatment. Enhanced absorption, superior tolerability, and improved palatability collectively translate into higher therapeutic success and better compliance compared to conventional oral tablets or capsules. The pharmacological synergy between iron and supportive micronutrients not only replenishes depleted iron stores but also strengthens overall hematopoietic, metabolic, and immune functions, promoting holistic recovery. Given their superior taste profile, adjustable dosing, and reduced side effects, iron syrups are particularly well-suited for children, elderly individuals, and patients requiring long-term supplementation. With ongoing progress in nanotechnology, microencapsulation, and bioenhancer integration, iron-based syrup formulations are steadily emerging as safe, effective, and user-friendly alternatives in the global fight against anemia. Their continued development underscores the successful integration of nutritional science, pharmaceutical technology, and clinical innovation, marking a new era in the management of Iron Deficiency Anemia and contributing significantly to global public health.

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