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# TOOTH DISCOLORATION ASSOCIATED WITH ORAL IRON SUPPLEMENTATION: MECHANISMS, RISK FACTORS AND PREVENTIVE STRATEGIES - A NARRATIVE REVIEW

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## ABSTRACT

Oral iron supplementation is widely used for the prevention and treatment of iron deficiency, particularly in infants and young children. Liquid iron formulations may cause extrinsic tooth discoloration, which can raise esthetic concerns and potentially reduce treatment adherence. This narrative review aimed to summarize current evidence on the mechanisms of iron-associated tooth discoloration, identify formulation-, administration-, and tooth-related risk factors, and evaluate available preventive and management strategies. A structured literature search was conducted using PubMed/MEDLINE, Web of Science, Scopus, and Google Scholar for publications available from database inception to August 2026, with priority given to clinical and laboratory studies directly evaluating iron-related dental staining. The available evidence indicates that discoloration is predominantly an extrinsic phenomenon related to local interaction of iron-containing formulations with the tooth surface. Its severity appears to depend on formulation characteristics, iron concentration, duration of contact, and enamel condition. Some liposomal and polysaccharide formulations may cause less staining than conventional ferrous salts, although findings are inconsistent. Dilution of liquid iron may reduce discoloration, whereas evidence for toothbrushing and enamel coatings remains limited or conflicting. Professional prophylaxis appears effective for removing established stains. Tooth discoloration should not lead to discontinuation of medically indicated iron therapy, but further clinical studies are needed to establish evidence-based preventive recommendations.

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## KEYWORDS

Oral Iron Supplementation, Tooth Discoloration, Dental Staining, Ferrous Sulfate, Enamel, Preventive Dentistry

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## 1. Introduction

Iron deficiency (ID) and iron-deficiency anemia (IDA) remain among the most common nutritional disorders and are encountered across a wide range of age groups. Oral iron is generally preferred when replacement can be achieved through the gastrointestinal route because it is effective, widely available, and less resource-intensive than intravenous treatment. Ferrous sulfate remains the most established and commonly used oral preparation, while other ferrous salts, ferric complexes, polysaccharide preparations, ferric maltol, liposomal products, and sucrosomial formulations have expanded the range of available therapies (Iolascon et al., 2024; Leone et al., 2026; Pantopoulos, 2024). In pediatrics, liquid drops and syrups are especially important because they permit age- and weight-adjusted dosing in children who cannot reliably swallow tablets or capsules. This practical advantage also creates prolonged or repeated direct contact between the medication and the oral environment.

The adverse effects of oral iron therapy are usually discussed in relation to gastrointestinal intolerance, metallic taste, or dark stools. Dental discoloration is less medically serious, but it is relevant because it is immediately visible and may be interpreted by patients or caregivers as evidence of dental damage. Pediatric recommendations acknowledge temporary darkening of teeth after some oral ferrous preparations and advise measures aimed at reducing contact of the formulation with the teeth or removing residual material after administration (Chaber et al., 2024). The esthetic impact may also influence adherence. In a randomized clinical trial in anemic children, liquid ferrous sulfate drops were associated with more caregiver-reported tooth staining and poorer adherence than micronutrient powders containing microencapsulated iron (Christofides et al., 2006). In addition, survey data indicate that parents frequently have incomplete knowledge concerning the relationship between iron supplementation, tooth staining, and dental caries (Talebi et al., 2012). These observations suggest that a problem that is biologically superficial can nevertheless affect continuation of an otherwise necessary therapy.

Iron-associated dental discoloration is usually considered an extrinsic staining phenomenon. This distinction is important. Extrinsic discoloration develops on the external tooth surface or within deposits associated with the acquired pellicle and is potentially removable by mechanical cleaning. Intrinsic discoloration, in contrast, results from incorporation of chromogenic substances into enamel or dentin during tooth formation or from later changes within the dental tissues (Alazmah, 2021). Iron-related staining should also be differentiated from bacterial black stain, a distinct form of extrinsic pigmentation typically characterized by dark dots or lines near the cervical third of the tooth and associated with a particular biofilm and salivary environment (Al-Shareef et al., 2025; Żyła et al., 2015). The two conditions may share iron-containing deposits as part of their chemistry, but they should not be treated as synonymous.

The mechanism of discoloration following oral iron administration is incompletely defined. Several processes probably act together. Iron may adsorb to the acquired pellicle or enamel surface, accumulate in superficial irregularities, and participate in the formation of dark insoluble compounds. The local availability of iron may be modified by the chemical form of the supplement and by the pharmaceutical formulation. Acidic pH may alter the enamel surface, while demineralization or increased porosity may provide additional sites for retention. Oral bacteria and their metabolic products have also been proposed to contribute to formation of dark iron-containing deposits. Experimental studies support parts of this model but do not establish a single pathway that explains all clinical staining (Babaei et al., 2021; Hekmatfar et al., 2018; Nazemismalman et al., 2023; Pani et al., 2015).

The evidence has also changed substantially during the last several years. An earlier systematic review evaluated iron-containing products in relation to dental caries, enamel microhardness, and discoloration, with discoloration representing only one component of a broad dental analysis and the underlying search extending through 2018 (Asgari et al., 2020). More recent studies have compared conventional and newer formulations, examined the role of pH and viscosity, assessed sound and demineralized enamel, investigated surface coatings and dilution, and extended laboratory observations from primary to permanent teeth (Abou Karam & Chedid, 2026; Bansal et al., 2023; Khalid et al., 2026; Vahedi et al., 2025). These studies provide a basis for a more focused synthesis centered specifically on iron-associated tooth discoloration.

Accordingly, the aim of this narrative review is to summarize current evidence concerning the clinical characteristics and mechanisms of tooth discoloration associated with oral iron supplementation; identify formulation-, administration-, tooth-, and patient-related factors that may modify staining; evaluate preventive and therapeutic strategies; and define the major limitations of the present evidence base. Particular attention is given to the distinction between findings that are supported by direct clinical evidence and those derived primarily from *in vitro* models.

## 2. Methods

A structured literature search was conducted using PubMed/MEDLINE, Web of Science, Scopus, and Google Scholar for publications available from database inception to August 2026. Search terms included combinations of "oral iron", "iron supplementation", "iron drops", "iron syrup", "ferrous sulfate", "iron polymaltose", "liposomal iron", and "sucrosomial iron" with "tooth discoloration", "dental staining", "enamel discoloration", and "black stain". Reference lists of relevant original studies and reviews were screened to identify additional publications.

Priority was given to clinical and laboratory studies directly evaluating iron-associated tooth discoloration. Studies addressing iron adsorption, enamel demineralization, microhardness, physicochemical properties of oral iron formulations, preventive strategies, or stain removal were included when they contributed to interpretation of the mechanism or clinical management of staining. Contemporary reviews and clinical recommendations were used to provide context regarding oral iron formulations and patient counseling. Because of substantial heterogeneity in experimental design, dentition, iron formulation, exposure protocol, and color-assessment methods, the evidence was synthesized narratively rather than quantitatively.

## 3. Clinical Characteristics and Mechanisms of Iron-Induced Tooth Discoloration

### 3.1. Clinical presentation and differential diagnosis

Tooth discoloration associated with oral iron is most consistently described as an extrinsic dark brown, gray, or black surface stain. It is particularly recognized after use of liquid drops and syrups, which directly bathe the erupted tooth surfaces. The distribution can vary according to the way the product is administered and the surfaces exposed, and reports describe staining of anterior primary teeth as a common clinical concern. A published case involving an infant receiving several iron-fortified dietary sources documented black staining of the external surfaces of the anterior teeth; the deposits were mechanically removed and did not recur after the excessive iron exposure was reduced (Adcock & Hogan, 2008). Although such case reports cannot estimate incidence, they illustrate the superficial and potentially reversible nature of the condition.

Most laboratory research has focused on primary incisors because liquid iron supplementation is widely used in early childhood and because extracted primary teeth are available for experimental models. The predominance of studies on deciduous teeth should not be interpreted as proof that permanent teeth are resistant. Khalid et al. (2026) exposed permanent teeth to two commercially available iron formulations and found significant discoloration relative to artificial saliva. The study therefore provides direct experimental evidence that permanent enamel can also be affected, although the clinical frequency and severity of this problem in adolescents and adults remain uncertain.

Differential diagnosis is important because dark surface staining may be mistaken for active caries, arrested caries, chromogenic bacterial stain, or other medication-related discoloration. Classic bacterial black stain generally appears as a dark line or incomplete coalescence of small dark dots near the cervical third, often following the gingival margin. Contemporary reviews associate this condition with a distinctive microbial community, particularly *Actinomyces* species, and with differences in salivary composition, including higher concentrations of iron and other minerals (Al-Shareef et al., 2025). Iron-supplement staining may be more diffuse and temporally related to initiation of an iron-containing product. Nevertheless, there may be overlap in appearance, and clinical diagnosis should consider history, distribution, surface texture, and the response to professional cleaning rather than color alone.

The distinction from dental caries is especially relevant for counseling. Extrinsic iron deposits are not themselves synonymous with demineralized carious tissue. Experimental research on iron and dental caries is complex and has produced findings ranging from erosive effects of acidic medicines to potentially cariostatic effects of iron in selected models (Asgari et al., 2020). Consequently, the presence of a dark stain should not be used as an indicator that oral iron has directly caused a carious lesion. Equally, the presence of iron staining does not exclude coexisting caries. The two processes require separate clinical assessment.

### **3.2. Local iron deposition and interaction with the tooth surface**

A central feature of the proposed mechanism is local exposure. Iron that remains in contact with the tooth surface can be retained within the acquired pellicle or adsorb to superficial enamel. Pani et al. (2015) demonstrated that several iron-containing solutions produced measurable color changes in primary teeth under standardized in vitro conditions, whereas control teeth stored in artificial saliva did not develop comparable staining. Importantly, the degree of discoloration increased over time during the 72-hour exposure. Although continuous laboratory immersion exaggerates clinical contact, the time-dependent effect supports the concept that repeated or prolonged local exposure can progressively increase surface discoloration.

Babaei et al. (2021) extended this concept by measuring both color change and iron associated with the specimens. Five commercially available iron drops were evaluated, and all produced visible discoloration. The amount of iron detected by atomic absorption was correlated with discoloration, providing experimental support for a relationship between local iron accumulation and the observed change in color. This does not prove that all detected iron was bound in the same chemical form, but it provides a measurable link between exposure, surface-associated iron, and staining.

The acquired pellicle may be an important intermediary rather than an inert surface. Salivary proteins adsorbed to enamel can bind ions and organic chromogens and influence subsequent attachment of plaque. Mechanistic literature on extrinsic metal-associated staining proposes that reactions involving metal ions may occur within or on this pellicle. In the context of oral iron supplementation, a reasonable model is therefore that iron first interacts with salivary or pellicle components and then becomes incorporated into visible deposits. Direct confirmation of the precise molecular species in supplement-related stain is still limited, and the mechanism should be described as probable rather than definitive.

### **3.3. Microbial contribution and iron-sulfur compounds**

Microbial metabolism provides a second plausible pathway. Black-stain literature has long implicated reactions between iron and sulfur-containing bacterial metabolites. Modern reviews continue to identify Actinomyces as a prominent component of bacterial black-stain biofilms and describe iron deposition as a central chemical feature (Al-Shareef et al., 2025; Żyła et al., 2015). Hydrogen sulfide and related sulfur products generated by oral bacteria may react with available iron to produce dark, poorly soluble iron-containing compounds. If oral iron supplementation increases the amount of locally available iron, the same chemical environment could plausibly promote surface pigmentation.

However, evidence from bacterial black stain cannot simply be transferred to iron-supplement staining. Bacterial black stain develops in individuals who may not be taking iron medications and appears to depend on a characteristic biofilm and salivary profile. Conversely, experimental staining can be produced by exposing extracted teeth to iron formulations in the absence of a living oral microbiome. This indicates that microbial activity is not required for every form of iron-associated discoloration. A more defensible interpretation is that bacterial metabolism may amplify or modify stain formation in vivo, while direct iron-pellicle-enamel interactions can produce discoloration independently. Future clinical studies incorporating microbiome or metabolomic analysis would be needed to determine how important this pathway is in patients receiving oral iron.

### **3.4. Acidity, enamel surface alteration, and susceptibility to stain retention**

Many pediatric liquid medicines, including iron preparations, are acidic. Acid exposure can alter superficial enamel by increasing mineral solubility, reducing microhardness, or producing microscopic surface irregularities. Pashar et al. (2015) found reduced microhardness after exposure of primary enamel to several iron and multivitamin drops, with marked changes in the most erosive preparation. Sahebazar et al. (2022) similarly demonstrated that the effect on primary-enamel microhardness differed between a conventional iron drop, the same product diluted with juice, and a sucrosomial formulation. These studies do not directly measure staining, but they provide a mechanistic basis for the hypothesis that an altered, rougher, or more porous enamel surface could retain more iron-containing material.

Direct evidence linking surface condition and iron retention comes from Nazemiasalman et al. (2023). Primary incisors subjected to an artificial cariogenic challenge demonstrated greater iron uptake than teeth maintained in saline, and scanning electron microscopy showed more fractures and structural porosity in the challenged specimens. The investigators interpreted this increased porosity as a factor facilitating iron uptake and subsequent discoloration. The measured difference in color between cariogenic-challenge and saline groups did not reach conventional statistical significance in all comparisons, so the strongest conclusion from

this study concerns increased iron uptake and structural susceptibility rather than a precise magnitude of additional staining.

The role of pH itself is more uncertain. Babaei et al. (2021) found an association between pH and discoloration across five iron products, whereas Hekmatfar et al. (2018), evaluating pH, titratable acidity, and iron uptake, did not identify a significant correlation between acidity and the amount of iron absorbed by primary enamel. Commercial formulations differ simultaneously in iron concentration, iron chemistry, excipients, sweeteners, viscosity, and buffering capacity. Therefore, low pH may increase susceptibility by altering the tooth surface, but existing comparative studies cannot isolate acidity as an independent determinant of staining. The current evidence is most consistent with a multifactorial process in which iron availability, local contact, pellicle interactions, enamel condition, and possibly microbial metabolism contribute to the final clinical appearance.

## **4. Risk Factors for Tooth Discoloration**

### **4.1. Iron formulation and chemical form**

The staining potential of an oral iron product cannot be inferred simply from the elemental iron dose. Different salts, complexes, and delivery systems differ in solubility, oxidation state, stability, excipients, taste-masking strategies, and the proportion of iron that can interact directly with oral surfaces. Contemporary oral iron therapy includes conventional ferrous salts, ferric complexes, polysaccharide-based preparations, and newer encapsulated formulations such as liposomal and sucrosomial products (Leone et al., 2026; Pantopoulos, 2024). Although these technologies are primarily designed to optimize absorption or tolerability, they may also alter dental exposure.

Pani et al. (2015) provided early experimental evidence that formulations with approximately standardized iron content can differ substantially in their capacity to stain primary enamel. Ferric oxide polymaltose produced greater discoloration than ferrous fumarate in their model, while a mixed formulation produced a different staining profile again. This finding is important because it demonstrates that a simple hierarchy based only on ferrous versus ferric iron is unlikely to be universally valid. Pharmaceutical formulation matters, and conclusions concerning a specific commercial product should not automatically be generalized to all preparations containing the same nominal iron compound.

Recent comparative work strengthens this point. Vahedi et al. (2025) studied liposomal iron, ferrous sulfate, sucrosomial iron, and an iron polysaccharide complex at standardized iron concentrations. Ferrous sulfate and the sucrosomial product generated the greatest mean color changes, whereas the liposomal and polysaccharide formulations produced less discoloration. The type of formulation explained a substantial proportion of the variability in color change. Gupta et al. (2025) similarly observed greater staining after ferrous sulfate than after an iron polymaltose complex, although that study had less detailed methodology and should be regarded as supportive rather than decisive evidence.

The results for encapsulated formulations deserve careful interpretation. Yılmaz et al. (2025) observed less darkening with a microencapsulated liposomal iron product than with a conventional Fe<sup>2+</sup> supplement. This is consistent with the hypothesis that encapsulation may reduce the fraction of iron that directly interacts with the tooth surface. However, sucrosomial products have not shown uniformly low staining. Vahedi et al. (2025) reported relatively high discoloration for SiderAl, whereas Farzandi et al. (2026) found minimal color change and no evident surface defects with Sideral during a short exposure protocol. Differences in exposure duration, concentration, product composition, and color-assessment thresholds may explain part of this discrepancy. Consequently, the appropriate conclusion is that some encapsulated formulations appear promising, but no technology can currently be considered consistently non-staining on the basis of laboratory evidence alone.

Clinical comparisons are limited. Christofides et al. (2006) randomized anemic children to different micronutrient powders or liquid ferrous sulfate drops and reported greater staining in the drops group. This study is valuable because it demonstrates a real-world difference in caregiver-reported staining, but it does not isolate formulation chemistry: the interventions differed in physical form, administration with food, iron compound, and local oral exposure. The result therefore supports the importance of delivery system as a whole rather than proving that microencapsulated ferrous fumarate is intrinsically non-staining.

#### **4.2. Physicochemical properties of oral iron formulations**

Beyond iron chemistry, the physicochemical properties of the vehicle may modify how long a product remains on teeth and how it interacts with enamel. The main characteristics discussed in the literature are pH, titratable acidity, viscosity, iron concentration, and the amount of readily available iron. Pediatric drops may reach very low pH values because acids are used for stability, buffering, taste, or solubility (Hekmatfar et al., 2018). Theoretical concern arises because an acidic preparation can transiently alter enamel and because a viscous formulation may have slower oral clearance.

Babaei et al. (2021) measured pH and viscosity of five commercial iron drops before exposing primary teeth to the formulations. All were acidic, viscosity ranged widely, and the products produced visible discoloration. Color change correlated with pH and with iron detected by atomic absorption. These observations suggest that physicochemical characteristics matter, but the study did not standardize elemental iron concentration or independently manipulate pH and viscosity. As a result, the correlation cannot be interpreted as proof that modifying pH alone would proportionally reduce staining.

Hekmatfar et al. (2018) provide an important counterbalance. Despite substantial differences in the acidity and titratable acidity of five iron drops, no statistically significant relationship was found between these variables and enamel iron uptake. The findings imply that acidity and iron deposition are not interchangeable concepts. Acidic formulations may contribute to enamel changes, but deposition depends on additional chemical interactions. This distinction is important when translating laboratory findings into recommendations: neutralizing or diluting a product may reduce one component of risk, but it may not eliminate iron binding or staining.

Viscosity is biologically plausible as a contact-time modifier, but direct evidence is weak. A viscous syrup may clear more slowly from tooth surfaces than a less viscous solution, yet commercial comparisons change several variables simultaneously. Khalid et al. (2026) compared two iron products on permanent teeth and documented significant discoloration with both. Although the product with lower pH and lower viscosity produced numerically greater color change, the difference between the two iron formulations was not statistically significant. Therefore, that study confirms susceptibility of permanent enamel but does not establish either lower pH or a specific viscosity range as a causal predictor of staining.

Concentration is more directly relevant because it determines the amount of iron available during a given contact episode. Studies specifically manipulating concentration or dilution provide stronger evidence than cross-product correlations. This issue is addressed in Section 4.3 and is particularly important because it represents a potentially modifiable administration-related factor.

#### **4.3. Mode of administration, concentration, and contact time**

The local-exposure model predicts that staining should be influenced by how the medication is delivered. Drops placed directly against anterior teeth, slowly sipped syrups, or repeated small exposures may produce a different oral contact pattern than capsules swallowed intact or powders mixed with food. This concept is supported indirectly by the randomized trial of Christofides et al. (2006), in which liquid ferrous sulfate was associated with more tooth staining than powdered micronutrient interventions. It is also consistent with the fact that the dental adverse effect is emphasized mainly for liquid preparations in pediatric guidance (Chaber et al., 2024).

Contact duration has a clear effect in laboratory models. Pani et al. (2015) observed progressive increases in color change during continued exposure, demonstrating that staining is cumulative under experimental conditions. The absolute exposure times in such immersion studies should not be equated with days or months of clinical use, because saliva, swallowing, drinking, eating, and oral hygiene continuously modify the oral environment. Nevertheless, the direction of the effect is relevant: more intense and longer cumulative surface contact increases the opportunity for deposition.

The best direct experimental evidence for concentration comes from Abou Karam and Chedid (2026). Primary anterior teeth were exposed to concentrated or diluted ferrous sulfate syrup, with or without standardized toothbrushing. Concentrated syrup produced the greatest color change, and the effect of concentration remained strong throughout the simulated exposure period. Dilution reduced discoloration more consistently than brushing. Farzandi et al. (2026) also found less staining when a conventional iron drop was diluted with apple juice than when used undiluted, although the use of fruit juice introduces additional variables such as acidity and carbohydrate exposure and should not be translated directly into a recommendation to administer iron with juice.

These studies make concentration and local contact among the most plausible modifiable risk factors identified to date. However, a distinction is needed between dilution as an experimental manipulation and changing the prescribed dose. The therapeutic elemental iron dose should not be reduced without medical indication. When dilution is considered, the full prescribed dose must still be consumed, and the accompanying liquid should not adversely affect absorption or dental health. Controlled clinical trials are required before a specific dilution protocol can be recommended broadly.

#### **4.4. Tooth- and patient-related factors**

Enamel condition appears to modify susceptibility. Nazemisalman et al. (2023) found greater iron uptake after artificial cariogenic challenge and demonstrated more surface defects in challenged enamel. Bansal et al. (2023) similarly evaluated sound and artificially demineralized primary teeth and found different staining behavior depending on enamel condition and the protective coating applied. Collectively, these findings suggest that demineralized, hypomineralized, eroded, or otherwise roughened surfaces may provide more sites for retention of iron-containing deposits. Direct clinical confirmation in children with early caries, white-spot lesions, developmental defects, or erosion is still lacking.

Primary and permanent teeth also differ in thickness, mineralization, and surface morphology. The current literature is too imbalanced to establish a reliable comparative risk. Primary teeth dominate the evidence base, whereas Khalid et al. (2026) provide one of the few direct studies of permanent enamel. It is therefore inappropriate to state that iron staining is specifically a problem of primary dentition; rather, primary dentition is the setting in which the problem has been studied most frequently.

Plaque, acquired pellicle, saliva, and oral microbiota are likely to influence stain retention in vivo. An individual with substantial plaque accumulation may retain iron differently from an individual with meticulous oral hygiene, and salivary flow and protein composition may change the clearance and binding of iron. Black-stain research demonstrates that differences in microbiota and saliva can be associated with iron-rich pigmentation (Al-Shareef et al., 2025). Nonetheless, direct clinical studies of these variables in patients taking iron supplements are scarce. At present, they should be regarded as biologically plausible modifiers rather than established risk factors.

Age, dietary habits, concurrent chromogenic exposures, and the use of other acidic or staining medicines may further influence clinical appearance. These variables are rarely controlled in laboratory studies and are incompletely recorded in clinical reports. Their omission is one reason why estimates derived from extracted-tooth experiments cannot be converted into a reliable prediction of which individual patient will develop visible staining.

## **5. Prevention and Management**

### **5.1. Modification of administration technique**

Prevention should be guided by the predominantly local and extrinsic nature of iron-associated staining. The practical objective is not to reduce medically indicated iron therapy but to minimize unnecessary contact between concentrated liquid iron and erupted teeth. Pediatric clinical recommendations already acknowledge tooth discoloration as a temporary adverse effect of selected ferrous preparations and suggest measures such as rinsing the mouth or using neutral liquids after administration (Chaber et al., 2024). These recommendations are clinically sensible, although the strength of direct dental evidence varies among individual techniques.

Dilution has the strongest recent laboratory support. In the study by Abou Karam and Chedid (2026), diluted ferrous sulfate produced significantly less discoloration than the concentrated syrup, and concentration had a more consistent influence on final color than toothbrushing. Farzandi et al. (2026) reported a similar directional effect when a conventional iron drop was mixed with apple juice. The latter study should be interpreted cautiously because fruit juice is acidic and may have cariogenic implications, and because a single short exposure differs substantially from chronic use. The useful principle is therefore reduction of local concentration during contact, not endorsement of a specific acidic beverage.

Other commonly proposed measures include placing drops toward the posterior part of the mouth, avoiding prolonged holding or swishing of the medication, swallowing the preparation promptly, and using a straw for appropriate older children or adults. These measures are mechanistically reasonable because they reduce exposure of the labial surfaces of anterior teeth. However, controlled studies directly comparing these

administration techniques are lacking. They should be presented as practical options rather than evidence-based standards.

Rinsing with water after administration is low-cost and is supported by pediatric guidance as a way to reduce residual medication on tooth surfaces (Chaber et al., 2024). It also avoids the potential problem of brushing immediately after exposure to an acidic formulation. If the product has substantially lowered the local pH and transiently softened the enamel surface, immediate mechanical abrasion could theoretically be undesirable. The exact duration of such softening after iron preparations has not been established, so firm waiting-time recommendations cannot be justified from the available evidence.

Any advice concerning administration must preserve therapeutic efficacy. Some oral iron preparations have product-specific instructions concerning food, beverages, or timing because absorption may be influenced by coadministration. Preventive dental recommendations should therefore be compatible with the prescribing information and the clinical goals of iron replacement. The dentist should not independently reduce the elemental iron dose or advise discontinuation of therapy because of staining.

## **5.2. Oral hygiene measures**

Regular plaque control remains reasonable because extrinsic pigments are more likely to accumulate on retentive surfaces and within surface deposits. Nevertheless, the intuitive recommendation to brush immediately after every iron dose is not strongly supported by direct evidence. Abou Karam and Chedid (2026) found an early reduction in staining with brushing in one diluted group, but the effect was not sustained and pooled analysis did not demonstrate a significant final benefit of brushing. This suggests that mechanical removal after each exposure may be less important than reducing the concentration and duration of contact in the first place.

Heidari et al. (2019) provide additional information relevant to home care after stains have formed. In extracted primary teeth with experimentally induced iron staining, conventional and whitening toothpastes did not remove the deposits effectively, whereas professional prophylaxis completely removed visible staining. The study does not mean that toothbrushing is unimportant for general oral health; rather, it indicates that established iron deposits may be resistant to routine dentifrice-based cleaning. Patients and caregivers should therefore be advised not to intensify abrasive home cleaning in an attempt to remove persistent dark stains, because excessive brushing could cause unnecessary wear or gingival trauma.

## **5.3. Enamel surface protection**

The possibility of preventing staining by creating a barrier on enamel has been tested experimentally. Bansal et al. (2023) evaluated MI Varnish, GC G-Coat Plus, and GC Equia Forte Coat on sound and artificially demineralized primary teeth. Selected coatings reduced color change, with the most favorable material differing according to whether enamel was sound or demineralized. These findings support the concept that a physical or chemical barrier can reduce direct interaction between iron and enamel.

However, the evidence is not sufficient to recommend routine coating of teeth solely because a patient has been prescribed oral iron. Laboratory protocols involve carefully prepared surfaces, standardized coating application, and prolonged controlled exposure that may not reflect wear, salivary effects, or biofilm in vivo. Furthermore, not all coating studies have produced uniform results, and the durability of protection during months of supplementation is uncertain. Fluoride varnish or other preventive interventions may of course be indicated for caries prevention based on the patient's overall risk, but their use specifically as anti-staining therapy remains investigational.

## **5.4. Management of established discoloration**

When staining has already occurred, the conservative nature of treatment should be emphasized. Because uncomplicated iron staining is predominantly extrinsic, professional cleaning and polishing are logical first-line measures. The case described by Adcock and Hogan (2008) was managed by simple mechanical removal. In the laboratory study by Heidari et al. (2019), prophylaxis paste completely removed experimentally induced iron stains, whereas tested toothpastes were substantially less effective. These findings are consistent with clinical experience that professional debridement can remove superficial chromogenic deposits.

Yilmaz et al. (2025) compared professional dental prophylaxis with a peroxide-based bleaching intervention after staining produced by iron products and black tea. Both professional prophylaxis and bleaching improved color, with bleaching producing a greater whitening effect in that laboratory model. The

result demonstrates that oxidation can modify residual color, but it does not establish bleaching as standard therapy. In children, and particularly in primary dentition, the superficial and removable nature of staining favors mechanical treatment over chemical bleaching. In permanent teeth, bleaching might be considered only in selected esthetic cases when discoloration persists after adequate professional cleaning and after other causes of discoloration have been excluded.

Patient education is an essential component of management. Visible staining can be alarming, especially when it develops soon after a new medication is started. Clinicians should explain that superficial iron staining is different from caries and that stopping effective iron treatment without medical advice may expose the patient to the consequences of untreated ID or IDA. Communication between the prescribing clinician and dentist is particularly useful when staining is severe, when the medication is poorly tolerated for other reasons, or when an alternative formulation is already clinically acceptable. The goal is to manage the dental adverse effect while maintaining effective systemic treatment.

## 6. Discussion

The present review indicates that tooth discoloration associated with oral iron supplementation is a real but incompletely characterized adverse effect. The most consistent finding across the literature is that direct exposure of teeth to liquid iron can produce measurable extrinsic color change. This conclusion is supported by multiple laboratory studies using primary teeth, by newer work on permanent enamel, and by limited clinical observations including a randomized trial in young children (Christofides et al., 2006; Khalid et al., 2026; Pani et al., 2015; Vahedi et al., 2025). The evidence is therefore sufficient to recognize staining as a clinically relevant phenomenon, but not sufficient to provide a reliable incidence rate or to predict individual susceptibility.

A central interpretation emerging from the evidence is that staining should be viewed as a property of the entire exposure system rather than of elemental iron alone. Iron chemistry matters, but so do pharmaceutical formulation, concentration, excipients, pH, viscosity, method of administration, contact duration, enamel condition, pellicle, saliva, and possibly microbial metabolism. This explains why studies comparing nominally similar categories can produce different results. It also cautions against simple statements such as "ferrous iron stains but ferric iron does not" or "encapsulated iron does not stain teeth." The experimental literature does not support either generalization (Babaei et al., 2021; Nazemisalman et al., 2023; Pani et al., 2015; Vahedi et al., 2025).

The comparison of newer formulations illustrates this problem clearly. Liposomal iron produced relatively low discoloration in both Babaei et al. (2021) and Vahedi et al. (2025), and a microencapsulated product produced less darkening than conventional Fe<sup>2+</sup> in Yilmaz et al. (2025). These convergent findings are encouraging. However, results for sucrosomial iron are inconsistent: Vahedi et al. (2025) reported substantial discoloration, whereas Farzandi et al. (2026) found minimal change under a much shorter exposure protocol. The difference could reflect formulation-specific excipients, concentration, exposure time, measurement method, or differences between products carrying a similar technological label. Consequently, clinicians cannot assume equivalence between all liposomal or sucrosomial products, and claims of lower staining should ideally be supported by product-specific clinical evidence.

The role of acidity also requires careful interpretation. Several iron drops have pH values below the critical range for enamel mineral stability, and laboratory studies demonstrate that acidic liquid medicines can reduce enamel microhardness or produce microscopic surface alteration (Hekmatfar et al., 2018; Pasdar et al., 2015; Sahebnazar et al., 2022). It is therefore biologically plausible that acid-induced roughening or porosity facilitates retention of iron-containing deposits. Yet direct comparisons are inconsistent: Babaei et al. (2021) found an association between pH and discoloration, while Hekmatfar et al. (2018) did not find a relationship between pH or titratable acidity and iron uptake. The more defensible conclusion is that acidity may modify susceptibility but is unlikely to be the sole determinant of staining.

Enamel condition may be particularly relevant in patients who already have demineralized surfaces. Nazemisalman et al. (2023) demonstrated greater iron uptake after an artificial cariogenic challenge, and Bansal et al. (2023) observed different staining and coating effects between sound and demineralized enamel. These findings suggest a clinically plausible interaction between pre-existing enamel changes and stain retention. This may matter in young children with early childhood caries risk, white-spot lesions, erosive exposure, or developmental enamel defects. At present, however, no prospective clinical study has quantified

whether these patients experience more severe staining during iron therapy. This represents a useful target for future research because it could identify a subgroup that benefits most from preventive dental review.

Among modifiable factors, concentration and contact time currently have the clearest experimental support. Pani et al. (2015) demonstrated a time-dependent increase in discoloration, while Abou Karam and Chedid (2026) showed a strong effect of syrup concentration and a more consistent benefit from dilution than from brushing. The direction of these findings is coherent with the extrinsic-staining model. They also provide a rationale for practical counseling: administer the medication in a way that minimizes unnecessary coating of the teeth and remove residual liquid after the dose. Nevertheless, evidence is still insufficient to specify an optimal dilution ratio, a universal volume of water, or an exact timing of rinsing or brushing.

The distinction between prevention and treatment is also important. Routine toothbrushing remains essential for dental health but should not be presented as a proven method for preventing iron staining. The experimental brushing study did not show a sustained final protective effect, and established deposits were not effectively removed by the dentifrices tested by Heidari et al. (2019). Professional prophylaxis, by contrast, repeatedly appears capable of removing superficial stain (Adcock & Hogan, 2008; Heidari et al., 2019; Yilmaz et al., 2025). This supports a conservative clinical pathway in which persistent esthetic discoloration is assessed and mechanically removed rather than prompting discontinuation of iron or aggressive home whitening.

The clinical significance of the problem should be framed proportionately. Tooth staining is generally reversible and does not carry the systemic consequences of untreated iron deficiency. The priority therefore remains effective iron replacement. However, dismissing staining as trivial may be counterproductive because it can affect parental concern, patient satisfaction, and adherence. In the trial by Christofides et al. (2006), the liquid drops group had both more reported staining and lower adherence than groups receiving powdered formulations. Although multiple aspects of acceptability differed between interventions, the result illustrates how visible oral adverse effects can influence treatment experience. Clear anticipatory guidance before starting therapy may therefore have practical value even when the discoloration itself is medically minor.

There are several reasons why the evidence base remains weak despite a growing number of publications. First, most studies are *in vitro*. Extracted teeth are commonly immersed in iron solutions for hours, days, or weeks, whereas clinical exposure is intermittent and modified by saliva, tongue movement, swallowing, food, water intake, toothbrushing, and pellicle turnover. Long immersion protocols are useful for demonstrating potential and comparing groups, but they may exaggerate absolute staining. Conversely, short single-exposure protocols may underestimate cumulative clinical effects. There is no validated laboratory model that translates a specific immersion duration into months of oral therapy (Abou Karam & Chedid, 2026; Asgari et al., 2020; Pani et al., 2015; Vahedi et al., 2025).

Second, outcome measurement is heterogeneous. Several studies use spectrophotometric CIELAB or CIEDE2000 systems, whereas others rely on shade guides, photography, or categorical visual assessments. Thresholds for perceptibility and clinical acceptability are not always applied consistently. Different instruments, background conditions, hydration status of enamel, and measurement sites further limit comparison of  $\Delta E$  values across studies (Heidari et al., 2019; Khalid et al., 2026; Pani et al., 2015; Vahedi et al., 2025; Yilmaz et al., 2025). Future research should adopt standardized color methodology and clearly report both statistical and clinically perceptible changes.

Third, commercial products introduce confounding. Investigators often compare marketed formulations that differ simultaneously in elemental iron concentration, iron compound, flavoring agents, acids, sweeteners, viscosity, and other excipients. A finding that product A stains more than product B therefore cannot identify which component caused the difference. Factorial experimental designs that independently manipulate pH, iron concentration, oxidation state, viscosity, and encapsulation would help separate these effects. Product-specific analyses of iron release at oral pH could also improve mechanistic understanding (Babaei et al., 2021; Khalid et al., 2026; Vahedi et al., 2025).

Fourth, the patient perspective is underrepresented. There are few studies measuring the incidence of clinically visible staining, time to onset, severity, quality-of-life effect, parental concern, or treatment discontinuation in routine practice. The available pediatric trial was not designed primarily as a dental study, and its staining outcome was caregiver reported (Christofides et al., 2006). Well-designed prospective cohorts or randomized comparisons could incorporate standardized dental photographs or spectrophotometry at baseline and follow-up while simultaneously recording dose, formulation, administration technique, oral hygiene, caries risk, diet, and adherence.

Fifth, permanent dentition remains understudied. The 2026 study by Khalid et al. demonstrates that permanent enamel can discolor *in vitro*, but adult and adolescent clinical data are insufficient. This matters because oral iron is commonly prescribed outside childhood, including to menstruating women, pregnant patients, blood donors, and individuals with chronic iron deficiency. Liquid formulations may be less common in adults, but chewable, soluble, or liquid preparations are still used, and the interaction between restorative

materials and iron formulations may also be relevant. A broader clinical evidence base would allow the review of iron staining to move beyond pediatric dentistry.

The present literature also leaves unresolved the role of the microbiome. Iron-rich bacterial black stain has a recognizable microbial signature, and iron-sulfur chemistry provides a plausible pathway for pigment production (Al-Shareef et al., 2025). Yet no contemporary clinical study has directly compared microbiota in patients who do and do not develop staining during identical iron therapy. Such studies could determine whether bacterial metabolism is a major determinant of susceptibility or merely one of several modifiers. Salivary iron, pH, flow rate, and pellicle composition could be assessed simultaneously.

From a practical standpoint, the current evidence supports a limited set of cautious recommendations. Patients and caregivers can be informed in advance that liquid iron may cause temporary extrinsic staining. Administration should minimize unnecessary prolonged contact with anterior teeth, and residual medication can be rinsed away with water when compatible with product instructions. Dilution may reduce staining in experimental models, but the prescribed elemental iron dose must be maintained and the method should not compromise absorption or introduce excessive sugar or acid exposure. Regular oral hygiene should continue, while aggressive brushing or abrasive whitening products should not be promoted as solutions to established stain. Persistent discoloration can usually be managed conservatively by a dentist with professional cleaning or polishing (Abou Karam & Chedid, 2026; Chaber et al., 2024; Heidari et al., 2019; Iolascon et al., 2024; Yilmaz et al., 2025).

These recommendations should remain subordinate to medical management of ID and IDA. Selection of an iron formulation should primarily consider indication, efficacy, tolerability, dosing, cost, age, and adherence. Dental staining can be included as an additional factor when several therapeutically appropriate alternatives are available, particularly in a patient with previous severe staining or substantial esthetic concern. Current evidence is not sufficient to recommend switching every patient from ferrous sulfate to a newer formulation solely to prevent discoloration. Such a strategy would require clinical comparative data demonstrating both reduced staining and equivalent hematologic effectiveness in the relevant population (Iolascon et al., 2024; Leone et al., 2026; Pantopoulos, 2024; Vahedi et al., 2025).

Future research should therefore prioritize clinically representative designs. The most informative study would prospectively compare commonly used formulations at therapeutic doses, include standardized baseline dental examination and objective color measurement, record administration technique and adherence, and follow patients long enough to determine onset and reversibility of staining. Stratification by primary versus permanent dentition and by sound versus demineralized enamel would clarify susceptibility. Parallel laboratory studies could then isolate the physicochemical variables responsible for observed clinical differences. This combined approach would allow current mechanistic hypotheses to be translated into evidence-based preventive recommendations (Asgari et al., 2020; Khalid et al., 2026; Vahedi et al., 2025).

## 7. Conclusions

Oral iron supplementation, particularly in liquid form, can cause extrinsic tooth discoloration through local interaction of iron-containing formulations with the tooth surface. The severity of staining appears to be influenced by multiple interacting factors, including the pharmaceutical formulation, local iron concentration, cumulative contact time, and enamel condition. Direct deposition of iron on the pellicle or enamel is likely central, while acidity, surface porosity, and microbial iron-sulfur reactions may modify stain formation and retention.

Current evidence suggests that minimizing prolonged contact with concentrated liquid iron and rinsing residual medication from the mouth are reasonable preventive principles. Dilution reduces discoloration in laboratory models, but product-specific administration instructions and the prescribed elemental iron dose must be preserved. Evidence for toothbrushing as a specific anti-staining intervention is weak, and enamel coatings cannot yet be recommended routinely. Once discoloration develops, professional cleaning and polishing appear to be effective conservative management strategies.

Most importantly, iron-associated staining is generally an esthetic and manageable adverse effect and should not lead to unsupervised discontinuation of medically indicated iron therapy. The evidence base remains dominated by heterogeneous *in vitro* studies on primary teeth. Prospective clinical studies using standardized color assessment are needed to establish the incidence of staining, identify susceptible patients, compare contemporary oral iron formulations, and define preventive protocols that are both dentally safe and compatible with effective iron replacement.

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