

Review articles

Iron deficiency anemia in swine: pathogenesis, diagnosis,
and preventive measuresK. L. Kostushkevych[#], V. H. Yefimov, E. V. Yesina

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Abstract. Iron deficiency anemia (IDA) in piglets remains a pressing issue in modern industrial swine production. The primary causes are the physiologically low iron levels present in newborn piglets and the imbalance between iron reserves, intake, and the animal's requirements during the suckling period. Contributing factors include the enhancement of productivity traits in pigs, such as increased litter sizes, accelerated growth rates during the suckling period, and restricted access to natural environmental elements, particularly soil. This review examines the mechanisms of iron homeostasis with an emphasis on intestinal iron absorption. Blood testing remains the cornerstone of anemia diagnosis in piglets. Hemoglobin (Hb) concentration is considered the key diagnostic indicator, and its measurement is increasingly conducted via point-of-care testing. Other important tests include red blood cell and reticulocyte counts, hematocrit, serum iron concentration, total iron-binding capacity (TIBC), and unsaturated iron-binding capacity (UIBC). Preventive strategies continue to focus on identifying the most effective and safe iron-containing preparations. In current industrial swine farming, the most commonly used preventive measure is a single intramuscular administration of complex iron-carbohydrate preparations on the third day of life at a dose of 200 mg per piglet. However, several issues remain under discussion. One such issue is the potential to influence neonatal iron levels through the maternal organism. Another is the need to evaluate the comparative efficacy of parenteral iron formulations based on iron dextran and gleptoferron. Due to the known toxicity of iron preparations, alternative administration approaches are being explored, such as combining parenteral and oral routes. Split dosing strategies and/or additional injections during the suckling period are also being proposed.

Keywords: hemoglobin; piglets; prophylaxis; iron dextran; gleptoferron.

Залізодефіцитна анемія у свиней: патогенез, діагностика і превентивні заходи

Анотація. Питання залізодефіцитної анемії поросят є проблемою сучасного промислового свиначарства. Встановлено, що причинами є фізіологічно низький рівень заліза в організмі поросят на момент народження та невідповідність запасів, надходження та потреб тварин у залізі у підсисний період. Сприяючими факторами розвитку є вдосконалення продуктивних якостей свиней, зокрема, збільшення кількості отриманих поросят від свиноматки, підвищення темпів росту у підсисний період та обмеження у доступі до природних умов існування, зокрема, ґрунту. Розглянуто механізми регуляції забезпечення організму залізом шляхом регуляції його абсорбції у кишечнику. Показано, що дослідження крові залишаються основою для діагностики анемії у поросят. Значення гемоглобіну вважається основним, а його вимірювання усе частіше проводиться на місці («point-of-care testing»). Серед додаткових лабораторних показників важливим є кількість еритроцитів та ретикулоцитів, гематокрит, уміст сироваткового заліза, загальна та ненасичена залізов'язувальна здатність сироватки крові. У превентивних стратегіях розвитку анемії поросят продовжуються пошук найбільш ефективних і безпечних залізовмісних препаратів. З'ясовано, що у сучасному промисловому свиначарстві найбільш поширеним заходом профілактики є ін'єкційне використання комплексних препаратів заліза з вуглеводами одноразово на 3-тю добу життя у дозі 200 мг на одну тварину. Проте, залишається низка дискусійних питань. Серед них слід виділити можливість управління рівнем заліза у поросят на момент народження через організм свиноматок. Крім того, важливим питанням є вивчення порівняльної ефективності парентеральних препаратів заліза, створених на основі декстрану заліза та глептоферону. Наявність токсичних властивостей у препаратів заліза спонукає до пошуку нових підходів до їх введення, зокрема, шляхом поєднання парентеральних і оральних засобів. Пропонується також роздільне введення загальної дози заліза та/або додаткової ін'єкції упродовж підсисного періоду.

Ключові слова: гемоглобін; поросята; профілактика; декстран заліза; глептоферон.

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Introduction

Current management of industrial pig farming and the continuous genetic improvement of production traits in pigs are the main causes that determine the application of permanent monitoring of the physiological parameters in pig herds. Over the past few decades, the number of live-born piglets per litter has increased from 11–12 to 17–18 or more piglets (Sell-Kubiak, 2021). Moreover, the number of weaned piglets has also risen; however, their survival rate during the pre-weaning period has declined (Laothong et al., 2024). Growth rates of piglets from birth to slaughter, along with lean meat yield in the carcass, have also improved. It is likely that such changes affect the physiological state of pigs and may influence the pathogenesis and clinical manifestation of diseases.

Even with thorough past studies of certain pathologies, the need to correlate their clinical course, results of specialized blood tests, and autopsy findings with contemporary scientific literature remains essential. This is particularly important as modern research methods now allow for the discovery of previously unknown levels of interaction between various organs and systems of the body. The use of such advanced techniques enables the identification of new biochemical mechanisms regulating complex physiological processes and contributes to a fundamentally new understanding of disease pathogenesis and treatment.

Iron deficiency anaemia is one of the most critical issues in the early rearing of piglets (Costa et al., 2023), especially in industrial operations where animals lack access to soil, and consequently, to the natural iron enrichment pathway (Egeli & Framstad, 1999). The disease has a significant impact on growth, development, survival, and the economic efficiency of pork production. In piglets, iron deficiency can be viewed as a consequence of genetic selection over recent decades for increased litter size and higher birth weights. As a result, sows are no longer able to supply sufficient iron to the growing number of piglets during both prenatal and early postnatal development (Bhattarai et al., 2019). Notably, even when sows have a normal iron status, an average of 27% of piglets are born anaemic (Hb <9 g/dl), and up to 75% have Hb levels between 9 and 11 g/dl (Sánchez-Piñeyro et al., 2025).

Studies conducted in Canada revealed that piglets with iron deficiency were found at weaning on 19 out of 20 commercial farms, with an average anaemia prevalence of 6.4% (Perri et al., 2016). Other researchers carried out a large-scale investigation of sows and found that 47.1% of them showed signs of anaemia (Hb below 9 g/dl) at the time of weaning (Sperling et al., 2021).

This review aims to analyse the current state of research on IDA in pigs under industrial farming conditions, focusing on its pathogenesis, diagnostic approaches, and the effectiveness of preventive strategies.

Iron requirements and metabolism in piglets

Iron deficiency in young pigs has been a long-standing issue in swine production, first identified as early as the late 19th century (Mazgaj et al., 2024). Later, in 1924, a causal relationship between iron deficiency and anaemia was established (McGowan & Crichton, 1924). In the classical study by Venn and coauthors (1947), it was demonstrated that a piglet's body contains approximately 50 mg of iron at birth. However, to maintain normal growth, a piglet must receive around 7 mg of iron per day. At the same time, the authors noted that sow's milk can supply no more than 1 mg of iron daily. This discrepancy between iron demand and supply leads to the development of anaemia. For instance, by day 11 of life, piglets not treated with iron supplements had Hb concentrations drop to 5.50 g/dl, indicating severe anaemia in over 90% of animals (Sánchez-Piñeyro et al., 2025). According to other sources (Meng et al., 2025), Hb levels between days 1 and 21 of life ranged from 47 to 63 g/l, confirming the presence of severe anaemia throughout the entire suckling period.

However, piglets reared with unrestricted access to soil tend to have higher iron content in their organisms. This may also clarify the peat-based feed additives supplementation beneficial effect on the Hb and iron levels improvement in piglets (Yefimov et al., 2017).

The iron content in sow milk increases from day 1 to day 16 of lactation, ranging from 1.68 to 8.61 mg/kg (Hu et al., 2018). A meta-analysis by Hurley (2015) indicates that the iron concentration in colostrum is 1.7–5.4 µg/ml, which is higher than in milk – 1.27–4.6 µg/ml. Other studies report iron levels in milk ranging from 1.70 to 2.97 mg/kg (Csapó et al., 1996). Similar information was provided by Novais and coauthors (2016), although they did not observe a significant difference in iron levels between colostrum and milk on day 17 postpartum. Furthermore, the authors found no increase in colostrum iron concentration even when additional iron was supplemented to the sows. However, it has been noted that administering iron supplements to pregnant sows results in higher iron levels not only in their blood serum and milk but also in the tissues of newborn piglets (Xing et al., 2023).

Prenatal iron transfer to piglets appears to be limited, likely due to the presence of a barrier to intrauterine iron transport, which is not compensated for by the iron provided in colostrum after birth (Matte & Audet, 2020).

In late gestation, the sow's need for iron increases rapidly due to the expansion of her red blood cell mass, which delivers iron to the developing fetus (Mahan et al., 2009). After the third farrowing, iron levels in sows gradually decrease and remain low for the rest of their lives (Gannon et al., 2011; Peters & Mahan, 2008). Nevertheless, iron injections or high dietary iron supplementation during late gestation did not result in increased iron levels in the offspring (Ducsay et al., 1984). These interventions also had limited effects on Hb levels, which may be attributed to restricted transplacental iron transport from the mother to the fetus (Mazgaj et al., 2024).

Thus, the effectiveness of iron supplementation in pregnant sows as a preventive measure against iron deficiency anaemia (IDA) in piglets remains a matter of debate.

Iron metabolism is unique, mainly due to the lack of efficient excretory pathways (Fig. 1). Therefore, regulation of iron absorption in the intestine is the primary engine to maintain iron homeostasis (Ji et al., 2019).

Specialized mechanism facilitates efficient iron uptake: duodenal cytochrome B metallo-reductase converts ferric iron (Fe³⁺) into the soluble ferrous form (Fe²⁺) that particularly realized on the apical membrane of enterocytes (McKie, 2001). The apical membrane protein divalent metal transporter 1 (DMT1) serves as the main entry point for Fe²⁺ into the cell. The iron is then exported into the bloodstream via the basolateral membrane, primarily through ferroportin 1 (FPN1) (Leong et al., 2003). Multicopper oxidases such as ceruloplasmin and/or hephaestin play key roles in transporting iron across the basolateral membrane by oxidizing Fe²⁺ to Fe³⁺ for subsequent binding and transport. While the interaction mechanisms between FPN1 and ceruloplasmin are not yet fully understood, the essential role of copper in facilitating iron absorption is well established (Ward & Kaplan, 2012). The main iron transport protein in plasma is transferrin, which can bind two Fe³⁺ ions with high affinity (Gkouvatsos et al., 2012).

Iron deficiency and hypoxemia stimulate the production of erythropoietin in the kidneys. Erythropoietin, in turn, promotes erythropoiesis and increases the production of erythroferrone in the red bone marrow. Erythroferrone enhances iron absorption and suppresses the synthesis of hepcidin in hepatocytes. Hormone hepcidin is a key regulator of iron metabolism. Its production is stimulated by bone morphogenetic protein 6 (BMP6) in response to iron detection by liver endothelial cells in the absence of the inhibitory effect of erythroferrone (McMillen et al., 2022; Wang & Babbitt, 2019). Hepcidin controls intestinal iron absorption by binding to FPN1 on the basolateral membrane surface, leading to its degradation (Ji et al., 2019).

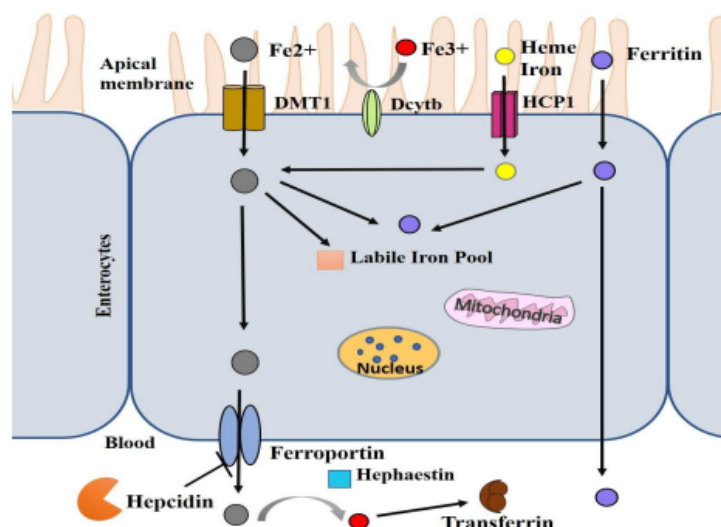


Fig. 1. Mechanism of intestinal iron absorption (Sawhney et al., 2023).

Several results reported that expression of the duodenal iron transporters DMT1 and FPN1 is very low during the first days of a piglet's life (Lipiński et al., 2010). Researchers believe this is an additional factor contributing to the development of anemia.

IDA in Pigs: Clinical Manifestation and Contributing Factors

IDA in pigs can pass in both chronic and acute forms. In chronic cases, signs include pale and wrinkled skin, pallor of the snout and ears, coarse hair coat, lethargy, and poor growth. In acute cases, spasmodic breathing may develop, and in extreme situations, death can occur due to hypoxia (Sawhney et al., 2023; Zimmerman et al., 2012; Svoboda & Drabek, 2005). Clinical signs of anemia typically appear between 10 and 14 days of age. Initially, pallor of the mucous membranes, particularly the conjunctiva, becomes noticeable. In the next stage, pallor appears on the outer surface of the ears. In critic stages, the skin becomes pale across the entire body, and there is marked dyspnea, lethargy, and increased amplitude of the apical heartbeat following physical exertion (Svoboda & Drabek, 2005).

Early-onset IDA in pigs leads to a significant reduction in feed intake and negatively impacts growth rate. Particularly, a lack of growth rate is dependent on the duration of the anemic state itself—even after hematocrit and Hb levels have returned to normal parameters (Knight & Dilger, 2018)

Depletion of iron stores in piglets results in reduced activity of the enzyme ribonucleotide reductase, which is iron-dependent and responsible for DNA synthesis and cellular replication. Additionally, iron influences the production of interleukin-2, which regulates the proliferation and differentiation of lymphocyte populations. This may partly explain the reduction in both cellular and humoral immunity observed in anemic suckling piglets (Masiuk et al., 2024). Consequently, there is a high incidence of infectious diseases, particularly colibacillosis (Svoboda & Drabek, 2005).

In organic pig herds with prolonged suckling periods, the onset of iron intake from feed is delayed. As a result, a single injection of 200 mg of iron (in the form of iron dextran) on day 3 of life led to the lowest hematocrit and serum iron levels by day 28, along with the lowest average daily weight gain until weaning. In contrast, piglets receiving an additional iron injection demonstrated improved outcomes (Heidbüchel et al., 2019). Thus, the longer the suckling period, the higher the risk of anemia in piglets due to the

exhaustion of iron reserves.

Moreover, seasonal effect on Hb levels was observed at three days of age in piglets raised outdoors, that suggest the effect of climate and season factors on the anemia development (Fjelkner et al., 2024). Negative correlations were identified between piglet birth weight and Hb levels (-0.37 ± 0.32), as well as between sow Hb levels and average piglet birth weight (-0.60 ± 0.34) (Hollema et al., 2020).

In addition to iron deficiency, other factors may contribute to the development of IDA. One such factor is infection with hemotrophic mycoplasmas (hemoplasmas). The pathogenic mechanisms primarily involve erythrocyte destruction through adhesion, invasion, eryptosis, and indirect erythrocyte lysis due to immune-mediated events and immune dysregulation processes (Ade et al., 2024).

Gastrointestinal pathologies may also lead to anemia. Ulceration in the cardiac part of the stomach while pathogenesis observed both chronic and subacute phase that can result in anemia due to blood loss (Krepelková et al., 2024). Proliferative hemorrhagic enteropathy (PHE) that caused by *Lawsonia intracellularis* and typically observed in pigs of 4–12 months of life. The clinical picture is often characterized by sudden death associated with anemia and hemorrhagic diarrhea (Luppi et al., 2023).

Diagnostic Approaches to IDA

Hematological and biochemical blood analyses remain the cornerstone for diagnosing anemia in piglets. Currently, Hb concentration is considered the primary indicator for diagnosing anemia in swine. A Hb level below 9 g/100 ml is regarded as latent anemia, necessitating iron supplementation before it drops below 8 g/100 ml, which is then classified as clinical anemia (Noblett et al., 2021). Hb concentrations of 10 g/100 ml or higher are considered within the normal range.

Growth retardation has been observed when Hb levels fall below 7 g/100 ml, with values under 6 g/100 ml classified as severe anemia. Levels below 4 g/100 ml are associated with increased mortality (Zimmerman et al., 2012). According to Bhattarai & Nielson (2015), Hb concentrations below 110 g/l indicate IDA, whereas levels below 90 g/l are indicative of clinical anemia. Wei and coauthors (2005) defined severe anemia as an Hb concentration below 60 g/l, while Svoboda & Drabek (2005) proposed 80 g/l as the diagnostic threshold for anemia. Similar evaluation criteria

based on Hb levels include: anemia—below 9 g/dl; subclinical status – between 9 and 11 g/dl; and optimal Hb levels – 11 g/dl for piglets and 10 g/dl for sows (Sperling et al., 2021).

The normal Hb range in sows is 10–16 g/dl, with values below 10 g/dl indicative of anemia (Noblett et al., 2021). Notably, wild boars exhibit high Hb (140 g/l) and erythrocyte counts (8–10 T/l), suggesting sufficient supply of trace elements essential for erythropoiesis (Ulyzko & Todorov, 2014).

Hb levels tend to decline during early lactation, making anemia more prevalent in this period, while levels begin to rise in later stages of lactation (Noblett et al., 2021). A linear decline in mean Hb levels – from 11.7 g/dl to 10.8 g/dl – was recorded with increasing parity in hyperprolific sows, indicating poor recovery of iron stores between farrowings (Auvigne et al., 2010).

In addition to Hb concentration, other hematological parameters used to detect IDA in piglets include red blood cell (RBC) count, total and differential leukocyte count, platelet count, hematocrit (Hct), hemoglobin distribution width (HDW), mean corpuscular hemoglobin concentration (MCHC), mean corpuscular hemoglobin (MCH), mean corpuscular volume (MCV), and red cell distribution width (RDW).

Reported erythrocyte counts for suckling piglets range from 5.62 to $7.84 \times 10^{12}/l$ (Zhang et al., 2022), while other researchers provide a broader reference range of 4.08 to $8.29 \times 10^{12}/l$ (Friendship et al., 1984; Ventrella et al., 2016). For sows, reference ranges are 4.98–8.29 and $4.98–7.50 \times 10^{12}/l$ (Zhang et al., 2022; Bhattarai et al., 2019). A study conducted in Slovenia confirmed that erythrocyte counts in the local pig population matched the regional reference values—ranging from 5.0 to $8.1 \times 10^{12}/l$ (Ježek et al., 2018).

Modern-generation hematology analyzers allow for predictive assessments of erythrocyte function based on reticulocyte indices. Of particular interest is the mean Hb content in reticulocytes, a parameter commonly used in human medicine and now applicable to veterinary diagnostics, particularly for diagnosing IDA in piglets (Godyn et al., 2016). Compared to conventional markers such as Hb, packed cell volume (PCV), and RBC, reticulocyte indices respond more rapidly to disruptions in erythropoiesis. The response of MCV and MCH is comparable to that of reticulocyte indices. In piglets with severe iron deficiency, significant increases in both traditional (Hb, PCV, MCV, and MCH) and reticulocyte indices were observed within 48 hours of iron supplementation. In cases of mild iron deficiency, reticulocyte indices responded more quickly than erythrocyte parameters (Svoboda et al., 2008). In suckling piglets, IDA is typically a hypochromic microcytic anemia characterized by a reduction in reticulocyte (erythrocyte) indices (Mazgaj et al., 2024).

In veterinary medicine, point-of-care testing (POCT) methods have gained popularity due to their ability to deliver immediate results using minimal blood volumes. Conductivity-based Hb measurement consistently underestimated Hb values, whereas the photometric method demonstrated superior accuracy and is thus considered more reliable for on-site Hb measurement in pigs (Kutter et al., 2012).

Measuring serum iron concentration provides essential data for evaluating iron status. However, it is not considered the most reliable standalone test for detecting iron deficiency. This is due to the considerable individual biological variability in serum iron levels (21%), which is higher compared to ferritin (13%), transferrin (4%), and soluble transferrin receptor (sTFR) (7%) (Rusch et al., 2023).

Total iron-binding capacity (TIBC) is an important laboratory test for diagnosing iron metabolism disorders. This parameter reflects the maximum amount of iron required to fully saturate plasma or serum transferrin (Yamanishi et al., 2003) and is effectively an indirect measure of transferrin levels (Faruqi et al., 2024). Some studies indicate that although TIBC and transferrin levels are significantly correlated in humans, direct measurement

of transferrin is preferable (Kasvosve & Delanghe, 2002). However, given that transferrin quantification relies on immunochemical methods, the authors caution that errors may occur in populations with substantial genetic variability in this protein.

Unbound iron-binding capacity (UIBC) is considered more accurate than TIBC and transferrin saturation percentage for diagnosing iron deficiency. According to Åsberg and coauthors (2021), UIBC is a more precise test than sTFR for assessing iron deficiency in non-inflamed female subjects. Conversely, for the evaluation of iron overload, ferritin measurement is deemed more appropriate (Soman & Adiga, 2018).

Mass spectrometric analysis has been proposed for the quantitative determination of hepcidin-25 a peptide hormone that regulates iron metabolism – in the plasma of pigs. An increase in iron availability leads to the recovery of piglets from IDA and correlates with elevated plasma hepcidin-25 levels (Starzyński et al., 2013).

Thus, various parameters are employed to assess iron sufficiency in the body. However, in the context of evaluating pigs with IDA, the most reliable, informative, and accessible indicators are serum iron, TIBC, and UIBC. These not only provide insight into iron levels but also reflect the response of plasma transport proteins – primarily transferrin – and the degree of their saturation.

Current strategies for the prevention and treatment of IDA

For optimal functioning of the body, piglets require from 7 to 16 mg of iron per day, since the intensity of metabolic processes and, accordingly, the number of erythrocytes increases from birth to weaning. Iron reserves in the piglet's body are limited. They are mainly concentrated and estimated at 50 mg. These levels are considered the lowest among newborn mammals (Venn et al., 1947). If no external iron supplement is administered, the chances of piglets developing IDA increase significantly (Lipiński et al., 2010).

For the prevention of IDA, iron, manganese, copper, and cobalt salts were previously administered orally. Iron fumarate salt licks, iron-containing briquettes based on chalk, and granulated feed with iron glycerophosphate were also used for feeding piglets (Ulyzko & Todorov, 2014). In addition, earlier sources pointed out the importance of keeping suckling piglets on natural soil (Gendreau, 1938), or introducing turf, including that sprayed with iron sulfate, into pens to create an environment similar to the natural one (Mitchell, 1940). However, not all soils, particularly sandy ones, have such an effect (Heitman, 1948). For a time, the effect of liver extracts with anti-anemic properties was studied, presumably due to the cyanocobalamin they contained (Braude, 1949).

With the study of causes and mechanisms of anemia development in piglets, the stage of using various iron compounds began. In particular, as early as the 1940s, for the prevention of anemia, aqueous solutions of iron sulfate were recommended to be applied to sow teats and introduced into feed mixtures (Gendreau, 1938; Hamilton et al., 1933). Since then, inorganic, organic, and complex iron-containing compounds have been used for oral and parenteral administration. However, the search for effective and safe preparations continues to this day.

In biological systems, iron utilization is associated with two problems: the first – low solubility of free metal ions and the formation of toxic compounds. Most of the iron in feeds is in the form of non-heme ferric ion (Fe^{3+}). Such feed components as phosphates, phytates, carbonates, and oxalates significantly reduce iron bioavailability, as they form insoluble compounds with it (Somsok et al., 2005). Iron absorption in tissues can be increased by forming an iron complex with sugars (Gyurcsik & Nagy, 2000).

Iron-containing preparations are classified by the route of administration into oral forms (iron salts, or their combination with cobalt and copper salts, vitamins) and parenteral forms

(iron complexes with dextran, vitamins). In terms of form, iron-containing preparations include inorganic compounds (ferrous sulfate and ferric chloride) and organic iron (II) compounds – gluconate, fumarate, xylitol, sorbitol, dextran, dextrin – and iron (III) compounds – ferroprotein (Svoboda & Píšťková, 2018).

Inorganic iron salts (particularly ferrous sulphate) are chemically unstable and easily react with other feed ingredients. This leads to limited biological availability of iron and the easy formation of free radicals, which intensify lipid peroxidation and may cause gastrointestinal disorders (Oates & Morgan, 1996).

Second-generation iron feed additives (salts of iron and organic acids), such as ferrous lactate, are absorbed in the form of iron ions and molecular chelates. However, these salts may cause adverse reactions, have low stability, and poor intestinal absorption (Cancelo-Hidalgo, 2013).

Recently, metal compounds with organic carriers have gained popularity worldwide. Metal-organic complexes have been collectively termed chelated compounds. Chelated iron, as a new type of iron-derived supplement constructed with polysaccharides component binding. Similar complexes have attracted considerable attention due to its unique gastrointestinal tolerability and high level of iron absorption. Numerous studies have demonstrated the positive effects of iron chelate for the treatment of anemia, reduction of free radical formation, and modulation of immune response. Moreover, preliminary research has shown that feed supplements with polysaccharide iron chelate can improve the reproductive performance of sows and promote faster growth in piglets (Feng et al., 2024).

Iron chelated with polysaccharides, polypeptides, and amino acids are the main products of the third generation of iron supplements. The high bioavailability of these preparations (amino acid iron chelates) may be attributed to their structure. This type of iron preparation exhibits higher stability and absorption rates compared to the previous two generations of iron supplements. It is assumed that chelated iron may pass through the enterocyte membrane with mechanism which is similar to small peptides absorption in the small intestine (Yu et al., 2019).

Despite certain limitations in oral iron administration to piglets, the search for new iron-containing supplements remains actual task. The issues of high bioavailability and overcoming intestinal absorption barriers remain relevant. In this regard, the application of heme appears promising. It is a complex of divalent iron and porphyrin compound, which serves as a prosthetic group in various proteins (including Hb) (Xing et al., 2022). More than 60 years ago, efficient absorption of heme from feed was confirmed, and since then, it has been known that in mammals, its absorption is significantly more efficient than inorganic iron uptake (Anderson et al., 2005). However, the use of heme iron for the prevention of IDA in piglets has not led to its widespread adoption in swine production.

Another direction in the development of oral iron preparations is the creation of iron encapsulated with maltodextrin. The core of the microparticles consisted of ferrous sulfate heptahydrate (non-heme iron) and bovine erythrocytes (heme iron). The use of this supplement, in comparison with parenteral administration, showed similar results. However, the requirement for fourfold administration of these substances renders them impractical (Churio et al., 2018).

The formation of iron complexes with polysaccharides and polyols has been extensively studied, as polysaccharides are capable of stabilizing ferric oxide (Fe^{3+}) and maintaining a stable concentration of soluble iron under physiological conditions. The first iron-dextran complex was discovered in 1953, when an attempt was made to synthesize a ferritin analogue by replacing its protein component with a polysaccharide. This combination later became the most widespread method for treating hypochromic anemia in humans (London, 2004). Iron dextran has been used

parenterally as a polysaccharide iron supplement for piglets since 1954 to prevent anemia (Feng et al., 2024).

The study and discussions continue regarding the frequency and dosage of iron-containing preparations (Heidbüchel, 2019). For instance, some authors did not observe differences in piglet weaning weight when comparing single (on day 3 of life) versus double (on days 3 and 21) administration of iron dextran (Bruininx et al., 2000). On the other hand, Chevalier and coauthors (2023) found a positive effect on daily weight gain in piglets with an additional 200 mg dose of iron dextran administered at 8 days of age.

For instance, the dosage and injection number were tested in comprehensive study while the iron dextran was administered to piglets at a dose of 200 mg once (on day 3), twice (on days 3 and 14), and three times (on days 3, 14, and 21). No differences in piglet weight gain were observed by day 28 after birth. However, piglets that received only one injection of the preparation had significantly lower weight gains at weaning on days 40–45 of life. At the same time, no differences were found between the two- and three-time administration groups (Heidbüchel et al., 2019). It was also established that a single iron treatment (in the form of gleptoferron) on day 4 of life is insufficient to meet the iron needs of all piglets. Animals that had daily access to iron-enriched peat moss or received a repeated 200 mg dose of an iron-containing preparation were fully supplied with iron during the suckling period (Friendship et al., 2021).

The result of study in which piglets injected with iron preparations on days 1, 3, and 4 of life showed varying data. Piglets that exposed to iron dextran on the first day had significantly higher Hb concentrations compared to other animals on day 7 of life. At the same time, on days 14 and 21, no differences were found between the groups. This data evidence that some piglets are anemic at birth and consequently they need the iron injections on the first day of life to prevent IDA (Egeli & Framstad, 1999).

Separated administration of iron dextran on days 3 and 14 of life at a dose of 40 mg per kg of body weight was proposed to reduce the toxic effects of iron preparations. The results showed that modifying the protocol with two small doses of iron for newborn piglets increased their weight gain and survival, and also maintains intestinal wall development (Chen et al., 2019).

Iron dextran-based preparations for injectable use have several advantages, making them the most widely used for the prevention and treatment of IDA in piglets. At the same time, iron dextran has certain disadvantages. In particular, it is difficult to formulate such therapeutic compositions that contain more than 10% iron. In addition, side effects occasionally occur, and correction of low Hb levels may require prolonged administration (Alsop et al., 1970). Sporadically, iron dextran may cause anaphylactic reactions in piglets, triggered by a response to the sugar component (Szudzik et al., 2018).

A fairly widespread form of polysaccharide–iron complex is the formulation contained gleptoferron as a rule last decade. This formulation is a sterile colloidal solution of β -ferric oxyhydroxide and dextran glucoheptonic acid. The approximate molecular mass is about 2 million, and the average particle size is 50×20 nm (Movat & Wasi, 1985). Dextran heptonic acid is produced by a reaction with cyanide ions to form cyanohydrin followed by hydrolysis. It is then used for the synthesis of gleptoferron (Alsop et al., 1970).

Iron dextran is identified by the Chemical Abstracts Service (CAS) number 9004-66-4 and is chemically defined as an iron hydroxide complex (α 1,3- α 1,6-glycan) with the molecular formula $(C_6H_{10}O_5)_n \cdot [Fe(OH)_3]_m$. Gleptoferron is registered under CAS number 57680-55-4, with the molecular formula $C_{13}H_{25}FeO_{15}$. The structural formulas of both aforementioned compounds depicted in Figure 2.

Studies on absorption and bioavailability of iron in suckling piglets have shown that the use of gleptoferron produces better

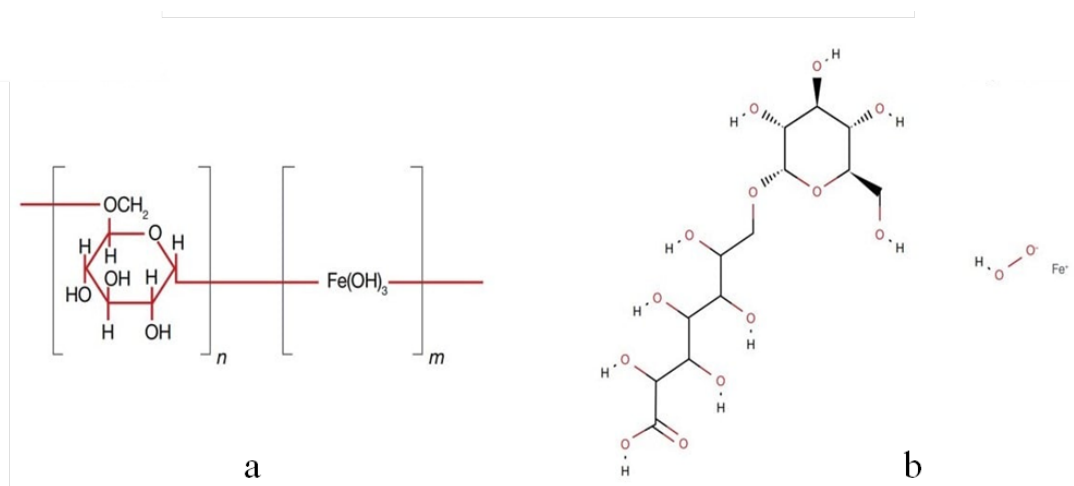


Fig. 2. Structural formula of iron dextran (a) and gleptoferron (b).

results than iron dextran. In particular, total iron absorption is 4.6 times higher compared to iron dextran. This leads to higher serum iron concentrations in piglets and a longer maintenance time of those levels (Morales et al., 2018).

Iron preparations based on gleptoferron are also were administered parenterally at a dose of 200 mg of iron at 3–4 days of age. The efficacy of administration is not inferior to that of dextran (Anderson et al., 2005). At the same time, certain results indicate that gleptoferron outperformed iron dextran effect on the prevention of anemia in piglets (Sperling et al., 2018). Recently, combined preparations of gleptoferron with toltrazuril have gained widespread use. This combination is an effective means of preventing both IDA and cystoisosporosis and is more practical (Karembe et al., 2024). At the same time, although the combination of gleptoferron with toltrazuril and iron dextran had the same effect on Hb levels in piglets, it is noted that in cases where an additional iron injection is needed, iron dextran products have an advantage (Hennig-Pauka et al., 2025).

Along with the development of new iron-containing drugs, their side effects are also being studied in respect to their known therapeutic and preventive effects. The study of the side effects caused by intravenous administration of iron dextran to several groups of patients for therapeutic purposes demonstrated detrimental outcomes including sarcoma, sterile abscess, tissue necrosis, and sudden death, associated with subsequent administration of iron dextran (Kumpf & Holland, 1990). When iron intake exceeds the binding capacity of transferrin in the serum, redox-active iron appears. When the amount of iron entering cells exceeds the capacity of iron-binding proteins, iron behaves as redox-active iron. As a result, lipid peroxidation intensifies, mitochondrial DNA is damaged, and cell apoptosis occurs (Stockwell, 2018; Kawabata, 2022). Taking this into account, some researchers suggest divided iron injection as a possible strategy both to meet the iron needs of piglets before weaning and to reduce toxic reactions during the suckling period (Albers et al., 2022). The combine treatment with oral supplementation and iron injection is recommended manner that accompanied by oxidative stress reduction and contributes to increased weight gain, Hb levels, and serum iron concentration (Meng et al., 2025). Taking into the account aforementioned data, iron-organic complexes contained dextran are the main tool to treatment and prophylaxis IDA in swine farming.

Conclusion

IDA is widespread disease among pigs across various production groups in the industrial swine farming. The most susceptible group is suckling piglets, nearly 100% of which develop severe anemia in the absence of preventive managements. The pathogenesis is primarily driven by the mismatch between the iron requirements of rapidly growing piglets and the limited iron reserve at birth. Additionally, a lack of iron intake from colostrum and milk is a weighted cause also. Other contributing factors include lack of access to soil, high litter sizes, and fast postnatal growth rates.

The principal diagnosis criteria is Hb concentration, typically assessed via point-of-care devices. A Hb level below 9 g/100 ml in piglets is classified as latent anemia. This anamnesis requires obligatory an iron supplementation to prevent the level decline is below 8 g/100 mL taking into the account that is a limit level of clinically anemia. Anemia is diagnosed in sow while Hb decline is below 10 g/dl. Additional laboratory markers commonly used to confirm anemia are red blood cell and reticulocyte counts, serum iron, TIBC, and UIBC. The predominant preventive approach remains the injectable treatment with iron-carbohydrate complex on the third day of life in a dose of 200 mg per piglet. Ongoing research is evaluating the comparative efficiency of iron dextran and gleptoferron-based drugs. Due to concerns regarding iron toxicity, current tasks are directed toward optimizing exposure suckling piglets to combined feed additives and injectable formulations.

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Conflict of interests

The authors of this article declare no conflict of any interests or personal relationship regarding this manuscript.

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