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Applied Biochemistry

THEME

Contribution on recent research in anemia disease and it treatment

Presented by:

RACHED Lamia & BERRETIMA Amira

In front of the jury composed of.

President :	BELMASOUD Rachid	…….	Echahid Hamma Lakhdar University of El-Oued
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- Academic year 2022/2023 -

Dedication

After five years of diligence, perseverance and striving, today I am reaping the fruits of my labor, which I dedicate:

I dedicate this research to the spirit of my father, **Berretima Saide**, who I wished would be present with me on such a special day

I also dedicate this research to the sweetheart of my heart, the light of my eyes, and the balm for my wounds, to my dear mother, **Saliha masri**, may God prolong her life.

And I do not forget my brothers **Belkacem** and **Fares berretima**, the source of my energy

I conclude my dedication to my beloved sisters **Iman, Djouhara**, **Sana**

who have always been by my side and always with me in my joy and sorrow

Finally, I extend my sincere thanks to everyone who advised me, directed me, and guided me to complete this work

Amira BERRETIMA

Dedication

As a token of love and affection, I dedicate this modest work with great pride to all those who are dear to me:

Dear Father "**Khemissi Rached** ", who can be proud of and finds here the result of many years of sacrifices and hardships to help me move forward in this life. May God bless you and give you long life.

Dear mother "**Louiza Lalmi**", who worked for my success, through her love, continuous support and all the sacrifices she made in my life. I ask God for good health and longevity for you

My dear sister**" Farah**" and dear brothers " **Mohammed, Ayoub,Rabie** and **Moustafa** " , may God bless your hearts and grant you health, happiness and success

To all my dear family, friends and loved ones. And everyone who helped me accomplish this humble work from near or far.

RACHED Lamia

special thanks

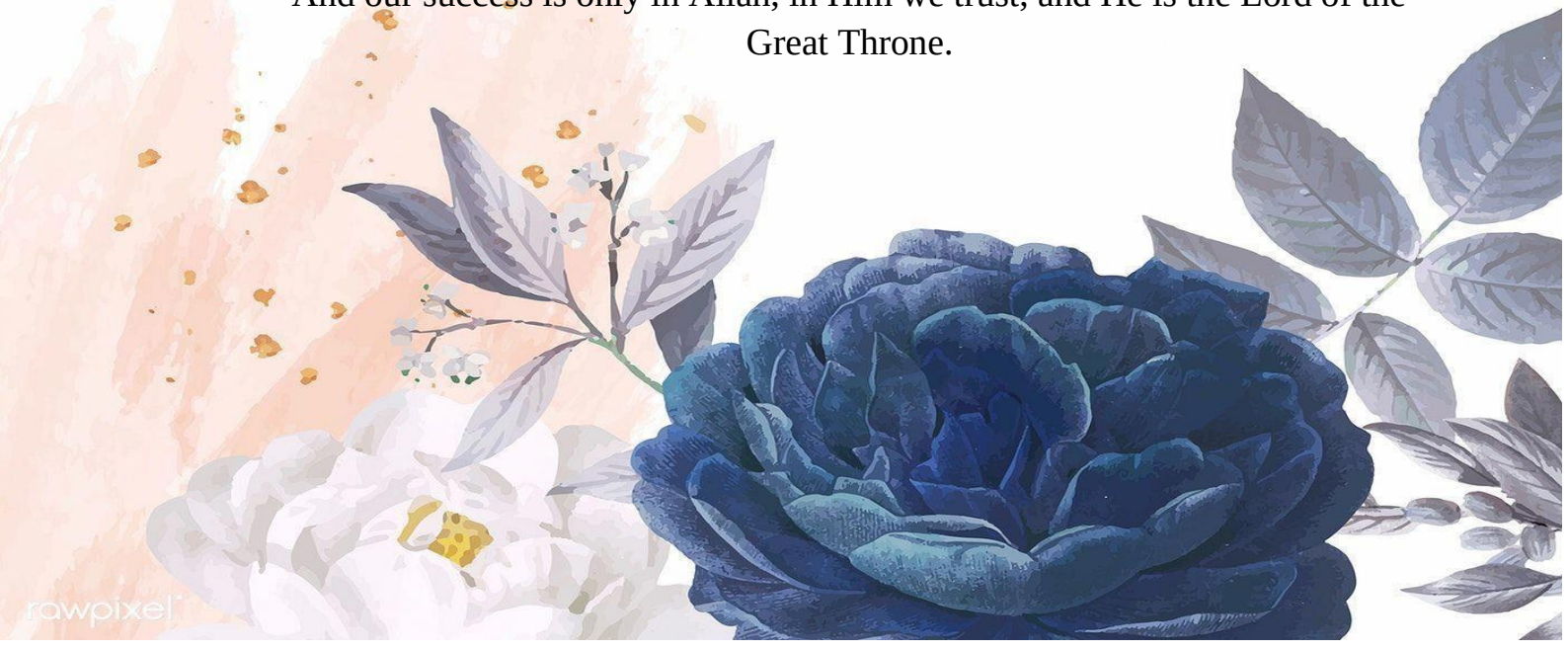
Praise be to God, Lord of the worlds, and prayers and peace be upon the most honorable of messengers, our master Muhammad, the last of the prophets and messengers.

We are pleased and honored to extend our sincere thanks and gratitude to our esteemed teacher* **Beya BOURAS***, who honored us with supervising this work and for the valuable guidance and care she gave us that helped us complete this memorandum. May God bless and perpetuate it as a beacon of knowledge, enlightened by its light.

Great thanks to the doctor **ZAATER Abd Malek**,We also extend our sincere thanks and gratitude to all our honorable professors from whom we learned, especially the professors of the College of Natural Sciences and Life.

Thanks are extended to all the library and administration workers of Hama Lakhdar University - Al- Ouad - may God reward them.

And our success is only in Allah, in Him we trust, and He is the Lord of the Great Throne.



Abstract

Abstract

Anemia is a global public health problem that has gained a lot of studies and research in recent years.

We conducted this study with the aim of identifying anemia and identifying the most important groups at risk of infection with this disease. This study also aims to bring together the most important and latest research and studies on anemia, in addition to highlighting the various treatments recommended globally.

According to what we have reached through this study, women from the age of 15 to 49 years and children under the age of five are the most affected by anemia. We also concluded that this disease can be treated in many different ways, whether by using some types of plants in what is known as alternative medicine, or through chemical medicines.

Finally, it is recommended to develop prevention and awareness methods in order to avoid this disease.

Key words: Anemia, disease, treatment methods.

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SUMMARY

Introduction

Blood is life. The heart pumps it into the arteries and veins. **(Preetha & Atanu, 2020)** It is necessary for the proper functioning of the body's organs (such as the brain, muscles, bones, and many others). Whole blood contains red blood cells, white blood cells, and platelets. These components are found within a protein fluid known as plasma. Red blood cells are also called red blood cells, which in turn contain the protein hemoglobin. **(Z. Al-Attar, Jasim & Hashim, 2020).** And any decrease in the number of healthy red blood cells or the hemoglobin they contain may expose the person to what is known as anemia. (**Khalid, & al., 2019)**

Anemia is a global public health problem that affects all developing and developed countries and has serious consequences for human health. It is a condition in which the number of red blood cells or the level of hemoglobin they contain is less than normal.**(Khalid N *& al.*, 2019)** . It occurs in all stages of the life cycle and is more common in pregnant women and young children **(Hench, 2020)**. , as it also affects other groups such as vegetarians (**World Health Organization, 2019)**. , the elderly and people with chronic diseases, and anemia (also known as low hemoglobin) may make you feel tired and debilitated. There are several types of anemia, each with its own cause. Anemia may be temporary or long-term and range from simple to severe. This disease often occurs for more than one reason, but iron deficiency anemia is one of the most important and common causes.

Anemia has taken a great deal of continuous research to find and understand the sources and methods of treatment of the latter, and for this we have made a summary of the most important recent studies on this disease, so this note is centered on 3 parts, which are the following:

Chapter 1: Anemia disease

Chapter 2: treatments of anemia

Chapter 3: Recent research in treatment anemia disease

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Chapter 01

Anemia disease

A range of health problems can arise from nutritional deficiency. Among these health problems is known as anemia. Is a common nutritional deficiency disorder and global public health problem which affects both developing and developed countries with major consequences for human health and their social and economic development. Therefore, in this part we will learn about anemia, types, causes and their symptoms

1. Definition of anemia

anemia may be defined as a reduction in haemoglobin concentration below that which is normal for the individual, due to an inadequate supply of haernopoietic nutrients **(Obeagu Emmanuel Ifeanyi, 2018)**. The Word << anaemia » explain It self « an >> mean without and « aemia » mean red blood cells, which means that Anaemia is a condition in which you lack healthy red blood cells that transfer proper amount of oxygen to all the parts of the body. **(Khalid, *& al.*, 2019, Natasha,2019)** As we find that the decline in the number of circulating erythrocytes and / or hemoglobin per unit of blood volume below normal for a given age and gender **(Z. Al-Attar, Jasim & Hashim, 2020)**.

2. Different types of anemia

The classification of anemia based on two factors: Red cell morphology and Etiology of anemia

2.1. Anemia Classification Based on Morphology

Morphological classification of anemia is based on: red cell size (Normocytic, microcytic, or macrocytic), and degree of hemoglobinization, reflected by the color of red cells (normochromic or hypochromic). As described in **(Figure 1)**.

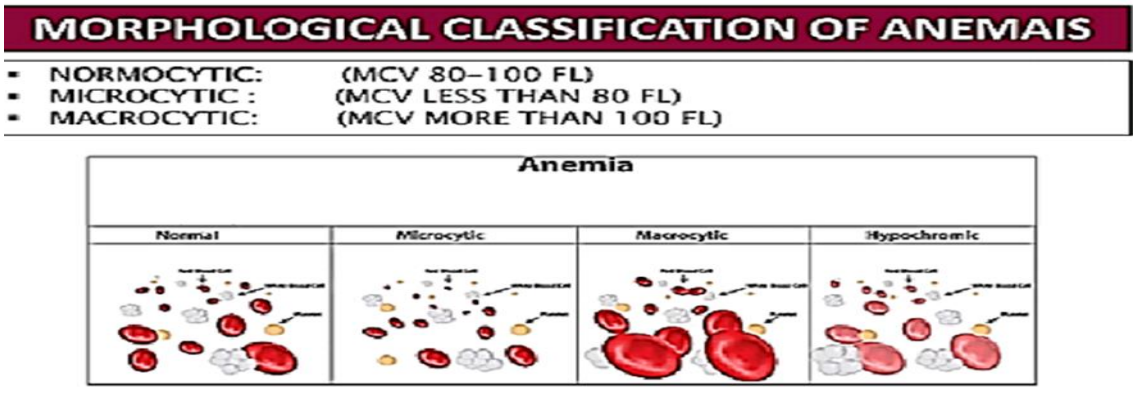

Figure 01: Morphological classification of anemia **(Al-Attar *& al.*, 2020)**

2.2. Anemia Classification Based on Etiology

The following are the different types of anemia as a matter of etiology and are the arranged from the least to the most dangerous types, which are: Vitamin deficiency anemia (Is a lack of healthy red blood cells caused by lower than usual amounts of vitamin B - 12 and folate). **(Preetha & Atanu, 2020),** Iron-Deficiency Anemia (**Sant -Rayn *& al.*, 2021),** anemia of chronic disease (ACD)or anemia of inflammation, **(Alhboob *& al.*, 2017, Sajidah, 2019),** Hemolytic Anemia. **(Bradley *& al.*, 2002),** Aplastic Anemia. **(Escalante *& al.*, 2019, Fatemeh *& al.*, 2023),** Megaloblastic anemia**. (Quratulain & Getrude, 2021),** Pernicious anemia (PA)**. (Htut *& al.*, 2021).** Sickle cell anemia(figure 02), **(Juliana *& al.*, 2018, Sagar *& al.*, 2021),** Thalassemia. **(Soundarya & al., 2016)**

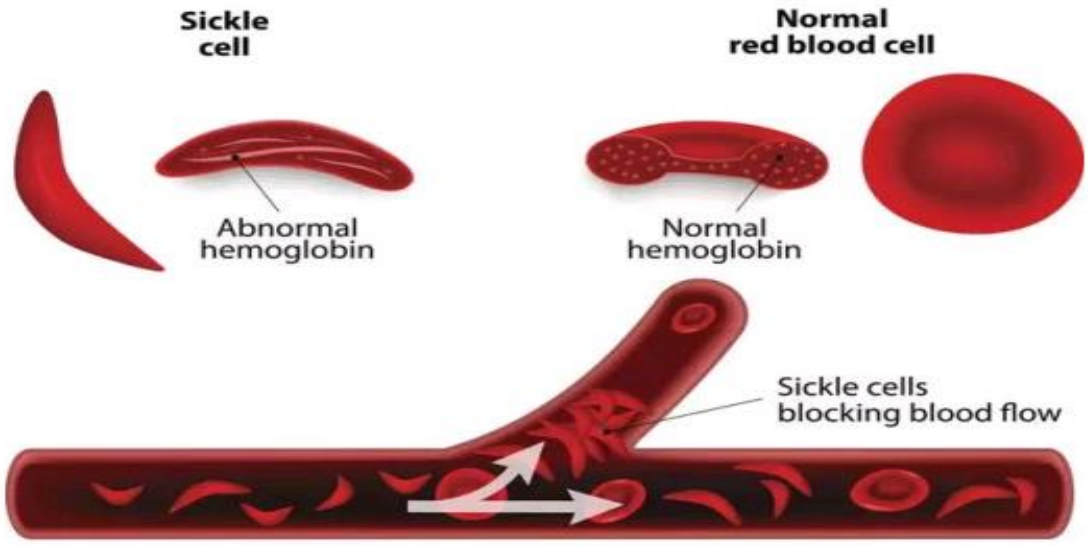

Figure 02: Blood Flow of Sickle Cells**. (Sagar *& al.*, 2021)**

1.3. Symptoms and signs associated with anemia

Anemia signs and symptoms vary depending on the cause and severity of anemia, at first, anemia can be so mild that you don't notice it. But symptoms worsen as anemia worsens. Among the most common symptoms of anemia is fatigue, and a decrease in the number of red blood cells can also cause shortness of breath in addition to dizziness, and other symptoms such as palpitations, pale skin and fainting spells **(Faiza *& al.*, 2019).**

On the other hand, we cannot rely on these symptoms as specific to anemia only, because they can indicate other diseases as well, while we find that there are specific symptoms that confirm the existence of anemia and differ according to the types of anemia. This is why

knowing and understanding the different classifications can help in recognizing the symptoms of anemia **(Soundarya *&* *al.*, 2016).**

1.4. Causes of anemia

There are many causes of Anemia but malnutrition is the main cause. The other factors that cause Anemia are the iron deficiency which is mostly found in infants and middle-aged women **(Alaliwi *&* *al.*, 2018,),** vitamin deficiency like Vitamin B12 deficiency is another important cause of nutritional anemia that affects elderly. **(Alaliwi *&* *al.*, 2018)**, chronic diseases, huge bleeding due physical injuries and during menstruation that leads to loss of red blood cells, in some cases your body It self destroy the red blood cells and the body does not form the red blood cells. Certain infectious diseases, pregnancy and age also cause severe Anemia **(Khalid *&* *al.*, 2019; Nicolai *&* *al.*, 2019; Luigia *&* *al.*, 2020)**

1.5. Definition of iron

Iron is a chemical element with the symbol Fe and atomic number 26. It is a metal that is essential for human health and plays a crucial role in various biological processes, including the production of hemoglobin, the protein in red blood cells that carries oxygen throughout the body (Zoroddu & al., 2019).

1.6. Cellular iron homeostasis

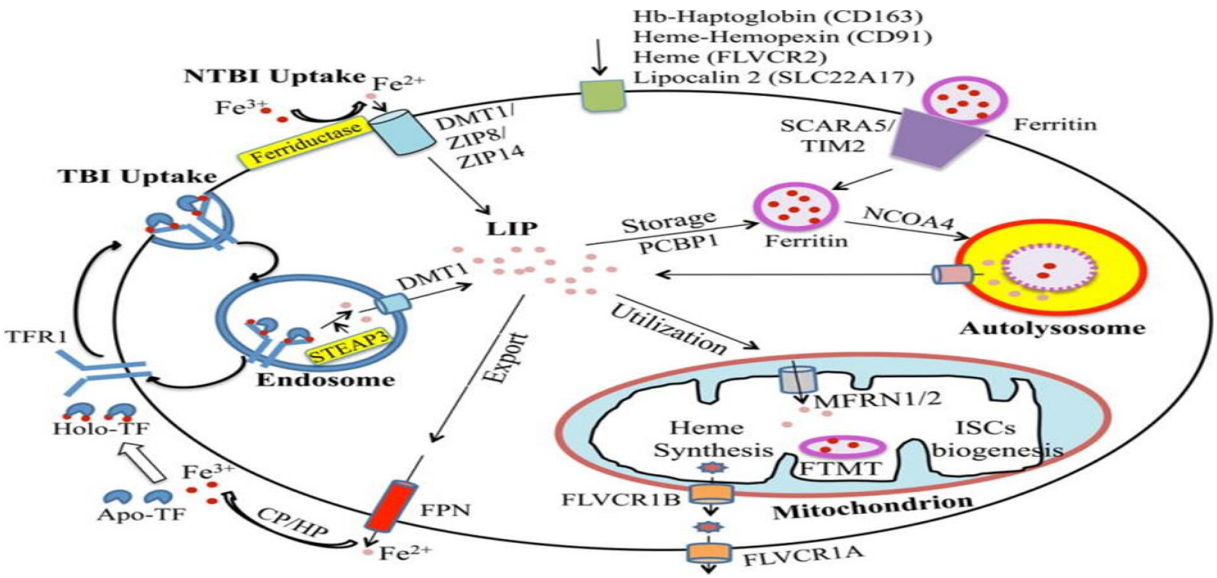

Figure 03. Cellular iron homeostasis **(Dev & Babitt, 2017).**

Depicted cell is an amalgam of many cell types; not all proteins/pathways are present in all cells. Iron enters into cells primarily by transferrin receptor 1 (TFR1)-mediated endocytosis. In endosomes, iron is freed from TF and reduced by a ferriductase (STEAP3) before exiting into the cytosol via divalent metal transporter (DMT1). TF and TFR1 are recycled back to the cell membrane for further cycles. DMT1 and other transporters (ZIP8, ZIP14) function in non-TF bound iron (NTBI) uptake pathways in some cell types. Other iron acquisition pathways in some cell types include uptake of hemoglobin(Hb)-haptoglobin, heme-hemopexin, heme, lipocalin 2, and ferritin via CD163, CD91, FLVCR2, SLC22A17, SCARA5, and TIM2 receptors respectively. In the cytosol, iron enters the labile iron pool (LIP), and is then utilized, stored, or exported out of the cell. Cytoplasmic iron transport is assisted in some cases by the chaperone poly (rC) binding protein 1 (PCBP1). Iron is mainly utilized by mitochondria for heme synthesis and iron-sulfur clusters (ISCs) biogenesis, with mitoferrins (MFRN1/2) playing a role in mitochondrial iron import and FLVCR1B playing a role in mitochondrial heme export. Excess iron in the cytosol is stored safely in ferritin. A mitochondrial form of ferritin (MTFT) is also expressed in some cell types. When the demand arises, ferritin can be targeted for autophagic turnover by nuclear receptor coactivator 4 (NCOA4) to release iron into the cytosolic LIP. Iron is exported out of the cell by ferroportin (FPN), assisted by ferroxidases ceruloplasmin (CP)/hephaestin (HP), followed by iron loading onto TF. FLVCR1A may play a role in heme export in some cell types.

1.7. Different categories most targeted by anemia

Iron deficiency anemia is a common type of anemia that occurs when the body does not have enough iron to produce sufficient hemoglobin (World Health Organization, 2019). It is a major public health issue that affects a variety of populations and can have serious health consequences, such as decreased physical and cognitive functioning and increased risk of infection (Wormser, 2019).

Here are some of the populations that are most commonly affected by iron deficiency anemia, with references:

1.Women of childbearing age:

Women who are pregnant, menstruating, or breastfeeding are at increased risk of iron deficiency anemia due to the additional iron demands of the developing fetus or infant (American College of Obstetricians and Gynecologists, 2018). Iron deficiency anemia during pregnancy can also lead to poor birth outcomes, such as low birth weight and preterm birth **(Hench, 2020).**

2 .Infants and children:

Growing children have increased iron needs and may develop iron deficiency anemia if they do not receive enough iron from their diet (World Health Organization, 2019). Iron deficiency anemia in childhood can lead to decreased physical and cognitive development and may have long-term consequences on health and wellbeing **(Wormser, 2019).**

3 .Vegetarians and vegans:

People who follow a vegetarian or vegan diet may be at higher risk of iron deficiency anemia due to the lower iron content of plant-based foods and the reduced bioavailability of iron from these foods (**Hench, 2020).**

4 .Elderly individuals:

Older adults may be at increased risk of iron deficiency anemia due to decreased ability to absorb iron from food and decreased iron stores in the body (**World Health Organization, 2019).**

5 .Individuals with chronic diseases:

People with certain medical conditions, such as inflammatory bowel disease or chronic kidney disease, may be at increased risk of iron deficiency anemia due to blood loss or decreased ability to absorb iron (Wormser, 2019).

It is important to diagnose and treat iron deficiency anemia promptly, as untreated anemia can lead to decreased physical and cognitive functioning and increased risk of infection and other health problems (American College of Obstetricians and Gynecologists, 2018).

Chapter 02

Treatment of Anemia

Evaluation of anemia has traditionally been performed by primary care physicians, internists, and hematological specialists.

this chapter is focused on treatment of Iron Deficiency and Vitamin Deficiency Anemia.

1.Iron Deficiency Anemia

Iron deficiency anemia (IDA) affects approximately 30% of the world's population. Although more prevalent in children and neonates, IDA remains extremely common in the adult population. **(Gasche, 2004).**

Treatment of iron deficiency should begin with dietary replacement (i.e., fortified cereals and breads, red meat, beans, green leafy vegetables), but when diet alone is inad equate to restore iron stores and Hgb to normal levels, or when anemia is severe, treatment with exogenous iron supplements should be implemented. Treatment is dependent on the urgency of the situation and the patient's presenting symptoms. If serum hemoglobin is $\leq$ 8 g/dl and the patient is symptomatic with shortness of breath, extreme fatigue, or signs of myocardial ischemia, then an immediate blood transfusion is warranted. When the patient is asymptomatic and the hemoglobin level is within an acceptable range, treatment should begin with oral iron. **(Zhu, 2010).**

1.1. Oral Iron

As the first-line treatment for IDA, oral iron is safe, cost effective, and convenient. Ferrous sulfate and ferrous glu conate are the two preferred oral preparations of iron, given the low cost and good bioavailability of elemental iron. To optimize iron absorption, ferrous salts should be taken with orange juice, since iron is better absorbed in an acidic environment. Furthermore, ascorbic acid reduces the oxidation of ferrous to ferric iron. Foods that reduce iron absorption include tea, coffee, phosphate-containing car bonated beverages, and medications that block gastric acid secretion (i.e., antacids, H2 blockers, proton pump inhibitors). Ferrous sulfate is typically taken in 300-mg tablets (60 mg elemental iron); ferrous gluconate is taken in 320- mg tablets (36 mg elemental iron) three to four times daily. Common adverse effects of oral iron supplements include nausea, epigastric discomfort, and constipation, all of which are dose-related. Adverse effects can occur in up to 20% of patients, impairing compliance. **(Zhu, 2010).**

Since the duodenum can maximally absorb 10–20 mg of iron daily, > 90% of ingested iron is not absorbed, where it can produce erosions and enteric siderosis (Haig, 2006). Successful iron repletion is possible with lower doses such as 15 mg elemental iron/day. Enteric-coated iron tablets are better tolerated but are less effective because the iron may not be released in the duodenum, where it is primarily absorbed. The therapeutic goal of oral iron therapy is to induce reticulocytosis within days and raise serum hemoglobin by 1–2 g/dl every 2 weeks, ultimately restor ing iron stores in approximately 3–4 months. In light of the foregoing considerations, decreasing the dose of oral iron preparations if adverse effects develop should be tried; if reticulocytes or RDW increase within 4 weeks, the dose is probably adequate. **(Zhu, 2010).**

Figure 4. Exemple of Oral Iron

Table 01 Common Oral Iron Preparations

Preparation	Dose (mg)	Elemental Iron Content (mg)	5000-mg Dose Cycle (Tablets)
Ferrous sulphate	324	65	75
Ferrous gluconate	300	36	140
Ferrous fumarate	100	33	150

The choice of delivery formulation is another source of confusion. Oral iron may be given as tablets or elixirs. Among the tablet preparations, there are nonenteric-coated pills and enteric-coated and prolonged-release formulations. Nonenteric-coated iron tablets are most commonly used as initial treatment because of their lower cost. Delayed release and enteric-coated iron

preparations have been advocated because they are better tolerated than the nonenteric-coated tablets. However, they are less effective because they may contain less iron and their

iron may not be released in the duodenum, where iron is absorbed. In fact, patients who have been treated unsuccessfully with enteric-coated and prolonged-release iron preparations may respond well to the administration of nonenteric-coated ferrous salts **(Alleyne, 2008).**

1.2. Intravenous Iron

Indications

When the patient fails oral iron therapy, parenteral iron therapy is indicated **(Maslovsky, 2005).** Indications for parenteral iron therapy in GI disease include: (1) high iron requirements due to chronic uncorrectable bleeding or chronic hemodi alysis; (2) iron malabsorption secondary to a GI condition (i.e., celiac disease, atrophic gastritis, gastric bypass); (3) IBD with ineffective erythropoiesis, poor absorption, and intolerance (also see below); (4) severe anemia with unwillingness to receive transfusions; (5) intolerance of or noncompliance with oral therapy; (6) need for rapid resti tution of iron stores (e.g., pre-operative), although some suggest that in the case of celiac disease, institution of a gluten-free diet is curative over 6–12 months, and (7) possibly in restless legs and related syndromes . **(Zhu, 2010).** Note that parenteral iron sucrose therapy is currently restricted by the US FDA to renal failure patients either undergoing dialysis or pre-dialysis who are receiving concurrent epoeitin therapy.

Preparations

Intravenous iron preparations are available as ferric gluconate, iron sucrose, iron dextran, and ferric carboxymaltose. Ferric gluconate (Ferrlecit) is effective in treating IDA patients on hemodialysis and IDA patients without renal disease (**Clark, 2008)**. For those who develop hypersensitivity reactions to ferric gluconate, iron sucrose (Venofer) may be given **)Charytan, 2004.(** Doses of iron sucrose for patients on hemodialysis are adjusted lower Also, iron sucrose appears to be a safe and effective alternative form of treatment that is able to rapidly restore iron stores in pregnant and postpartum women with IDA **(Zhu, 2010).** Iron dextran (INFeD, DexFerrum), unlike ferric gluconate and iron sucrose, is higher in molecular weight and releases iron more slowly to be bound by transferrin and to supply the bone marrow. Because of these properties, it has his torically had the advantage of being able to be administered in large doses (200–500 mg), satisfying the patient's total iron requirement with just one administration (total dose infusion), thereby saving cost and improving patient compliance.

Nevertheless, a smaller test dose is currently recommended due to reports of severe anaphylactic reactions in addition to adverse effects such as hypotension, myalgia, arthralgia,

nausea, vomiting, and fever. Therefore, iron dextran is rarely used as it is contraindicated in the pediatric population and discouraged in adults (Akarsu, 2006). A newly suggested alternative to total-dose iron dextran administration may be giving total-dose or high dose iron sucrose infusions that are equally effective and associated with fewer toxicities **(Wall, 2008).**

Ferric carboxymaltose (Ferinject R) is a novel intravenous iron preparation that can be administered in high single doses (of up to 1,000 mg iron per week) on a weekly basis at infusions rates much higher than for iron sucrose. To date, phase III studies support its safety and efficacy in diverse patient populations, including IBD patients with iron deficiency anemia **(Zhu, 2010).**

1.3. Recombinant Human Erythropoietin

Recombinant human erythropoietin (EPO) is most com monly used for and FDA indicated for the treatment of ACD in patients with chronic renal failure. These patients are supplemented with IV iron in order to compensate for the functional iron deficiency that is caused by increased erythropoiesis **(Macdougall, 1999).** In the setting of GI-related IDA, however, EPO may be indicated in several situations. In patients with GI cancer where IDA is common, inappropriate low levels of endogenous.

Table 02 Pharmacological properties of parenteral iron products **(Silverstein, 2004)**

	Iron dextran	Iron sucrose	Ferric gluconate
Bioavailability	+	++	++
$t_{1/2}$ (h)	6	5–6	1
Clearance (1,000-mg dose)	10–20 mg/h[a]	Unknown	Unknown
Volume of distribution (l)	Not reported	7.9	6
Dialyzed	Negligible	Negligible	Negligible
Safety profile	+	++	++
Pregnancy category (FDA)	C	B	B

2.Vitamin Deficiency Anemia

Vitamin B12 or B9 (commonly called folate) deficiency anaemia occurs when a lack of vitamin B12 or folate causes the body to produce abnormally large red blood cells that cannot function properly.

Red blood cells carry oxygen around the body using a substance called haemoglobin. Anaemia is the general term for having either fewer red blood cells than normal or having an abnormally low amount of haemoglobin in each red blood cell.

2.1. Causes

Vitamin deficiency anemia can occur if you don't eat enough foods containing vitamin B-12 and folate, or if your body has trouble absorbing or processing these vitamins.

Low levels of vitamin B-12 can be caused by:

Diet. Vitamin B-12 is mainly found in meat, eggs and milk, so people who don't eat these types of foods may need to take B-12 supplements. Some foods have been fortified with B-12, including some breakfast cereals and some nutritional yeast products.

•**Pernicious anemia**. This condition occurs when the body's immune system attacks cells in the stomach that produce a substance called intrinsic factor. Without this substance, B-12 can't be absorbed in the intestines.

•**Gastric surgeries**. If portions of your stomach or intestines have been surgically removed, that can reduce the amount of intrinsic factor produced and the amount of space available for vitamin B-12 to be absorbed.

•**Intestinal problems**. Crohn's disease and celiac disease can interfere with absorption of vitamin B-12, as can tapeworms that may be ingested from eating contaminated fish**. (mayoclinic.org, 2023).**

Folate deficiencies Also known as vitamin B-9, folate is a nutrient found mainly in dark green leafy vegetables and liver. A folate deficiency can occur when people don't eat foods containing folate or their bodies are unable to absorb folate from food.

Absorption problems may be caused by:

- Intestinal diseases such as celiac disease
- Surgical removal or bypass of a large part of the intestines
- Excessive alcohol consumption
- Prescription drugs, such as some anti-seizure medications

Pregnant women and women who are breastfeeding have an increased demand for folate, as do people undergoing dialysis for kidney disease.

A lack of folate can cause birth defects during pregnancy. However, folate deficiency is less common now in countries that routinely add folate to food products such as breads, cereals and pasta. **(mayoclinic.org, 2023).**

2.2. Treatment

Some vitamins are used to treat anemia vitamin B12 and folic acid can be given orally or parenterally. If there is no evidence of malabsorption, the generally preferred route for supplementation is oral. It is important to remember that oral supplementation takes time and should not be used in cases where urgent supplementation is required. In asymptomatic cases oral supplementation is sufficient. In patients with neurologic symptoms or those with increased demand such as pregnancy and in infancy, vitamin B12 and folic acid supplementation should be initiated parenterally. Patients with symptomatic anemia may require a blood transfusion to relieve symptoms, as vitamin B12 and folic acid supplementation do not correct anemia rapidly. Vitamin B12 is also available in a sublingual formulation, which may be appropriate for patients with intestinal malabsorption syndromes. **(Devalia, 2014).**

Figure 5. Vitamin B12 and folic orally Treatment

The recommended dose for vitamin B12 supplementation in children is 50 to 100 mcg parenterally once a week until the deficiency is corrected. They may require supplemental doses

every month or every other month thereafter, depending on the formulation used (cyanocobalamin versus hydroxocobalamin). In adults, the recommended dose is 1000 mcg parenterally once a week until the deficiency is corrected, followed by supplemental doses every month or every other month. An oral vitamin B12 dose of 1000 mcg daily is equally effective as the above parenteral regimen, provided that there is no intestinal malabsorption issue. **(Green, 2017).** A 2018 Cochrane review reported oral supplementation was equally effective in raising serum B12 levels as compared to intramuscular formulations, with the added benefit of it being a low-cost treatment. **(Wang, 2018).** The duration of treatment is dependent on the cause of the deficiency. If the root cause is correctable, supplementation can be stopped after serum B12 levels normalize. However, in cases with expected life-long deficiency (gastric bypass surgery patients, pernicious anemia, etc.) indefinite supplementation is warranted.

The recommended dose for folic acid supplementation is 1 mg orally once a day until the deficiency is corrected. If the cause of this deficiency is correctable, supplementation can be stopped after repletion. However, in cases with nonreversible causes, indefinite supplementation is recommended **(Devalia, 2014).**

With adequate supplementation and bone marrow response, hemolytic markers (if intramedullary hemolysis is present) will improve within 1 week and serum hemoglobin/hematocrit levels will completely normalize within 1 to 2 months. **(Stabler, 2013).** However, the neuropsychiatric symptoms take a longer period of time to recover (from 3 to 12 months) and according to some reports, there is transient clinical worsening of the neurological symptoms **(Stabler, 2013).** In some cases, the neurological symptoms may be irreversible. A 2006 observational study evaluating 57 patients with subacute combined degeneration reported only 14% clinical resolution after B12 treatment**. (Vasconcelos, 2006).** They did note that 86% of the patients had some clinical improvement. Subgroup analysis in the study revealed that absence of sensory dermatomal deficit, Romberg, and Babinski signs, age less than 50 years, and less than or equal to 7 segment involvements on magnetic resonance imaging, correlated with resolution of neurologic symptoms **(Vasconcelos, 2006).** This highlights the importance of early diagnosis and treatment as patients with severe/prolonged neurological symptoms tend to have persistence of symptoms despite treatment.

All patients with folate deficiency should be offered supplemental folic acid for the correction of the deficiency. Typically, oral folic acid (1 to 5 mg daily) suffices to treat folate

deficiency **(Green, 2017)**. Intravenous, subcutaneous, or intramuscular formulations of folic acid can be used for patients unable to tolerate oral medications. Folinic acid (also called leucovorin), a reduced form of folate, is primarily used to prevent the toxicities of methotrexate. The duration of therapy depends on whether the cause of the initial deficiency persists. Patients with malabsorption or short gut syndromes may typically require long-term treatment.

In patients who have a concomitant vitamin B12 deficiency, it is imperative to replete vitamin B12 as well. Folate treatment alone does not improve neurological symptoms and signs due to B12 deficiency, which, if untreated, may likely progress and cause permanent neurological damage (Okada, 2014). All patients should be encouraged to a diet rich in fruits and vegetables. (Khan, 2018).

3.Plants used in traditional treatment against anemia

Although the old research on anemia dealt with many treatments, if the research continued, they would find other ways to treat this disease. Modern methods of treating anemia such as Medicinal plant.

Anemia is a blood disease which is considered as the reduction of the total number of red blood cells in blood or decrease of their number according to blood volume (hemotocrit) or decrease of their total hemoglobin content (the hemoglobin concentration in the blood) and can be fairly seen in all countries. It may occur itself or can be the indicative or a symptom of an other underlying disease (1). Anemia may occur because of, chronic blood loss, bone marrow disorders, increased hemolysis, infection, malignancy, endocrine disorders and some other diseases. Many drugs can lead to anemia by causing toxic effect on blood cells, hemoglobin production or erythropoietic organs. Anemia may also occur by the inadequate intake of substances which are necessary for erythropoiesis such as iron, folic acid and vitamin B12 with diet.

in Erbay, 2016 there are 77 plants used by public for the treatment of anemia in turkey also Peter, 2014 make study about Ethno-medicinal knowledge and plants traditionally used to treat anemia in Tanzania and the largest effect is Lawsonia inermis, Aloe sp, Uvaria acuminata, Parinari curatellifolia, Ozoroa reticulata, Manihot esculenta, Canthium sp and Afzelia quanzensis were the plant species in which their claimed use for anemia.

In Arora, S., & Arora, S. **(2021)** they study about potential of Moringa oleifera in cas of iron deficiency anemia (IDA)

Table 03 : plants used traditionally to treat anemia

S/N	Botanical name	Family	Voucher specimen	Vernacular name	Part used	Frequency of use
1	*Amaranthus hybridus* L.	Amaranthaceae	5029	Mchicha	Leaves	2
2	*Ozoroa reticulate* (Baker f.) R and A. Fern	Anacardiaceae	5048	Mkutano	Root	1
3	*Uvaria acuminate* Oliv.	Annonaceae	5017	Msharifu	Roots	1
4	*Cocos nucifera* L.	Arecaceae	5027	Mnazi	Roots, leaves	5
5	*Bidens pilosa* L.	Asteraceae	5018	Myegelele	Leaves	1
6	*Kigelia Africana* (Lam.) Benth	Bignoniaceae	5024	Mlegeya	Stem barks	2
7	*Adansomia digitata* L.	Bombacaceae	5033	Mbuyu	Stem bark	1
8	*Afzelia quanzensis* Welw.	Caesalpiniaceae	5023	Mkongo	Roots	1
9	*Parinari curatellifolia* Benth.	Chrysobalanaceae	5054	Mbula	Leaves	1
10	*Ipomoea batatas* (L.) Lam.	Convolvulaceae	5035	Matembele	Leaves	2
11	*Cucurbita maxima* Duchesne.	Cucurbitaceae	5038	Maboga	Leaves	4
12	*Phyllanthus reticulatus* Poir.	Euphorbiaceae	5047	Madini	Leaves, root barks	1
13	*Manihot esculenta* Crantz.	Euphorbiaceae	5030	Kisamvu	Leaves	1
14	*Carica papaya* L.	Euphorbiaceae	5025	Papai dume	Roots	1
15	*Bridelia Micrantha* (Hochst.) Baill	Euphorbiaceae	5039	Mkalati	Stem bark	1
16	*Piliostigma thonningii* Schum.	Fabaceae	5026	Msekela	Stem bark	1
17	*Vigna unguiculata* (L.) Walp	Fabaceae	5037	Mbaazi	Leaves, seeds	6
18	*Cassytha filiformis* L.	Lauraceae	5014	Mlangamia	Stem	1
19	*Aloe sp*	Liliaceae	5049	Mwalovela	Leaves	1
20	*Lawsonia inermis* L.	Lythraceae	5052	Hina	Leaves	2
21	*Hibiscus sabdariffa* Linn.	Malvaceae	5036	Mdamu damu	Leaves, calyces	23
22	*Milicia excelsa* Welw C.C. Berg	Moraceae	5022	Mvule	Roots	1
23	*Syzygium cumini* (L.) Skeels	Myrtaceae	5041	Mkeche	Roots, stem bark	1
24	*Ximenia caffra* Sond.	Olacaceae	5040	Mpingi	Roots	1
25	*Passiflora edulis* Sims	Passifloraceae	5044	Mpesheni	Leaves	2
26	*Sorghum bicolor* (L.) Moench	Poaceae	5046	Mtama	Seeds	2
27	*Canthium sp*	Rubiaceae	5021	Bwanashokola	Roots	1
28	*Rhoicissus tridentata* Wild and Drum	Vitaceae	5020	Mkakaka	Leaves	1

Chapter03

Recent research in treatment anemia disease

I. Recent research in treatment anemia disease 2022-2023

1. Study 04 : Michel & al, 2022

- **Title:** Study of the Anti-anaemic Effects of a Dietary Supplement Based on Jatropha gossypiifolia Leaves in Wistar Rats

Details: The study evaluated the anti-anaemic properties of *Jatropha gossypiifolia* leaves (JGL) by inducing haemolytic anaemia in 4 groups of male Wistar rats and feeding them with normal diet, Ranferon®, 10% JGL, and 20% JGL. The results showed that JGL contained sterols, polyterpenes, phenolic compounds, flavonoids, quinones, catechic tannins, alkaloids, and saponosides. The aqueous leaf extract was not orally toxic, and JGL-based diets, like Ranferon®, partially or totally restored the various haematological parameters measured at the end of the experiment. These findings suggest that J. gossypiifolia has the potential to be used as an anti-anaemic agent.

Table 04. Composition chimique de *J. gossypiifolia*

Composés recherchés		**Réactifs/Test**	**Résultats**
Stérols et polyterpènes		Réaction de Liebermann	+
Composés phénoliques		Réaction au Chlorure ferrique	++
Flavonoïdes		Réaction à la Cyanidine	-
Quinones		Réactif de Bornstraeger	+
Tanins	Catéchiques	Réactif de Stiasny	++
	Galliques	Réactif de Stiasny + $FeCl_3$	-
Alcaloïdes		Réactif de Dragendorff / Réactif de Bouchardat	+
Saponosides		Mousse persistante	+

(+) : Faible présence ; (++) : Forte présence ; (-) :Absence

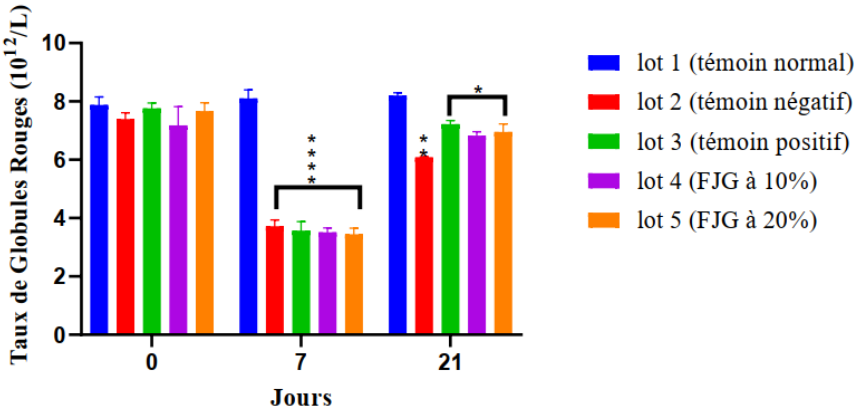

Figure 6. Effect of 2,4-DNPH and J. gossypiifolia leaves on red blood cell levels

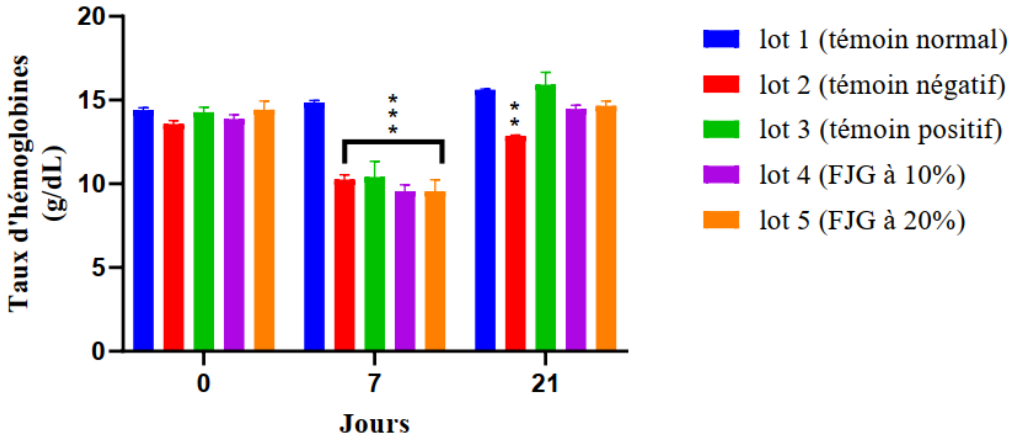

Figure 7. Effect of 2,4-DNPH and J. gossypiifolia leaves on hemoglobin levels

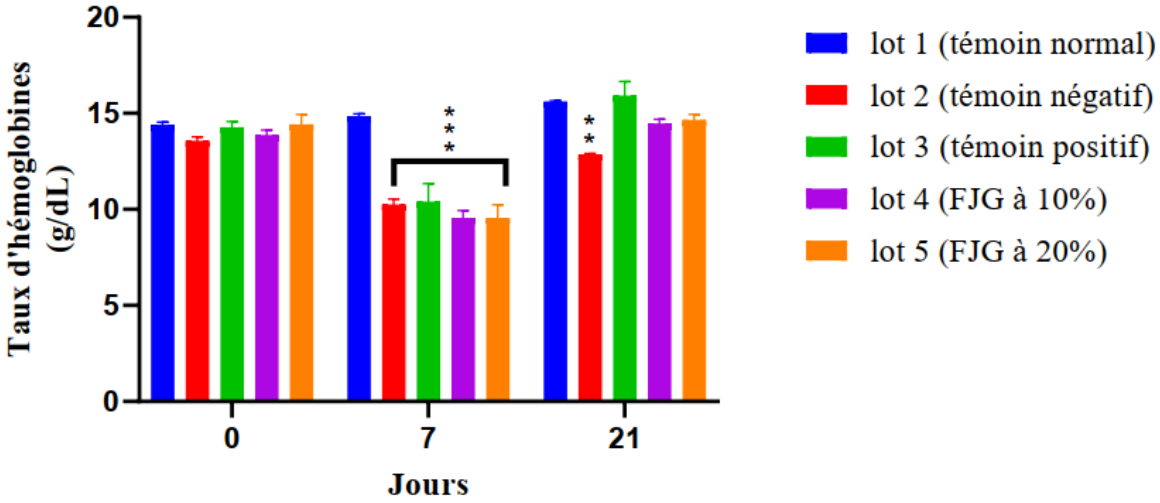

Figure 8. effect of 2,4-DNPH and J. gossypiifolia leaves on hematocrit

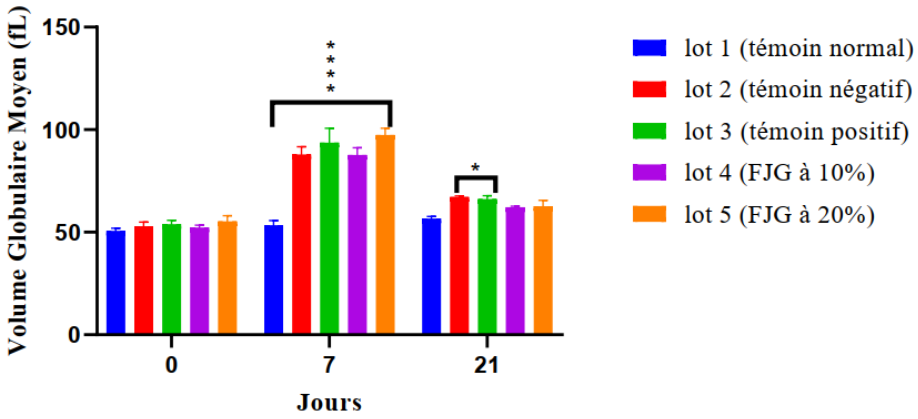

Figure 9. Effect of 2,4-DNPH and J. gossypiifolia leaves on mean globular volume

2. Study 02 : Ousaaid & al, 2022

- **Title:** Anti-anemic effect of antioxidant-rich apple vinegar against phenylhydrazine-induced hemolytic anemia in rats.

Details: The study found that apple vinegar contained high levels of polyphenols and flavonoids, which have antioxidant properties. These compounds are known to scavenge free radicals and reduce oxidative stress. The phytochemical analysis of apple vinegar revealed the presence of bioactive compounds, including arbutin, apigenin, sinapic, ferulic, and trans-ferulic acids. Ferulic and trans-ferulic acids were found to be the major antioxidant components in apple vinegar. In vivo, phenylhydrazine treatment induced changes in platelets, blood cell count, mean corpuscular volume, hemoglobin concentration, and mean capsulated hemoglobin. However, the co-administration of apple vinegar showed its capacity to ameliorate the changes induced by phenylhydrazine. Overall, the study suggests that apple vinegar use could have a positive impact on the prevention of hemolytic anemia induced by phenylhydrazine due to the antioxidant properties of its major components.

Table 05. Phenolic compounds and quantification of apple vinegar.

Phenolic Compounds in Apple Vinegar (%)					
Syringic acid	Gallic acid	Kaempferol	Rutin	Oleochantal	Hydroxytyrosol
ND	ND	0.192	0.125	0.132	0.019
Transferulic acid	Oleuropein	Hesperetin	Trimethoxyflavone	Arbutin	Rosmarinic acid
43.921	0.004	0.015	0.102	3.736	ND
Ursolic acid	Apigenin	Amentoflavone	Luteolin	Quercetin-3-*O*-glucoside	Quercetin-3-*O*-glucuronic acid
ND	2.539	0.047	ND	0.021	0.044
Kaempferol-3-*O*-glucose	Quercetin-3-*O*-hexose deoxyhexose	Isorhamnetin- 3-*O* Rutinoside	Isorhamnetin-7-*O*-Pentose / luteoilin 7-*O*-glucoside	Kaempferol-3-*O*-glucuronic acid	Narigin
ND	0.031	0.016	0.171	0.102	0.104
Kaempferol-3-*O*-hexose deohyhexose	Tyrosol	Protocathecoic acid	Vanillic acid	Syringic acid	*p*-hydroxybenzoic\ salicilic acid
0.054	ND	0.238	0.193 ± 0.002	0.953 ± 0.013	ND
Gentisic acid	Caffeic acid	Ferulic acid	Sinapic acid	Trans-cinnamic acid	Chlorogenic acid
0.153	ND	40.155	3.887	1.835	0.372
Cathechin\ epicathechin	Gallocathechin\ epigallocathechin gallate	Gallocathechin\ epigallocathechin	Cathechin gallate	Procianidin	Myricetin
0.213	0.255	0.128	ND	0.093	0.146

ND: Not determined.

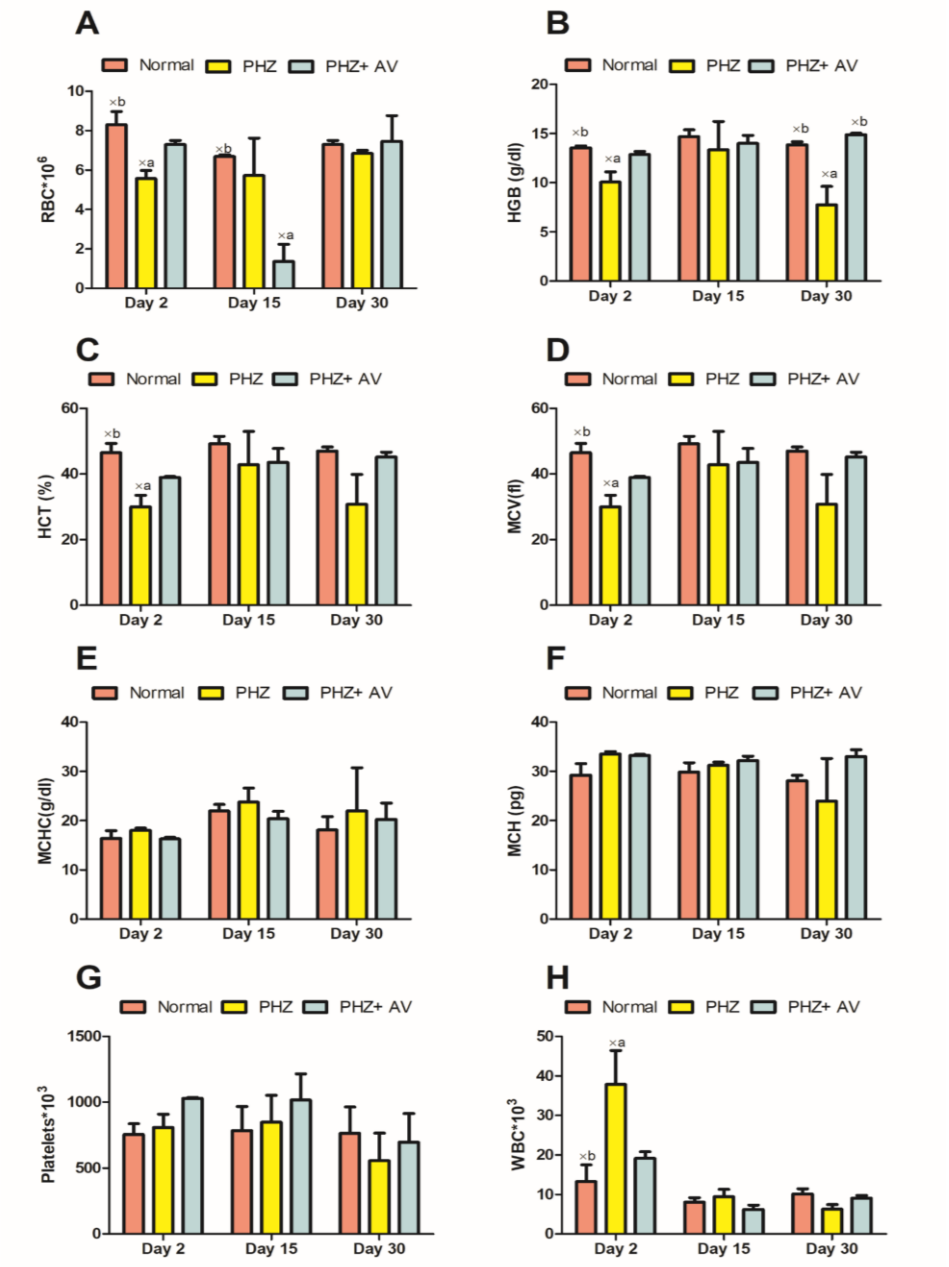

Figure 10. Effect of apple vinegar on hematological indices: A: effect of the interventions on red blood cells (RBC); B: effect of the interventions on hemoglobin (HGB); C: effect of the interventions on hematocrit (HCT); D: effect of the interventions on mean corpuscular volume (MCV); E: effect of the interventions on mean corpuscular hemoglobin concentration (MCHC); F: effect of the interventions on mean capsulated hemoglobin (MCH); G: effect of the interventions on platelets; H: effect of the interventions on white blood cells (WBC); ×a: comparison between normal and the two other groups; ×b: comparison between PHZ group and the two other groups (significance $p < 0.05$).

3. Study 03 : Kumar & al, 2022

- **Title:** Iron Deficiency Anemia: Efficacy and Limitations of Nutritional and Comprehensive Mitigation Strategies

Details: Iron deficiency anemia (IDA) is a major global public health problem that affects mainly young children and women of childbearing age, especially during pregnancy. IDA can lead to life-threatening loss of red blood cells, muscle function, and energy production, which causes weakness and impaired growth, motor, and cognitive performance, affecting the well-being of the young generation and the economic advancement of developing countries. Despite numerous strategic programs aimed at increasing iron intake, improvement of iron intake alone has not been sufficient to mitigate IDA. Emerging critical risk factors for IDA include cultural diets, infections, genetics, inflammatory conditions, metabolic diseases, dysbiosis, and socioeconomic parameters. The new multifactorial mechanism of IDA pathogenesis opens perspectives for the improvement of mitigation programs and relief of IDA in India and worldwide. In India, several IDA mitigation programs have been implemented, such as iron supplementation, food fortification, dietary diversification, and deworming. However, these programs have limitations, and the effectiveness of these programs is not significant. The new multifactorial mechanism of IDA pathogenesis opens perspectives for the improvement of mitigation programs and relief of IDA in India and worldwide.

Many government programs focused primarily on nutritional and population risks were developed and implemented to address Iron Deficiency Anemia from 1963 to 2021.

Table 06: National Iron Plus Initiative intervention and regime. IFA-syrup supplement of iron and folic acid (1 mL containing 20 mg iron/100 mg folic acid).

Age Group	Intervention/Dose	Regime	Service Delivery
6–60 m old	IFA syrup	IFA biweekly from 6 to 60 m old Deworming, children >12 m old	ASHA/ANM: inclusion in MCP card
5–10 y old	Tablet (45 mg iron/400 mg folic acid)	Weekly from 5 to 10 y old Deworming, biannually	Teacher for aged-school children AWC: children out of the school
10–19 y old	Tablet (100 mg iron/500 µg folic acid	Weekly from 10 to 19 y old Deworming, biannually	Teacher: school children AWC: children out of the school
Pregnant/lactating women	Tablet (100 mg iron/ 500 mg of folic acid)	Daily from 14 to 16 weeks of gestation. Repeated for 100 days during post-partum	ANC/ANM/ASHA: inclusion in MCP card
Women in reproductive age (WRA)	Tablet (100 mg iron/500 mg of folic acid)	Weekly throughout the reproductive period	FHW during a home visit for contraceptive distribution

4. Study 04 : Benkhnigue, & al, 2023

- **Title :** Ethnobotanical and ethnopharmacological study of medicinal plants used in treating some liver diseases in the Al-Haouz Rehamna region (Morocco).

Details: The study identified 48 medicinal plants used in traditional medicine against anemia disease, of which 12 were toxic. The inventoried species were distributed in 45 genera and belong to 27 botanical families, of which four predominated in the number of species: Apiaceae, Amaranthaceae, Fabaceae, and Asteraceae. The ethnobotanical indices, such as Use Value (UV), Family Use Value (FUV), and Plant Part Value (PPV), were determined. The study also found that 11 species were traditionally more used as effective plants against anemia, including *Rubia peregrina, Lens culinaris, Malva sylvestris, Beta vulgaris, Spinacia oleracea, Mercurialis annua, Hibiscus sabdariffa, Corrigiola telephiifolia, Nasturtium officinale, Cistus laurifolius, and Armeria mauritanica.*

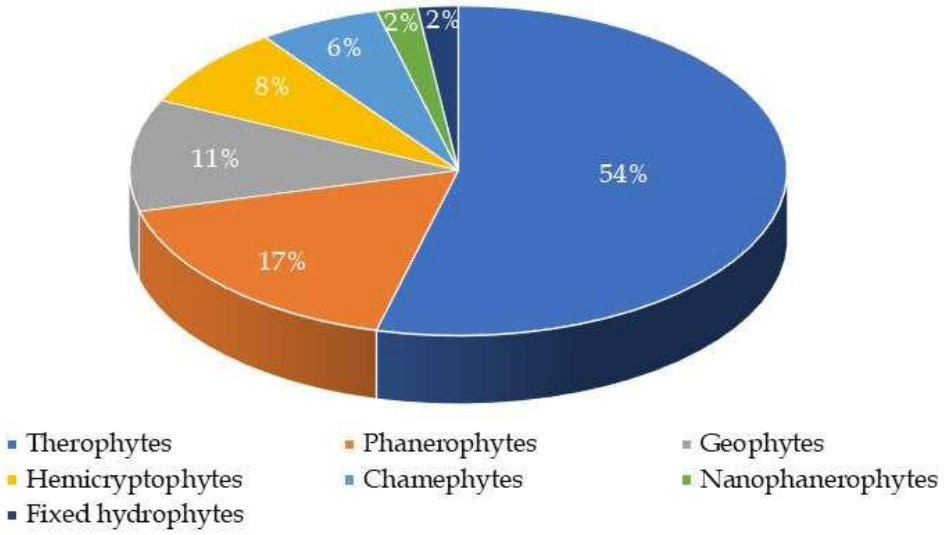

Figure 11. Distribution of the medicinal flora of the Al Haouz Rehamna region according to their biological types.

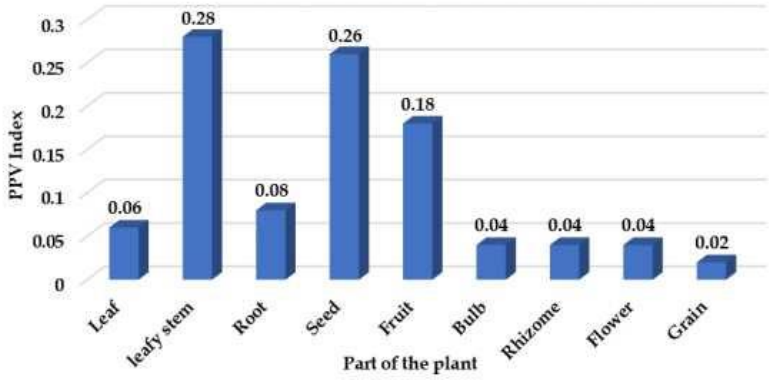

Figure 12. Plant parts used to treat anemia in study area.

5. Study 05 : Zakrzewska& al, 2023

- **Title :** Prebiotics, probiotics, and postbiotics in the prevention and treatment of anemia.

Details: Iron deficiency anemia (IDA) affects approximately 1/3 of the world's population, and research suggests that some probiotics. The review highlights that probiotics, prebiotics, and postbiotics can play a significant role in preventing and treating iron deficiency anemia. The study shows that probiotics, such as Lactobacillus acidophilus and Bifidobacterium longum, can improve iron absorption and influence the course of anemia. Prebiotics, including galactooligosaccharides (GOS) and fructooligosaccharides (FOS), can increase iron bioavailability and decrease its harmful effects on the intestinal microbiota. Additionally, postbiotics, such as vitamins, short-chain fatty acids (SCFA), and tryptophan, can regulate intestinal absorption and may impact iron status in humans. The review also discusses the latest findings on the mechanisms of action for probiotics, prebiotics, and postbiotics. Overall, the review suggests that probiotics, prebiotics, and postbiotics can be effective in preventing and treating iron deficiency anemia and that further research is needed to fully understand their mechanisms of action.

Table 07. Some of Summary of human studies on prebiotics in anemia mentioned in article

Prebiotic/ Author	Dose	Type of Administration	Subject Study Group (n)/Control Group (n)	Assessment Method	Main Result
FOS; Lobo AR. et al., (2014) [39]	7.5% FOS for 1 or 2 weeks	yacon flour or Raftilose P95	iron deficient anemic rats supplemented with FP assigned to RAF group (n = 16) or YF (n = 16)/control group (n = 16)	HRE, hepatic Fe stores	FOS supplementation increased Fe bioavailability measured by HRE and hepatic Fe stores, which were more pronounced in the RAF group at week 1 changes in Hb level in FOS-fed rats were greater than those in the FP group (p = 0.01) and similar to those in the FS group
FOS, Ohta A. et al., (1998) [41]	75 g/kg for 6 weeks	added to diet	rats after surgically stomach removing (n = 7) or sham operated rats (n = 7) fed the FOS diet/no FOS diet (n = 7)	Ht, Hb concentration, HRE	Ht, Hb concentration, and HRE were significantly lower in gastrectomized rats fed a diet without FOS compared to the other three groups FOS prevented anemia in totally gastrectomized rats
FOS; Zhang F. et al., (2017) [40]	5% (w/v) FOS = 1–2/g per day for 28 days	dissolved in water	non anemic rats fed regular diet + FOS (n = 6)/regular no FOS diet (n = 6) anemic rats fed regular diet + FOS (n = 6)/regular no FOS diet (n = 6) anemic rats fed low iron diet + FOS (n = 6)/low-iron no FOS diet (6)	Hb concentration	anemic rats fed low-iron diet + FOS had higher Hb level ($p < 0.05$) after 21 days, compared to control group in anemic rats fed regular diet, Hb returned to normal level after 14 days and FOS supplementation showed no additional effects

Table 08. Some Studies evaluating probiotics in anemia mentioned in article.

Study	Subjects	Intervention	Number of Patients	Duration of the Study	Outcome
Korcok D.J. et al., (2018) [25]	healthy humans, women	*L. plantarum* 299v 1.1×10^9 CFU vs. placebo	20	1 week	significant increase in serum iron level in the probiotic group
Adiki S.K. et al., (2019) [59]	animal model, rats	*L. plantarum* 299v in 0.5 g dose and 1.0 g dose vs. different diet and iron supplementation	42, 7 groups per 6 rats	4 weeks	significant increase in iron absorption in lower probiotic group vs. diet groups, no differences in iron absorption between the group with higher and lower doses of probiotics
Hoppe M. et al., (2017) [60]	healthy humans, women	*L. plantarum* 299v 10×10^{10} CFU vs. placebo	14, study 1 28, study 2	4 weeks	significant increase in serum iron levels in probiotic groups compared to placebo groups in both studies

Table 09. Some Studies evaluating postbiotics in anemia mentioned in article.

Compound/Authors	Study/Control Group	Method	Effect
FA; Strozzi G.P. et al., (2008) [66]	23 healthy volunteers were randomly assigned to 1 of 3 study group	determination of the folate concentration in feces evacuated within 48 h before and after administration strains	significant increase in FA concentration in all treated groups ($p = 0.004$, $p < 0.001$, $p = 0.049$)
FA; Mohammad O. et al., (2009) [48]	12 children in the study and control group	analysis of folate plasma concentration after 42 days *Lactobacillus acidophilus* supplementations	increased folate plasma concentration ($p < 0.01$), reduction in the percentage prevalence of anaemia ($p < 0.01$)
SCFA; Soriano-Lerma A. et al., (2022) [75]	20 male Wistar rats, 11 in the control group, 9 in the anemic group	diet induction IDA for 40 days. Measured SCFA concentration in GI tract.	Significant increase in AA, PA and BA in the colon ($p < 0.05$) in rats with anemia
SCFA; Dostal A. et al., (2012) [76]	40 male Sprague-Dawley rats. Thirty-seven rats in the study group, 3 rats in the control group	3 rats on a normal diet and 37 rats on a non-iron diet for 24 d. After 37 d. cecal SCFA measurement	the cecal concentration of butyrate was 87% lower and that of propionate was 72% lower compared to the control group ($p < 0.05$).

6. Study 06 : Magtalas & al, 2023

- **Title :** Ethnomedicinal plants used for the prevention and treatment of anemia in the Philippines: a systematic review.

Details : Medicinal plants are frequently used in developing countries, including the Philippines, to treat common community diseases such as anemia, which is characterized by a lower-than-normal level of red blood cell count. This systematic review identifies the medicinal plants used for anemia treatment in the Philippines. The study followed the PRISMA flow diagram, conducting data searches on electronic databases and screening the collected studies based on inclusion and exclusion criteria. The review included 20 ethnobotanical studies on medicinal plants used for anemia treatment from different provinces within the 12 regions of the Philippines. The most common plant family is Convovulaceae, with nine records (21.95%), followed by Cucurbitaceae, with six records (14.63%), and Moringaceae, with five records (12.2%). The most common plant part used was the leaves, with fruits and leaves being the most common combination. Drinking the decoction was the most common route of administration. The review also assessed the quality of the studies using a developed quality assessment tool.

Briefly, The review found that the most common medicinal plants used for anemia treatment in the Philippines are *Ipomoea batatas* (sweet potato), *Momordica charantia* (bitter gourd), and *Moringa oleifera* (malunggay). The study also found that the most common method of preparation was decoction, which involves boiling the plant parts in water and drinking the resulting liquid. The review assessed the quality of the studies using a developed quality

assessment tool. The quality assessment tool consisted of 10 criteria, and each study was rated as low, moderate, or high quality based on the number of criteria met. The studies were found to be of moderate to high quality.

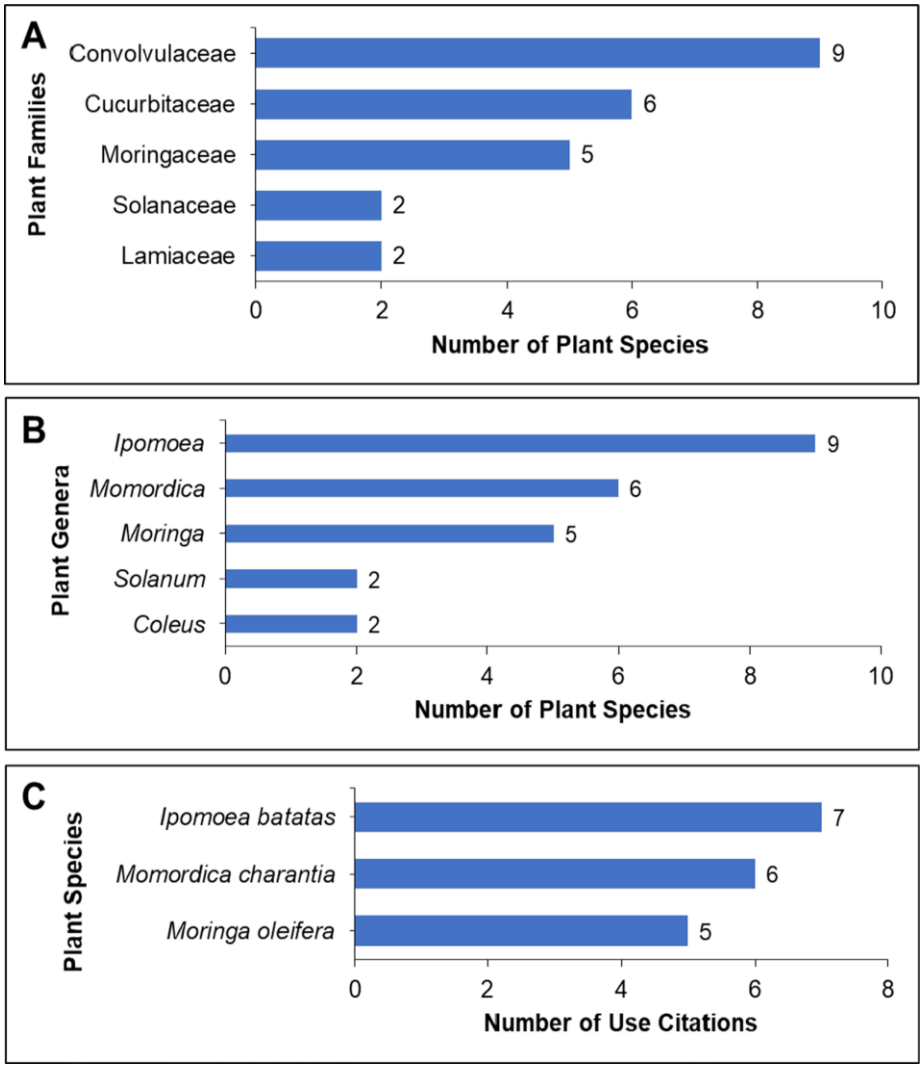

Figure 13. Most common families (A), genera (B), and species (C) of plants used for the prevention and treatment of anemia in the Philippine

7. Study 07 : Obaid & al, 2023

- **Title :** Efficacy of ferric carboxy maltose in treatment of iron deficiency/iron deficiency anaemia during pregnancy.

Details : This study evaluates the efficacy of ferric carboxy maltose (FCM) in treating iron deficiency/iron-deficiency anemia (ID/IDA) during pregnancy. Pregnant women who were ≥ 20 years old and diagnosed with ID (serum ferritin < 15 µg/l) and moderate IDA were included in the study. The participants received an FCM infusion to correct their ID/IDA. The study compared the pre-treatment ferritin, hemoglobin (Hb), and red blood cell (RBC) indices with the 6- and 12-week post-treatment values to evaluate the efficacy of FCM in treating ID/IDA during pregnancy. The study found that FCM infusion significantly increased the pre-treatment ferritin and Hb levels, as well as the pre-treatment RBCs mean corpuscular volume and RBCs mean corpuscular hemoglobin (MCH) levels.

In Summary, This study aimed to evaluate the effectiveness of ferric carboxy maltose (FCM) in treating iron deficiency and iron-deficiency anemia during pregnancy. The study included pregnant women who were at least 20 years old and had been diagnosed with ID (serum ferritin < 15 µg/l) and moderate IDA. The participants received an FCM infusion to correct their ID/IDA. The study compared the pre-treatment ferritin, hemoglobin (Hb), and red blood cell (RBC) indices with the 6- and 12-week post-treatment values to evaluate the efficacy of FCM in treating ID/IDA during pregnancy. The study found that FCM infusion significantly increased the pre-treatment ferritin and Hb levels, as well as the pre-treatment RBCs mean corpuscular volume and RBCs mean corpuscular hemoglobin (MCH) levels.

Table 10. The pre-treatment ferritin, haemoglobin, red blood cells mean corpuscular volume, and red blood cells mean corpuscular values compared to the 6-week post-treatment values

Parameters	Pre-treatment values (*N* = 110)	6-week post-treatment values (*N* = 110)	*p*-value (95% CI)
Pre-treatment ferritin [µg/l]	10.3 ±2.3	139.5 ±1.9	0.02* (–129.8, –129.2, –128.6)
Pre-treatment haemoglobin [g/dl]	7.99 ±0.6	14.04 ±0.45	0.001* (–6.2, –6.1, –5.9)
Pre-treatment RBCs-MCV [fl]	72.02 ±3.5	90.6 ±2.8	0.01* (–19.4, –18.6, –17.7)
Pre-treatment RBCs-MCH [pg]	23.9 ±1.9	29.98 ±1.5	0.007* (–6.5, –6.1, –5.6)

Table 11. The pre-treatment ferritin, haemoglobin, red blood cells mean corpuscular volume, and red blood cells mean corpuscular values compared to the 12-week post-treatment values

Parameters	Pre-treatment values (*N* = 110)	12-week post-treatment values (*N* = 110)	*p*-value (95% CI)
Pre-treatment ferritin [µg/l]	10.3 ±2.3	128.9 ±1.7	0.0008* (−119, −118.6, −118.1)
Pre-treatment haemoglobin [g/dl]	7.99 ±0.6	13.02 ±0.5	0.02* (−6.2, −6.03, −5.9)
Pre-treatment RBCs-MCV [fl]	72.02 ±3.5	89.5 ±2.9	0.02* (−18.3, −17.5, −16.6)
Pre-treatment RBCs-MCH [pg]	23.9 ±1.9	30.2 ±1.5	0.007* (−6.8, −6.3, −5.8)

8. Study 08: Lo & al, 2023

- **Title :** The role of oral iron in the treatment of adults with iron deficiency.

Details : Iron deficiency is a significant public health concern worldwide, with premenopausal women being the most commonly affected population. Oral iron supplements are the most commonly used treatment for iron deficiency. However, the optimal formulation, dosing strategy, and which patients should receive intravenous iron are still unclear. The hepcidin-ferroportin iron regulatory pathway is a complex system that regulates iron absorption and prevents iron overload. It can limit the efficacy of oral iron supplements, leading to side effects such as constipation and dyspepsia. To overcome this physiological bottleneck, low-dose and every-other-day dosing protocols have been developed, but they still result in low fractional iron absorption. This article reviews the pathophysiology of iron absorption and the current evidence for various oral iron preparations. It also highlights the need for further research to improve the management of iron deficiency.

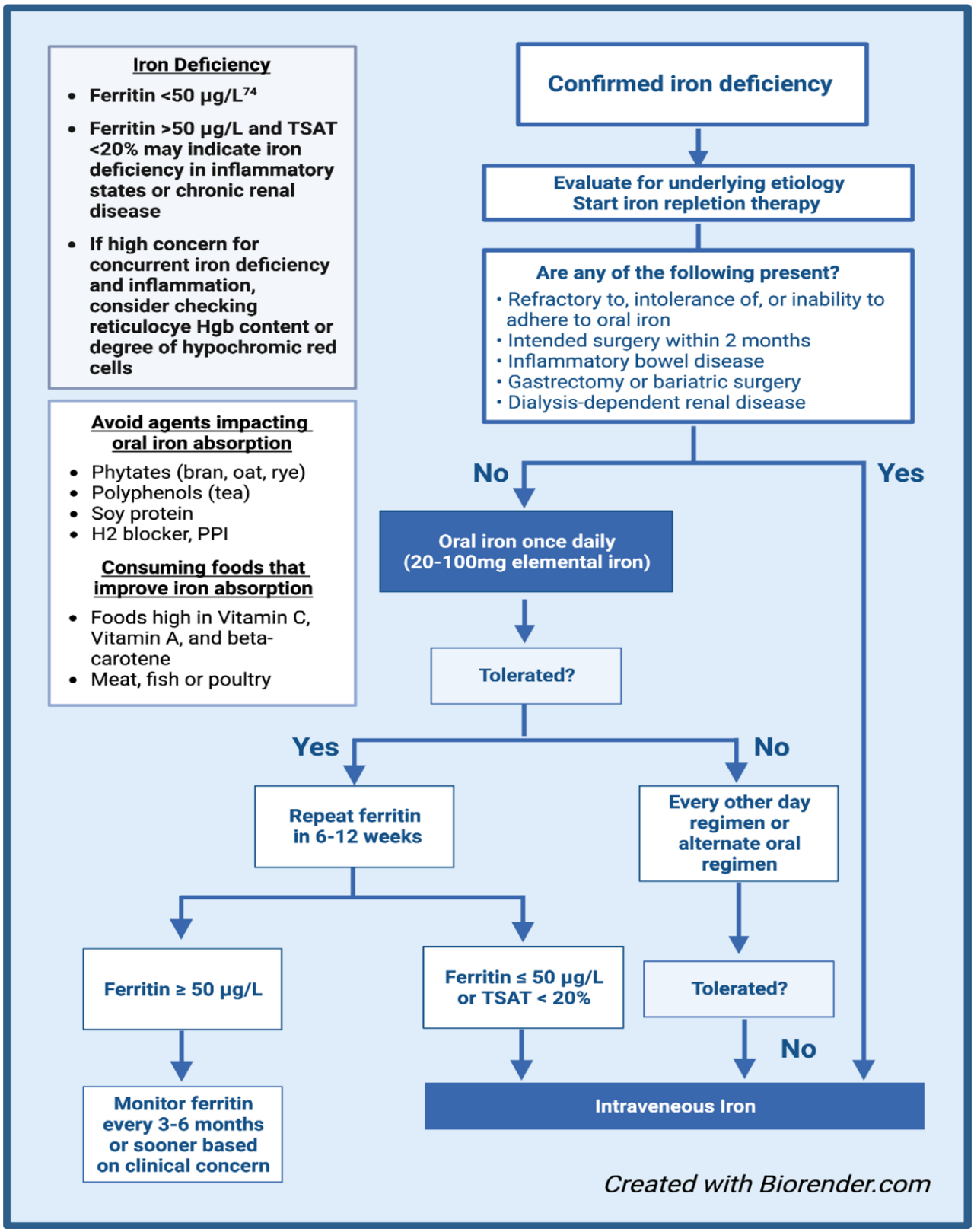

Figure 14. Proposed algorithm for treating iron deficiency

Conclusion

Conclusion

Through this work that we have done, we have come to the conclusion that anemia is a disease with a wide range that affects many of the world's population in different age groups. It has several reasons, so we shed light on the most important cause, which is iron deficiency, as we touched on knowing how to absorb, recycle and balance iron in the human body. Also, this disease has several types, and each type has symptoms that distinguish it from the rest. Anemia has many and varied treatments, which depend on the cause of its infection, between taking nutritional supplements and undergoing medical procedures, in addition to using some natural plants in treatment. However, research and studies are still in place in order to learn more about ways to prevent and treat anemia.

And as a perspective;

- Anti-anemic effects of JGL leaf extracts in El-Oued
- Role of Apple cider vinegar in combating anemia in women of childbearing age
- Statistics on medicinal plants used to combat and treat anemia in El-Oued
- Efficacy of ferric maltose in the treatment of ID/ IDA IN children and infants
- Role of intravenous iron in treating adults and improving the management of iron deficiency in the body

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ملخص

فقر الدم مشكلة صحية عامة عالمية اكتسبت الكثير من الدراسات والأبحاث في السنوات الأخيرة.

أجرينا هذه الدراسة بهدف تحديد فقر الدم وتحديد أهم المجموعات المعرضة لخطر الإصابة بهذا المرض. تهدف هذه الدراسة أيضًا إلى الجمع بين أهم وأحدث الأبحاث والدراسات حول فقر الدم، بالإضافة إلى تسليط الضوء على العلاجات المختلفة الموصى بها عالميًا.

وفقًا لما وصلنا إليه من خلال هذه الدراسة، فإن النساء من سن 15 إلى 49 عامًا والأطفال دون سن الخامسة هم الأكثر إصابة بفقر الدم. خلصنا أيضًا إلى أنه يمكن علاج هذا المرض بعدة طرق مختلفة، سواء باستخدام بعض أنواع النباتات فيما يعرف بالطب البديل، أو من خلال الأدوية الكيميائية. أخيرًا، يوصى بتطوير طرق الوقاية والتوعية لتجنب هذا المرض.

الكلمات مفتاحية: فقر الدم، الأمراض، طرق العلاج.

Résumé

L'anémie est un problème de santé publique mondial qui a fait l'objet de nombreuses études et recherches au cours des dernières années.

Nous avons mené cette étude dans le but d'identifier l'anémie et les groupes les plus importants à risque d'infection par cette maladie. Cette étude vise également à rassembler les recherches et études les plus importantes et les plus récentes sur l'anémie, en plus de mettre en évidence les différents traitements recommandés globalement.

Selon les résultats de cette étude, les femmes de 15 à 49 ans et les enfants de moins de cinq ans sont les plus touchés par l'anémie. Nous avons également conclu que cette maladie peut être traitée de différentes façons, que ce soit en utilisant certains types de plantes dans ce qu'on appelle la médecine alternative, ou par des médicaments chimiques.

Enfin, il est recommandé de développer des méthodes de prévention et de sensibilisation afin d'éviter cette maladie.

Mots clés : Anémie, maladie, méthodes de traitement**.**

Abstract

Anemia is a global public health problem that has gained a lot of studies and research in recent years.

We conducted this study with the aim of presenting the most important and latest research on anemia, as well as identifying the most important groups most vulnerable to this disease in recent times.

According to our findings, women from 15 to 49 years old and children under the age of five are the most affected groups with anemia.

Therefore, it is recommended to develop prevention and awareness methods about this disease, treatment methods, and limit its spread.

Key words: Anemia, disease, treatment methods**.**