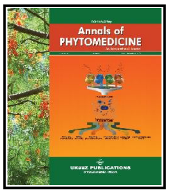
Annals of Phytomedicine 11(2): 75-81, 2022

DOI: http://dx.doi.org/10.54085/ap.2022.11.2.8

Annals of Phytomedicine: An International Journal
http://www.ukaazpublications.com/publications/index.php

Print ISSN : 2278-9839 Online ISSN : 2393-9885



Review Article : Open Access

Nutraceutical interventions for anaemia

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Article Info

Article history
Received 3 June 2022
Revised 19 July 2022
Accepted 20 July 2022
Published Online 30 December-2022

Keywords
Anaemia
Nutraceuticals
Nutrition
Superfoods
Iron

Abstract

Anaemia is a condition arising due to decreased red blood cells (RBCs) population, inadequate haemoglobin content, abnormal RBCs morphology, increased RBCs destruction, excessive blood loss, or a combination of these risk factors. As a result, there is insufficient oxygen supply in the body. The underlying factors can be nutritional deficiencies, acute/chronic disease conditions, or genetic disorders. These factors are generally used to classify anaemia under different categories. With a global increase in the disease burden, scientists and researchers are looking for better and novel therapeutic ways. Nutraceuticals are gaining considerable attention these days as they being food components, can additionally maintain health and help fight various disease conditions. Such products may range from nutrients and dietary supplements to genetically modified foods and herbal products. The current review focuses on the role of nutraceuticals in the management of anaemia.

1. Introduction

Iron is a common and essential mineral localized in the cytochrome of all cells of the body. It is involved in various cellular and metabolic processes including energy production and oxygen transport (Gupta, 2014). The total amount of iron in the human body is 2-4 g and varies with gender, body size, age and nutritional status (Clark, 2007). Different living organisms have different approaches to acquire, store and reutilize iron. In context to humans, iron from food comes in two forms: heme and non-heme. The heme-iron (derived from meat and fish) is directly absorbed in the large intestine by specific receptors whereas, the inorganic form (derived from plants, vegetables, fruits and iron-fortified foods) is first reduced in the gut and then absorbed by the divalent metal cation transporters of duodenal cells. Iron is stored in two forms: as ferritin in intestinal cells or as myoglobin in muscle cells (Anderson and Shah, 2013). Maintaining iron equilibrium is a tightly balanced process as both ends can affect human health. Both, iron overload and iron deficiency, may impair oxygen transport, induce tissue damage and disturb inflammatory responses (Verna *et al.*, 2021). The disturbing concentrations of iron can support inflammation and even hamper an effective immune response. The human body loses small quantities of iron on daily basis (by sweating or enterocyte shedding), but the loss is compensated through routine dietary intake. However, under abnormal conditions, reduced concentrations of iron and abnormalities in RBCs may lead to the development of anaemia (Ganz and Nemeth, 2006; Brune *et al.*, 1986; Longo and Camaschella, 2015). Taking into consideration the importance of iron for human health, scientists and researchers are working to find new nutritional strategies for the treatment of anaemia.

Hippocrates, the father of Western medicine, once said that "Let food be thy medicine", meaning "Let food be your medicine and medicine be your food". Our food plays an essential role in the healthy functioning of our body and helps maintain the health of an individual. Nutraceuticals are medicinal foods that can help enhance health, modulate immunity and prevent various diseases. Therefore, the concept of nutraceuticals can be envisioned for improving the health of an individual and is even scientifically supported by various research teams (Chintale Ashwini *et al.*, 2013). The current review focuses on anaemia, the concept of nutraceuticals, nutritional resources of iron and superfoods that can be used as nutritional supplements for anaemia.

2. Anaemia

A haematological abnormality characterized by decreased red blood cell (RBC) count and/or haemoglobin is termed anaemia. It is commonly found worldwide; approximately 1.6 billion people are currently affected. It can occur due to decreased RBC production, increased RBC destruction, abnormal RBC production, or excessive loss of red cells (Newhall *et al.*, 2020). Bone marrow is responsible for the production of RBCs and the process takes place in the presence of a hormone (erythropoietin) released from the kidney. Erythroid progenitor cells grow and differentiate into reticulocytes, which eventually mature into RBCs. These RBCs carry oxygen and supply it to the entire body. They circulate in the bloodstream and are destroyed by the macrophages after 120 days. Therefore, to maintain the equilibrium between loss and production of RBCs, the bone marrow produces about 50,000 reticulocytes/ml of whole blood each day. In conditions like gastrointestinal bleed, acute haemorrhage and haemolytic anaemia, the bone marrow is unable to compensate for the loss and meet the demands. The pathology of anaemia is often multifactorial and can be due to any underlying disease (Broadway-Duren and Klaassen, 2013).

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2.1 Classification of anaemia

Anaemia can be classified in numerous ways; however, a methodological approach is considered most suitable, even for clinicians. Two approaches are used for the determination of causality of anaemia: the kinetic and the morphologic approach.

2.1.1 The kinetic approach

This approach focuses on the mechanism that causes a decrease in the haemoglobin content and is divided into three heads: increased loss of RBCs, increased destruction of RBCs and decreased production of RBCs. Excessive blood loss can occur in conditions like chronic or acute haemorrhage, heavy menstruation, melenastools, traumatic injuries, hematemesis, slow-bleeding ulcers, gastrointestinal cancers, gross haematuria, *etc*. (Newhall *et al*., 2020). Increased RBC destruction can occure specially in haemolytic anaemias; they can be either acquired (autoimmune anaemia, splenomegaly, haemolytic uremic syndrome) or inherited (thalassemia, sickle cell diseases). Decreased RBC production can be a result of nutrient deficiencies (iron, vitamin B12 and folic acid), bone marrow suppression (due to chemotherapy or radiation therapy), disease within the bone marrow (aplastic anaemia, myelodysplastic syndrome), or hormonal deficiency (hypothyroidism and hypogonadism) (Broadway-Duren and Klaassen, 2013).

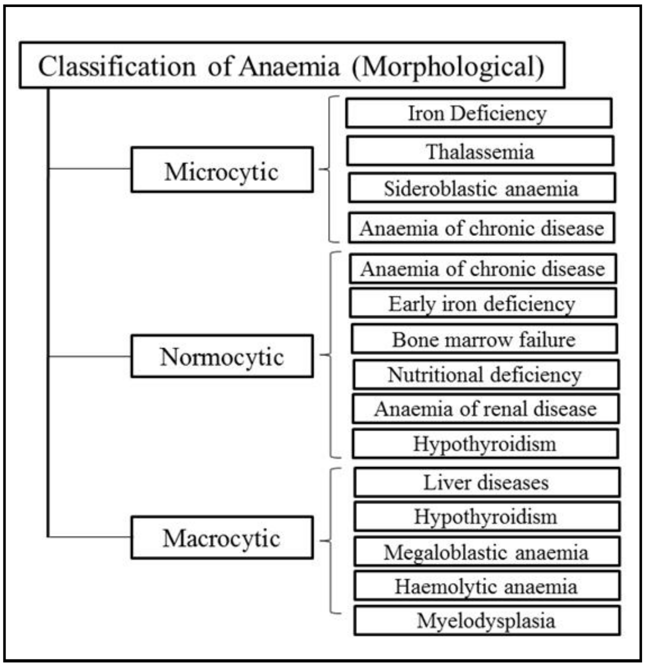

Figure 1: Classification of anaemia by morphologic approach.

2.1.2 Morphologic approach

This approach groups anaemia based on the mean corpuscular volume (MCV) of the RBCs. This approach has three categories: (i) microcytic anaemia (MCV < 80 fl); characterized by small hypochromic RBCs and decreased haemoglobin content (Newhall *et al*., 2020). Most common examples of microcytic anaemia are iron-deficient anaemia, thalassemia and chronic disease-linked anaemia, (ii) normocytic anaemia (MCV= 80 to100 fl) and (iii) macrocytic anaemia (MCV<100 fl); characterized by large RBCs, abnormal nucleic acid metabolism or RBC maturation (Figure 1).

2.2 Forms of anaemia

2.2.1 Iron deficiency anaemia

Iron deficiency anaemia (IDA) is considered a threat in many developing and low-income countries and affects 30% population of the total population. According to World Health Organization (WHO), IDA is the most prevalent nutritional deficiency and its reduction is one of the six priorities of WHO's Comprehensive Implementation Plan on Maternal, Infant, and Young Child Nutrition (Prentice *et al*., 2017; da Silva Lopes *et al*., 2021). IDA is a global health concern characterized by microcytic, hypochromic red blood cells. It affects women, children and the elderly population and is a common comorbidity with various medical conditions. The cause of IDA varies with age, gender, race and socio-economic status (Pasricha *et al*., 2013).The etiology of IDA is multifactorial; however, it may occur due to blood loss, low dietary intake, decreased iron absorption and increased systemic requirements, chronic diseases like obesity and kidney disorders, lifestyle factors, and parasitic infestation (Figure 2). A higher frequency of IDA has also been linked to *Helicobacter pylori* infection and inflammatory bowel disease. IDA slowly develops and progresses from iron deficiency and comes with decreased motor, physical and cognitive performance in patients (Yip and Ramakrishnan, 2002; Gasche *et al*., 2004; Jimenez and Gasche, 2019; Cappellini *et al*., 2020).

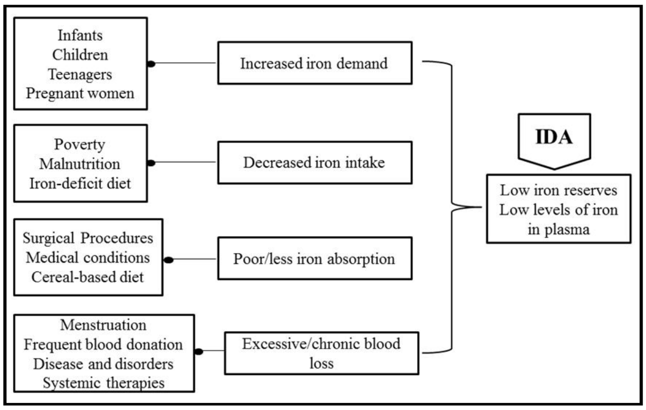

Figure 2: Aetiologies of iron deficiency anaemia (IDA).

Iron supplementation is used for iron deficiency and to improve the hemoglobin status of the population at risk. Four different oral supplementations are generally used: ferrous fumarate, ferrous gluconate, ferrous sulfate and ferric sulfate (Pena-Rosas *et al*., 2015). The recommended dose of iron supplement is 150-200 mg elemental iron/day. This dose can be achieved by the consumption of 325 mg of ferrous sulfate or gluconate thrice a day (Watson and Preedy, 2012). People at high risk of anaemia (such as pregnant women) may especially benefit from iron supplementation; however, oral supplementation has some limitations. Side effects such as epigastric pain, constipation, and nausea are commonly reported. Therefore, a lower dosage or intermittent supplementation can be preferred. Parenteral forms such as iron dextran, iron sucrose, and sodium ferric gluconate can be in cases where deficiency does not recover with oral supplementation (Watson and Preedy, 2012).

2.2.2 Haemolytic anaemia

Haemolytic anaemia covers broad categories of anaemias caused due to increased red cell turnover and their abnormal breakdown. This class includes haemolysis-associated inherited red cell disorders, microangiopathic haemolytic anaemias, transfusion-related haemolysis, autoimmune haemolytic anaemia and haemolysis as a result of infections, drugs, or burns. Other clinical markers helpful for the diagnoses of haemolysis are: increased levels of bilirubin and lactate dehydrogenase, low haptoglobins, and peripheral blood smear: bite cells, spherocytes, or schistocytes (Dhaliwal *et al*., 2004).

2.2.3 Macrocytic anaemia

The common causes of macrocytic anaemia include liver disease, B12, and folate deficiency, alcohol and antifolate drugs (methotrexate). It can be classified into megaloblastic and non-megaloblastic anaemia based upon their cause. Megaloblastic anaemia occurs due to defective DNA and RNA synthesis and is characterized by hypersegmented neutrophils and macro-ovalocytes on peripheral blood film. These abnormalities are not found in patients with non-megaloblastic anaemia. However, clinical examinations and history should be looked upon for the differential diagnosis. As an initial evaluation, serum vitamin B12 and folate, reticulocyte count and peripheral blood smear are generally recommended (Nagao and Hirokawa, 2017).

2.2.4 Normocytic anaemia

Normochromic normocytic anaemia occurs as a result of acute blood loss and is generally seen in hospitalized patients. However, chronic normocytic anaemia (termed as anaemia of chronic disease) can also occur due to any underlying systemic disorder. This is often seen secondary to any other disease like multiple myeloma, renal failure, hypothyroidism, and inflammatory and malignant diseases. The condition is often assessed by ferritin and haemoglobin levels, renal functions, thyroid function tests, immunoglobulins and protein electrophoresis in patients (Brill and Baumgardner, 2000).

2.2.5 Microcytic anaemia

One of the most common causes of microcytic anaemia worldwide is iron deficiency. Iron deficiency is a significant condition in many developing and developed countries. It prevails in men, women of all ages (post-menopausal, childbearing age, and pregnant), and the elderly population. Other causes of microcytic anaemia include haemoglobinopathies, chronic diseases and sideroblasticanaemias (DeLoughery, 2014).

2.3 Clinical presentation of anaemia

Some of the common symptoms of anaemia are fatigue, dyspnea, palpitations, weakness and hearing roaring in the ears. Other complications such as arrhythmias, angina, myocardial infarction, and congestive heart failure can be seen in serious cases. However, the severity depends on the rate of onset, oxygen demands and degree of anaemia. The clinical finding includes the investigation of skin pallor, palmar creases, nail beds and conjunctivae. Physical findings include jaundice caused by hemolyticanemia, postural hypotension secondary to intravascular volume loss and bone pain and/or organomegaly associated with infiltrative disease of the bone marrow. In pre-and post-menopausal women and male patients, abdominal pain, peptic ulcer disease and reflux disease are also reported (Newhall *et al*., 2020).

3. Concept of nutraceuticals

The term nutraceutical is a combination of two words: nutrition (a nourishing food/food component) and pharmaceutical (a medical drug). It is defined as any food or food component that has both health and medicinal benefits and therefore, can be useful for the prevention and treatment of disorders and diseases. The category includes dietary supplements, herbal products, genetically engineered "designer" foods, isolated nutrients and processed foods. Any non-toxic food supplement or extract that has scientifically-proven health benefits can be considered a nutraceutical (Pushpangadan *et al*., 2014). This concept of nutraceuticals is currently receiving enormous attention due to their presumed safety and nutritional and therapeutic benefits. Their usage eliminates or reduces the need for conventional medications and has lesser adverse effects (Chintale Ashwini *et al*., 2013).

For a drug to be introduced to the market, it has to pass pre-clinical and clinical trials. However, on the other hand, no such verification for nutrients is required. Recently, functional foods and nutraceuticals have been scientifically proven to be effective in lifestyle-related diseases as they might offer certain benefits: increase the health value of the diet, help live longer, are natural in origin, have psychological benefits, less unpleasant side effects, promote wellness, control symptoms and prevent malignant processes (Majeed, 2017).

3.1 Classification of nutraceuticals

Nutraceuticals are categorized as:

- **Nutrients:** Food components with established nutritional value. It includes minerals, vitamins, fatty acids and amino acids.
- **Herbs:** Herbal and botanical components which can be used as extracts and concentrates.
- **Dietary supplements:** Any dietary ingredient intended to add value to the food you eat. Examples include glucosamine/chondroitin for arthritis, black cohosh for menopausal symptoms, *Ginkgo biloba* for memory loss, weight-loss supplements, sports nutrients and meal replacements (Saloni *et al*., 2022; Chintale Ashwini *et al*., 2013).

3.2 Traditional and non-traditional nutraceuticals

Traditional nutraceuticals include those food components in which no changes are done. It is a natural food, other than the way the consumer uses it. Natural components of fruits, vegetables, dairy products, grains and meat have various benefits and properties beyond nutrition. Lycopene (from tomatoes), saponins (from soy), and omega-3 fatty acids (from salmon) are some examples of traditional nutraceuticals. Non-traditional nutraceuticals are modified food components; they are either artificially bred or certain nutritional content is added to them. Calcium-fortified juices and minerals/vitamins added to cereals are some of examples (Chintale Ashwini *et al*., 2013; Grabowska *et al*., 2019) (Table 1).

4. Nutraceuticals as an iron resource

To maintain iron homeostasis, ~25mg of iron is required by the human body; most of which is necessary for hematopoiesis (replenishing the blood system) (Camaschella *et al*., 2016). Dietary iron contains both heme and non-heme (inorganic) iron. Heme iron is absorbed by enterocyte carrier HCP1 (heme carrier protein 1) in the intestine. It, then, dissociates from the porphyrinic ring by the

HMOX1 (Heme oxygenase 1) protein. It is either stored as ferritin or transported to the blood *via* the FLVCR1 (Feline leukemia virus subgroup C receptor 1) transporter. It is easier to be absorbed than organic iron; however, can saturate its receptor in a dose-dependent manner. Even under 20 mg concentration, it can saturate its receptor on the enterocytes and significantly reduce its absorption rate (Przybyszewska and Zekanowska, 2014; Gomme *et al.*, 2005; Pizarro *et al.*, 2003). Heme iron is most commonly obtained from red meat, game meat, shellfish, liver and spleen and is considered the best source of daily iron (Valenzuela *et al.*, 2009). In the contrast, non-heme iron can be obtained from plant-based foods and has a very less absorption rate. This vegetarian dietary iron is commonly present in ferric (Fe^{3+}) form and is reduced to ferrous (Fe^{2+}) ions to be transported *via* DMT1 (divalent metal transporter 1) to the duodenal enterocytes. This reduction step occurs in the presence of vitamin C; as it gives an electron to luminal Fe^{3+} through cytochrome b (Dcytb) and converts it to Fe^{2+} ions (Dainty *et al.*, 2014; Przybyszewska and Zekanowska, 2014).

Table 1: Nutraceuticals and their importance

S. No.	Nutraceutical	Therapeutic benefits
1.	**Nutrients**	
	Vitamin A	Antioxidant, Vision, Cell growth and development, Immune function, Reproduction, Foetal development
	Vitamin B1	Antioxidant, Immune function, Provide energy
	Vitamin B2	Metabolize fats and protein, Eye health, Nerve function
	Vitamin B3	Provide energy, Nerve function
	Vitamin B12	RBC production, Nerve tissue health, Brain function
	Vitamin C	Antioxidant, Maintain healthy skin, blood vessels, bones and cartilage
	Calcium	Bone strength, Important in nerve, muscle and glandular functions
	Vitamin E	Antioxidant, Immune health, Form blood cells, muscles, lung and nerve tissue
	Vitamin K	Blood clotting
2.	**Herbals**	
	Aloe Vera	Anti-inflammatory, Antioxidant, Emollient, Wound-healing properties
	Ginger	Carminative, Cholagogue, Antiemetic
	Turmeric	Anti-inflammatory, Antioxidant
	Saffron	Anti-inflammatory, Antioxidant, Aphrodisiac, Improve mood, Treat depressive symptoms
	Garlic	Anti-inflammatory, Antibacterial, Antifungal, Antithrombotic, Hypotensive
	Ephedra	Bronchodilator, Vasoconstrictor
	Liquorice	Expectorant, Secretolytic

The availability of dietary iron depends on different dietary factors. It is suggested to consume the sources that enhance iron absorption and utilization and avoid the inhibitors. Certain fruits, vegetables, and animal-based foods are rich sources of iron. It includes green leafy vegetables, spinach, meat and organs from cattle and fish (Teucherl and Cori, 2014). Dietary supplements such as ferrous glycerate, fumerate, or sulphate are abundantly present in calf liver, beet greens, almonds, beans, green leafy vegetables and brewer's yeast. Eggs, meats, tuna, liver and cheese have high concentration of vitamin B12 and green leafy vegetables, orange juice, and grains have high folic acid content. Dietary sources such as citrus fruits, tomatoes, cauliflower and broccoli are rich in vitamin C. Ascorbic acid is known to enhance iron absorption due to its iron-reducing and chelating properties. Organic acids, including fumaric, malic, succinic and tartaric acids, are also known to enhance iron uptake in both $Fe^{3+}$and Fe^{2+} forms. Citric and oxalic acids increase ferric iron intake; however, decreases the uptake in ferrous form. Propionic and acetic acid increases ferrous iron uptake only (Teucherl and Cori, 2014; Naviglio *et al.*, 2018). On the other hand, food compounds such as unprocessed cereals (rich in phytates) and calcium inhibit iron uptake. Animal origin milk (contains phosphoproteins), milk proteins, albumin and egg proteins are the inhibitors of iron absorption (Verna *et al.*, 2021).

Most often anaemia is due to lack of iron and vitamins; introducing herbs and supplements in the routine usually help. Herbs are known since ages for their role in strengthening immune system and treating various diseases. However, they can interact with various drugs and can cause serious side effects; therefore should be taken under appropriate supervision. Blackstrap molasses (pregnancy tea) is rich in iron, vitamins, proteins and minerals and used as laxative and in iron deficiency. Spirulina (blue-green algae) is another 'nutritionally packed' dietary supplement, rich in flavonoids and sulfalipids. It modulates cytokine production and stimulates the immune system. In a study conducted on elderly population, spirulina ameliorated anaemia and immunosenescence in subjects (Selmi *et al.*, 2011). Another study showed its antianaemic effect among women in their second trimester of pregnancy (Marlina and Nurhayati, 2020). Other herbs include alfalfa, chamomile, dandelion root and leaves, mint, burdock, thyme, yellowdock and ginseng (Hamadia *et al.*, 2020). Gentian is a widely used herb for anaemia as it stimulates digestive tract to absorb iron easily. Leaves of *Telfairia occidentalis*, *Brillanthisianitens*, *Tectona grandis*, *Jatropa curcas* and *Flacourtia flaven*, stem of *Khaya senegalensi*, *Allophylus rubifolius* and *Bracken-ridge azangue baric* and whole herb of *Psoraspermum ferbrifugum* and *Combratum dolichopetalum* are some other examples of traditional supplements given for the treatment of anaemia (Ogbe *et al*., 2010).

Various studies have shown the effect of fortification on health and the economy. Fortification can be defined as the addition of nutrient-rich substances (salts, chelates, meat, or similar derivatives) to the product recipe to improve its nutritional status. In this technique, nutrients are either added to the food (in form of a sprinkle or micronutrient powder) before consumption or taken as lipid based supplements (Prentice *et al*., 2017). Breeding techniques and genetic alterations are also employed to increase the nutritional value of crops during their growth. In particular to iron, wheat and maize flour, cereals and infant formula are generally fortified with iron (Prentice *et al*., 2017; da Silva Lopes *et al*., 2018; Tripathi *et al*., 2017; Mounika and Hymavathi, 2021). The dose of iron required for fortification is less as compared to supplementation and therefore, the level of iron increases much slower; making it an overall safer iron form. However, there are certain technical difficulties associated with it. The most bioavailable iron forms are expensive, less palatable and react with food components. Replacing this form with cost-effective and less reactive forms decreases iron bioavailability (Hurrell, 2002; Zimmermann and Hurrell, 2007). Fortified foods and additives are available in the market to increase iron availability; however, are not available and successful for all anaemia subjects. Therefore, this demands research on newer foods that are easily absorbable and exert a protective effect against the condition.

5. Superfoods in the treatment of anaemia

The term 'superfood' came into existence in the early 20th century as a marketing strategy for bananas. Earlier bananas were considered a cheap and easily digestible source of nutrition. As its popularity increased, physicians endorsed bananas for the treatment of ailments like electrolyte imbalances (Verna *et al*., 2021). According to nutritionists and media, super foods can be defined as foods that have high nutrition, limited calories and antioxidant and anti-inflammatory properties in them. Examples include calcium and mineral-rich milk from camel and donkey, scarcely known wild leafy vegetables, omega-3 fatty acids obtained from nuts and fish, *etc*. (Proestos, 2018; Daugherty, 2011). These superfoods have shown great effect in the treatment of inflammatory diseases and are used as supplements in dietary routines. Among them, a large number of superfoods contain a significant concentration of iron, and thus can be used as supplements for anaemia (Verna *et al*., 2021). New approaches for the management of anaemia are super foods like algae, polysaccharide-iron complexes, probiotics, iron-enriched grains and liposomal iron (Table 2).

Table 2: Superfood categories and their health benefits

S. No.	Category of superfood	Examples	Beneficial effects	References
1.	Algae	Mankai alga Sargassum	High iron content increase in haemoglobin levels. Increase in iron absorption. Antioxidant anti-inflammatory	Appenroth *et al*., 2018
2.	Mushrooms	*Grifolafrondosa* *Aspergillusoryzae*	Antioxidant, anti-inflammatory and immunomodulatory activity improve blood parameters. Easy iron absorption	Verna *et al*., 2021
3.	Probiotics	*Bifidobacterium* sp. *Lactobacillus* sp.	Increase iron absorption. Increase haemoglobin levels. Increase iron absorption rates	Skrypnik *et al*., 2019; Rosen *et al*., 2019
4.	Vegetable sources	Amaranth, Cowpea and soybean leaves	High iron content. Anti-inflammatory Increase RBC content	Verna *et al*., 2021
5.	Fortified crops	Wheat, Rice	Increase iron content. Increase iron absorption	Verna *et al*., 2021

One of the algae, the Mankai alga (also known as duckweed), is been reported to restore hemoglobin and normal blood parameters within six months in a rat model of anaemia (Appenroth *et al*., 2018). Similarly, algae of the genus Gracilaria have a large amount of inorganic iron and bioactive components and have the potential to reduce inflammatory cytokine production (Nabil-Adam *et al*., 2020). Macroalgae of genera Porphyria, Sargassum and Ulva are known to possess the highest iron contents during spring. These levels even exceed the daily human requirements. Polysaccharides of Ulva conjugated with iron have the potential to protect mice from artificially induced anaemia. Microalgae such as Chlorella, Spirulina and Tetraselmis sp. CPT4 are very rich sources of iron, vitamins, micronutrients and antioxidants essential to the human body. CPT4 has a very rich biomass of iron, amino acids, vitamins, fibers, and antioxidants. It has good ferric reducing and radical scavenging activity and did not show any toxic effect in the microbiological and toxicological assay (Verna *et al*., 2021).

Polysaccharides, present in a variety of mushrooms, have the property of being easily chelated with iron ions. These polysaccharides, in combination with iron ions, show antioxidant, anti-inflammatory and immunomodulatory activity; the combination can even bypass the gastrointestinal side effects of oral therapy. Iron conjugated with *Grifola frondosa* has potential immunomodulatory activities and can release a high concentration of iron when exposed to an artificial duodenal environment. *Auricularia* complex improves blood parameters in the rat anaemia model and possesses antioxidant and anti-inflammatory effects. Similarly, *Aspergillus oryzae* has higher levels of iron when compared to $FeSO_4$ and is easily available and absorbable. It has better bioavailability and a longer iron release time. *Ganoderma lucidum* extracts significantly improve the hematological parameters in healthy rats and increase the leukocyte population; this probably could be because of the combination of its iron content and antioxidant and anti-inflammatory properties (Davis *et al*., 2012; Gao *et al*., 2019; Koyande *et al*., 2019; Pereira *et al*., 2019; Verna *et al*., 2021).

Successful probiotic strains that enhance dietary iron absorption include *Bifidobacterium bifidum* W23, *Bifidobacterium lactis* W51 and W52, *Lactobacillus plantarum*, *Lactobacillus acidophilus* W37, *Lactobacillus casei* W56, *Lactobacillus brevis* W63, *Lactococcus lactis* W19 and W58 and *Lactobacillus salivarius* W24. These probiotics are known to increase iron absorption by ~50% and also increase its stability and vitality. They significantly increase the hemoglobin levels and are found therapeutic in colonic inflammation and inflammatory bowel disease (IBD) (Skrypnik *et al*., 2019; Rosen *et al*., 2019; Hoppe *et al*., 2017).

Vegetable sources like *Colocasia esculenta*, amaranth and Cowpea leaves are potent sources of iron and antioxidants and are greatly beneficial in patients with IBD (Sarker and Oba, 2019; Gupta *et al*., 2019; Owade *et al*., 2020). Similarly, soymilk and soybean leaves contain a high concentration of iron and help increase the RBC count in borderline anaemia in women (Murray-Kolb *et al*., 2003). Cereals, legumes and meat are also great sources of iron; but this iron is poorly absorbed due to the polyphenol content. Hence, their correct processing and fortification can provide the right amounts of iron. Genetically modified iron and other micronutrient fortified crops are currently emerging to treat anaemia in many countries of the world. Wheat, rice, cowpea leaves, cassava, potatoes and sweet potatoes are examples of some of the plant-based products that are fortified to increase amounts of iron, and thus show an increase in the bioavailable iron (Tako *et al*., 2015; Narayanan *et al*., 2019; Hurrell, 2020).

6. Conclusion

Iron and RBC reserves in the body maintain the daily requirements; its shortage can be sensed by the body. Anaemia is a widespread condition affecting people of all age groups and gender. Many forms of therapies are available but our scientific community still has the challenge to find newer and more effective management strategies. To this line, important findings could come from products obtained from herbal sources, dietary supplements (nutrients), specific diets and processed foods (collectively called nutraceuticals). Therefore, the present review focussed on the anaemia, nutraceuticals and nutraceuticals used as iron resources.

Conflict of interest

The authors declare no conflicts of interest relevant to this article.

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Citation **Meenakshi Gupta and Maryam Sarwat (2022). Nutraceutical interventions for anaemia. Ann. Phytomed., 11(2):75-81. http://dx.doi.org/10.54085/ap.2022.11.2.8.**