

Ferrobine

COMPLEX



Normalising the haemoglobin levels



RED BLOOD CELLS



ANAEMIA



IRON AND VITAMINS

Anaemia is considered as the worldwide most common nutritional deficiency and in 95% of the cases it is associated with an insufficient diet in iron

The human body contains 30 to 40 mg / kg of body weight of iron. It is mainly contained in haemoglobin (Hb), ferritin and other haem- (i.e. myoglobin in the muscles) and non-haem proteins. Iron is an essential element, since it is a component of a variety of enzymes involved in redox reactions and oxygen supply. Red blood cells have the highest iron demand, compared to that of other cells, which is approximately more than half of the total iron content of the body.

The absorption of iron occurs only in the duodenum and the jejunum (small intestine). Most of the iron ingested in food is in the ferric form (Fe^{3+}) and requires a reduction to the ferrous form (Fe^{2+}) for its absorption through the mucosa. The factors that influence the absorption of iron in the intestine are: the form of the iron and its redox status within the food, the pH of the intestinal lumen, the presence or absence of chelating agents in food (for example, phytate or oxalate) and the levels of various iron carriers.

If the amount of iron absorbed is not sufficient to meet the requirements of erythropoiesis (production of red blood cells), iron will be recycled. The haem complexes are degraded in the liver and spleen by the cells of the monocyte-macrophage system (immunological cells).

The World Health Organization (WHO) defines anaemia as the concentration of Hb below 13 g / dl in adult men and 12 g / dl in adult non-pregnant women. The factors that determine an iron deficiency anaemia (IDA) are: inadequate diet in iron, micronutrients and vitamins (vitamins B12, folate, vitamin A and D), the use of drugs and foods that inhibit the absorption of iron, overweight and obesity, malnutrition, athletes, especially adolescents, blood loss, pregnancy and new-borns; abnormalities in the menstruation... etc.



Definition of Anaemia by WHO

Age range	Haemoglobin (g/dl)
Children (6 months - 5 years)	11.0
Children (5 - 11 years)	11.5
Children (12 - 14 years)	12.0
Non-pregnant women (>15 years)	12.0
Pregnant women	11.0
Men (> 15 years)	13.0

The iron demands related to erythropoiesis have three goals: the oxygenation of the tissue, the renewal of the erythrocytes and the compensation for the loss of erythrocytes due to hemorrhage. The first step in the IDA therapy is finding out and treating the underlying cause. The therapy with iron is used to replenish the iron reserve and restore the Hb concentrations to normal levels, preventing and treating the symptoms that arise, leading to a better quality of life, physical performance, thermoregulation and cognitive and immune function.



Ferrobine

C O M P L E X

L I Q U I D

Normalises the iron levels, improving the haemoglobin values and the organic function

EFFECTIVE NORMALISATION OF THE HAEMOGLOBIN RED BLOOD CELLS LEVELS, CONTRIBUTING TO THE OPTIMISATION OF THE ENERGY FUNCTION AND THE NEUROLOGICAL AND CARDIOVASCULAR HEALTH

THE COMBINATION OF THE FERROUS GLUCONATE AND VITAMINS HAS SHOWN A POWERFUL SYNERGIC ACTION, FAVOURING THE REMISSION OF ANAEMIA

CONVENIENT DOSAGE:
ONE TIME PER DAY

SUITABLE TO BE USED AT ANY AGE OR FOR INDIVIDUALS WITH SPECIAL REQUIREMENTS, SUCH AS IN THE CASE OF PREGNANCY OR ATHLETES... ETC.

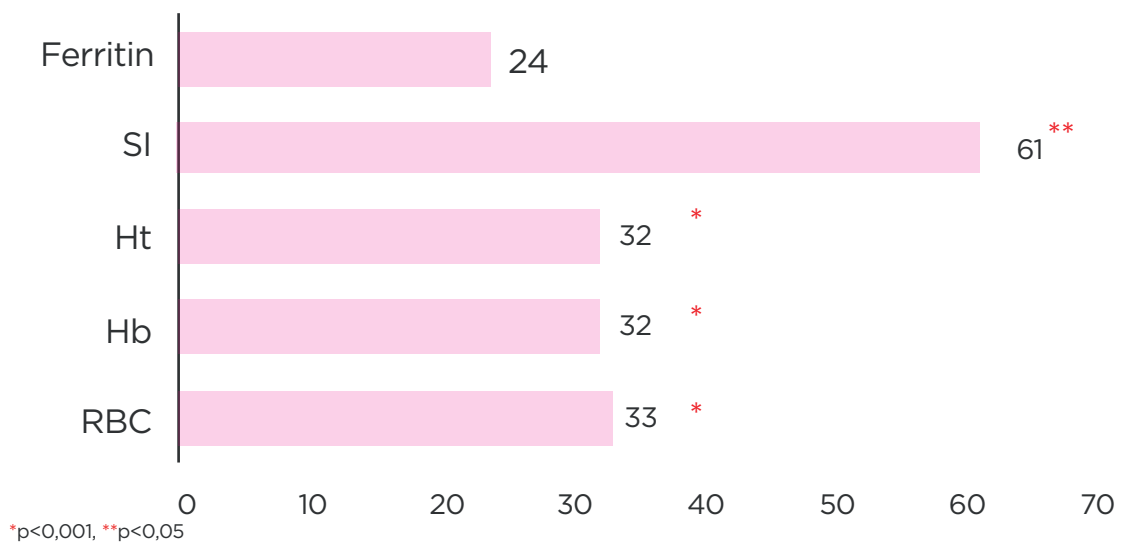
MAIN BENEFITS

Ferrobine Has been especially formulated for **normalising the iron levels, improving the haemoglobin values and the organic function**

Action of ingredients:

1. THE USE OF FERROUS GLUCONATE, IN SYNERGY WITH VITAMINS OF THE GROUP B, A, D, C AND E, SIGNIFICANTLY REDUCES THE ANAEMIA IN MORE THAN 60% OF INDIVIDUALS TREATED FOR AT LEAST 1 YEAR. ^{2,13,24}

Analysis of the therapeutic efficacy parameters
(% of improvement)



RBC= red blood cells; Hb = haemoglobin; Ht = hematocrit; SI: serum iron

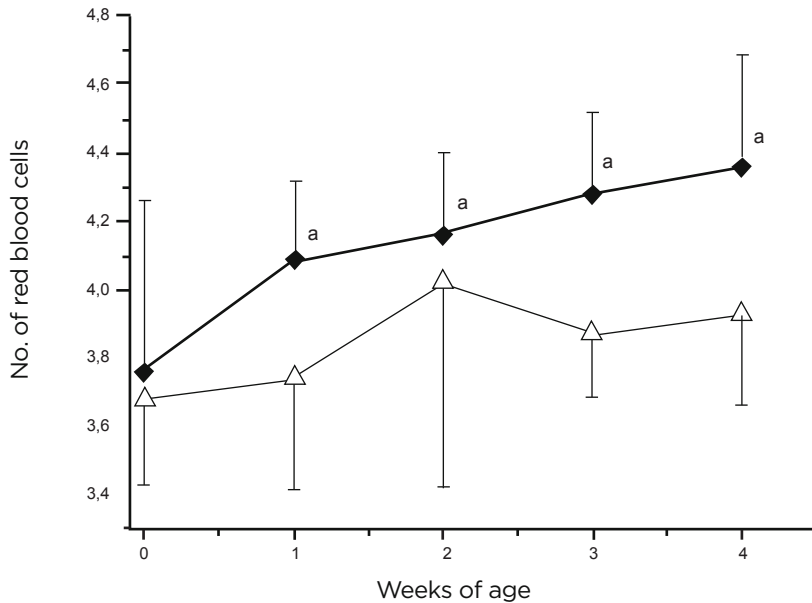
Adapted from Casparis D. Minerva Ginecol. 1996 Nov;48(11):511-8

- In children with anaemia, the use of Ferrous Gluconate increases haemoglobin levels in more than 20% in less than 6 months^{10,13,24}
- It has been shown that the preparations that contain ferrous salts are absorbed more easily than those containing ferric salts, since the former can be immediately absorbed by the duodenal mucosa^{3,10}
- **Ferrobine COMPLEX** contains a range of 27 different fruits, vegetables, cereals and some fructo-oligosaccharides that contributes to: the protection of vitamins and oligoelements of oxidation, improvement of the intestinal transit (prebiotic effect) and regulation of the absorption of fat

* Red grape, tomato, raspberry, rosemary, bilberry, **celery**, wild bilberry, black currant, carrots, strawberries, cherries, pineapple, apple, peach, apricot, lemon, lime, orange, grapefruit, **barley, rye, wheat**, broccoli, cabbage, brussels sprout and spinach.

2. THE B COMPLEX HAS PROVEN TO BE ESSENTIAL FOR THE MODULATION OF THE ENERGY METABOLISM AND CELLULAR PROLIFERATION, CONTRIBUTING TO NEUROLOGICAL AND CARDIOVASCULAR HEALTH^{5,7,11,16,18,19,21,22}

Evolution of the count of red blood cells in premature children with anaemia



The synergic action of iron and the B complex increases by 10% the number of red blood cells in premature new-borns with anaemia, after 4 weeks



◆ B complex + iron
△ Control

Adapted from Nadja Haiden. PEDIATRICS Volume 118, Number 1, July 2006

3. THE COMBINED ACTION OF THE VITAMINS A, C, E AND D CONTRIBUTE TO THE HOMEOSTASIS OF THE ERYTHROPOIETIC FUNCTION, PREVENTING THE OXIDATIVE DAMAGE AND MODULATING THE HORMONAL ACTIVITY^{1,4,5,8,11,20,26,27}

The activity of vitamins C, E and A decreases in more than 30% the action of oxidative enzymes²⁰

Vitamin D regulates the process of erythropoiesis, synergistically stimulating the progenitor cells of the red corpuscles with other hormones and cytokines, including erythropoietin (EPO)^{4,26}

The presence of vitamin A and C favours the absorption of iron^{1,5,8,11}





Recommended dosage according to age:
Children from 5 to 12 years: 5 ml per day before breakfast
Adolescents and adults: 10 ml per day before breakfast

FERROBINE / 250 ml		
INGREDIENTS	PER 10 ML	%NRV
Vitamin C	30 mg	38 %
Iron	14 mg	100 %
Niacin	9 mg	56 %
Vitamin E	5 mg	42 %
Pantothenic acid	3 mg	50 %
Vitamin B6	1 mg	71 %
Riboflavin	0.8 mg	57 %
Thiamine	0.7 mg	64 %
Vitamin A	400 µg	50 %
Folic acid	100 µg	50 %
Biotin	75 µg	150 %
Vitamin D	2.5 µg	50 %
Vitamin B12	0.5 µg	20 %

Source:

A: Retinol acetate

B1-Thiamine: Thiamine mononitrate
 B2-Riboflavin: Riboflavin High Flow; origin: fermentation

B3-Niacin: Nicotinamide

B5-Pantothenic Acid: Calcium Pantothenate

B6-Pyridoxine: Pyridoxine hydrochloride

B7-Biotin: D-biotin

B9-Folic acid: folic acid

B12-Cobalamin: Cyanocobalamin; origin: fermentation

C: L-ascorbic acid

D: Cholecalciferol; of animal origin, sheep fat and wool

E: DL- α -tocopherol acetate

%NRV (Nutrient Reference Value)

Proprietary Information for specialists. The distribution of this document, in whole or in part, is strictly prohibited.

1. Ana Cañete et al. Role of Vitamin A/Retinoic Acid in Regulation of Embryonic and Adult Hematopoiesis. *Nutrients* 2017, 9, 159.

2. C. R. Wall et al. Milk versus medicine for the treatment of iron deficiency anaemia in hospitalised infants. *Arch Dis Child* 2005;90:1033-1038.

3. Casparis D. et al. Effectiveness and tolerability of oral liquid ferrous gluconate in iron-deficiency anemia in pregnancy and in the immediate postpartum period: comparison with other liquid or solid formulations containing bivalent or trivalent iron. *Minerva Ginecol.* 1996 Nov;48(11):511-8.

4. Dominique J. Monlezun et al. Vitamin D Status and the Risk of Anemia in Community-Dwelling Adults. *Medicine.* Volume 94, Number 50, December 2015.

5. G.F.M. Ball. *Vitamins: Their Role in the Human Body.* Chapters 7, 11: Vitamin A: Retinoids and Carotenoids; Thiamin (Vitamin B1). 2004 by Blackwell Publishing Ltd, a Blackwell Publishing company. ISBN 0-632-06478-1.

6. Guideline: DAILY IRON SUPPLEMENTATION IN INFANTS AND CHILDREN. *World Health Organization* 2016. ISBN 978 92 4 154952 3.

7. Hilary J Powers. Riboflavin (vitamin B-2) and health. *Am J Clin Nutr* 2003;77:1352-60.

8. Human Vitamin and Mineral Requirements. Report of a joint FAO/WHO expert consultation, Bangkok, Thailand. Chapters 6, 9: Vitamin C; Vitamin E. 2001

9. Ilhami Berber et al. Evaluation of Ferric and Ferrous Iron Therapies in Women with Iron Deficiency Anaemia. *Advances in Hematology* Volume 2014, Article ID 297057, 6 pages.

10. Jaber L. et al. Iron polymaltose versus ferrous gluconate in the prevention of iron deficiency anemia of infancy. *J Pediatr Hematol Oncol.* 2010 Nov;32(8):585-8.

11. Janos Zempleni et al. *Handbook of Vitamins-Fourth Edition.* Chapter 9, 15: Pantothenic Acid; Ascorbic Acid. CRC Press, Taylor and Francis Group. International Standard Book Number-10: 0-8493-4022-5. 2007.

12. Jeffery L. Miller. *Iron Deficiency Anemia: A Common and Curable Disease.* Cold Spring Harb Perspect Med 2013;3: a011866.

13. Juan A Rivera et al. Effectiveness of a large-scale iron-fortified milk distribution program on anemia and iron deficiency in low-income young children in Mexico. *Am J Clin Nutr* 2010;91:431-9.

14. Lawrence Tim Goodnough and Stanley L. Schrier. *Evaluation and Management of Anemia in The Elderly.* *Am J Hematol.* 2014 January; 89(1): 88-96.

15. M.D. Ballesteros-Pomar y A. Arés-Luque. Déficit nutricionales carenciales. *Endocrinol Nutr* 2004;51(4):218-24.

16. Martino Luigi di Salvo et al. Vitamin B6 salvage enzymes: Mechanism, structure and regulation. *Biochimica et Biophysica Acta* 1814 (2011) 1597-1608.

17. Mary Wang. Iron Deficiency and Other Types of Anemia in Infants and Children. *Am Fam Physician.* 2016;93(4):270-278.

18. Matthias R. Baumgartner. Vitamin-responsive disorders: cobalamin, folate, biotin, vitamins B1 and E. *Handbook of Clinical Neurology, Vol. 113 (3rd series) Pediatric Neurology Part III,* 2013.

19. Nadja Haiden et al. A Randomized, Controlled Trial of the Effects of Adding Vitamin B12 and Folate to Erythropoietin for the Treatment of Anemia of Prematurity. *PEDIATRICS* Volume 118, Number 1, July 2006.

20. Nirjala Laxmi Madhikarmi and Kora Rudraiah Siddalinga Murthy. Antioxidant Enzymes and Oxidative Stress in the Erythrocytes of Iron Deficiency Anemic Patients Supplemented with Vitamins. *Iranian Biomedical Journal* 18 (2): 82-87 (April 2014).

21. Ping Xu and Anthony A. Sauve. Vitamin B3, the nicotinamide adenine dinucleotides and aging. *Mechanisms of Ageing and Development* 131 (2010) 287-298.

22. R. de Paz y F. Hernández-Navarro. Manejo, prevención y control de la anemia megaloblástica secundaria a déficit de ácido fólico.

23. Romilda Castro de Andrade Cairo et al. Iron deficiency anemia in adolescents: a literature review. *Nutr Hosp.* 2014;29(6):1240-1249.

24. Salvador Villalpando et al. Fortifying Milk with Ferrous Gluconate and Zinc Oxide in a Public Nutrition Program Reduced the Prevalence of Anemia in Toddlers. *J. Nutr.* 136: 2633-2637, 2006.

25. Sophia Taylor and David Rampton. Treatment of iron deficiency anemia: practical considerations. *Pol Arch Med Wewn.* 2015; 125 (6): 452-460.

26. Vasant Hirani et al. Cross-sectional and longitudinal associations between the active vitamin D metabolite (1,25 dihydroxyvitamin D) and haemoglobin levels in older Australian men: the Concord Health and Ageing in Men Project. *AGE* (2015) 37: 8.

27. Yoshinoto Iuchi. Chapter 4: Anemia Caused by Oxidative Stress. *Anemia, Dr. Donald Silverberg (Ed.), ISBN: 978-953-01-0138-3.* In Tech, Available from: <http://www.intechopen.com/books/anemia/anemia-caused-by-oxidative-stress>, (2012).