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Effects of Chlorella Supplementation in the Prevention of Iron Deficiency Anemia: A Review of Clinical and Experimental Studies

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Aims: This review aimed to evaluate the potential of *Chlorella* supplementation as a natural alternative for the prevention and treatment of iron-deficiency anemia, emphasizing its nutritional profile, bioactive compounds, and effects on hematological parameters.
Study Design: Systematic and descriptive-analytical review of clinical and experimental studies.
Place and Duration of Study: Studies published between 2014 and 2024, conducted in different regions, were included without geographical restriction.
Methodology: A total of 70 scientific articles were initially identified. After applying eligibility criteria and assessing methodological quality, 36 studies were selected for analysis. The review was conducted in PubMed, Web of Science, and Scopus databases using controlled descriptors and Boolean operators, such as ("nutritional profile" OR "nutritional composition") AND ("Chlorella vulgaris" OR "Chlorella spp"); ("Anemia" AND "Chlorella microalgae"); ("Iron Supplementation"); and ("proteins" OR "lipids" OR "carbohydrates" OR "amino acids" OR "antioxidants" OR "bioactive compounds").
Results: Evidence suggests that *Chlorella* supplementation may improve hematological parameters, particularly hemoglobin levels, due to its high iron bioavailability and additional nutrients such as vitamins, minerals, and antioxidants. Compared with conventional therapies, *Chlorella* was generally associated with better tolerability and fewer adverse effects, potentially improving adherence. However, the absence of large-scale, long-term trials and limited direct comparisons with pharmaceutical iron restrict the generalization of current findings.
Conclusion: *Chlorella* represents a promising complementary approach for the management of mild to moderate iron-deficiency anemia. Further multicenter and long-term clinical trials are required to confirm its efficacy, safety, and cost-effectiveness, as well as to define its potential role in standard therapeutic protocols.

Keywords: Microalga; Chlorella; iron-deficiency anemia; bioactive compounds.

1. INTRODUCTION

Anemia is a condition characterized by reduced hemoglobin concentration in the blood, Anemia is a condition characterized by a reduced concentration of hemoglobin in the blood, impairing oxygen transport capacity and negatively affecting overall health and quality of life. This morbidity presents with varying degrees of severity and diverse etiologies, one of which is iron-deficiency anemia, which occurs when dietary iron intake or its absorption by the body falls below clinically recommended levels. Low iron availability results in microcytic hypochromic anemia due to decreased synthesis of heme and hemoglobin (Marks et al., 2018). It is estimated that iron deficiency represents the leading nutritional cause of anemia worldwide. Other contributing factors include socioeconomic conditions, nutritional deficiencies, and chronic diseases, as well as challenges in accurate diagnosis and effective treatment. Iron-deficiency anemia is associated with severe fatigue, weakness, reduced exercise tolerance, pallor, tachycardia, and dyspnea, which collectively limit daily activities and physical performance. In adults, the condition leads to a marked reduction in productivity and an increased susceptibility to infections (Benson et al., 2021; Kumar et al., 2022). The prevalence of anemia varies significantly among population groups, such as children, adolescents, women of reproductive age, pregnant women, and postpartum women. It is estimated that 40% of children aged 6 to 59 months, 37% of pregnant women, and 30% of women aged 15 to 49 years worldwide are anemic, underscoring anemia as a major global public health concern (WHO, 2024).

Conventional treatments for anemia typically involve nutritional iron supplementation, either orally (e.g., ferrous sulfate) or intravenously, often combined with folic acid, which effectively increases hemoglobin levels. Vitamins such as B12 and B9 are administered orally or by injection, and vitamin A is recommended particularly for pregnant women and children (Marks et al., 2018). Supplementation with multiple micronutrients (MMN) is also beneficial, alongside the consumption of iron- and vitamin-

rich foods such as red meat, dark green vegetables, and citrus fruits. Although these approaches are accessible and effective, they frequently encounter limitations associated with side effects and poor treatment adherence, especially in oral therapy. Reported issues include inadequate absorption, poor compliance, and adverse effects such as nausea, vomiting, constipation, and abdominal pain (Camaschella, 2015; Maladkar et al., 2020). In this context, alternative and complementary approaches have gained relevance, offering potential solutions to overcome these barriers.

Nutritional interventions based on micronutrient-rich foods have shown promising results in anemia management. Among emerging resources, *Chlorella* stands out as a microalga rich in a wide range of nutrients and bioactive compounds that may provide significant health benefits and contribute to the prevention of various pathological conditions (Rani et al., 2018; Ru et al., 2020). These natural compounds present in *Chlorella* have the potential to serve as alternatives to synthetic drugs, offering natural options for essential nutritional supplementation.

Specifically, *Chlorella*-derived products represent a substantial source of iron (104 mg/100 g dry weight) and potassium (986 mg/100 g dry weight), both essential nutrients that, when consumed in adequate amounts, play a crucial role in anemia prevention (Camaschella, 2015). Although the iron in *Chlorella* is non-heme (as in all plants), its bioavailability varies significantly compared with other sources. The estimated absorption of non-heme iron in typical vegetarian diets is 5–12%, while heme iron (of animal origin) shows an absorption rate of 15–35% (Hurrell & Egli, 2010). However, *Chlorella* contains bioactive compounds such as vitamin C and proteins (approximately 60% of dry weight) that can enhance iron absorption. Studies suggest that *Chlorella* iron exhibits 2- to 3-fold greater bioavailability compared with vegetables such as spinach, which contain high levels of phytates, known inhibitors of iron absorption (Bito et al., 2020; Watanabe et al., 2014).

The present study aims to review and compile existing scientific evidence on the use of Chlorella in the treatment of iron-deficiency anemia. It seeks to evaluate its efficacy, advantages, and limitations in comparison with conventional therapeutic methods, providing a foundation for future therapeutic applications and public health interventions. Adopting a review-based approach allows for the integration and critical analysis of previously published studies, offering a comprehensive and up-to-date perspective on the topic, as well as identifying knowledge gaps and guiding future research directions.

2. MATERIALS AND METHODS

Initially, approximately 70 scientific articles related to the proposed topic were identified. After the rigorous application of eligibility criteria and a critical assessment of methodological quality, 36 studies were selected to form the reference base of this work. The bibliographic research was conducted systematically, using a descriptive-analytical approach, and carried out in the main international scientific databases PubMed, Web of Science, and Scopus, recognized for their comprehensiveness and relevance in the biomedical field.

The methodological process followed a protocol structured into eight successive stages, designed to ensure transparency, reproducibility, and consistency of the results obtained. First, the guiding research question was defined, serving as the foundation for the entire development of the review. Subsequently, a broad and meticulous bibliographic search was performed, employing controlled descriptors and free terms combined with Boolean operators to maximize both the precision and the scope of the search. The retrieved publications underwent an initial screening process, during which titles and abstracts were reviewed to exclude studies that were not directly related to the research topic.

In the next stage, potentially relevant papers were analyzed in full and selected according to the predefined eligibility criteria. A critical appraisal of the methodological quality of the included articles was then conducted, considering aspects such as experimental design, clarity of objectives, consistency of results, adequacy of statistical analysis, sample size, and overall scientific relevance. Following this evaluation, data extracted from the selected studies were systematically organized and synthesized, allowing for comparison of findings and identification of patterns and divergences within the reported evidence. The interpretation of results was carried out in a contextualized manner, linking the information obtained to the existing theoretical framework and to the specific objectives of the investigation. Finally, the

scientific report was prepared, and the documentary corpus was continuously updated to ensure the timeliness and relevance of the sources consulted.

The eligibility criteria included only original studies published in Portuguese or English between 2014 and 2024, with full-text availability and indexing in at least one of the selected databases. The search strategy was developed based on specific descriptors and free terms combined through Boolean operators, such as: ("nutritional profile" OR "nutritional composition") AND ("Chlorella vulgaris" OR "Chlorella spp"); ("anemia" AND "Chlorella microalgae"); ("iron supplementation"); and ("proteins" OR "lipids" OR "carbohydrates" OR "amino acids" OR "antioxidants" OR "bioactive compounds").

This methodological approach enabled a comprehensive, precise, and reproducible bibliographic prospecting process, ensuring the selection of scientifically robust studies aligned with the objectives of this investigation.

3. FINDINGS AND DISCUSSION

3.1 Characterization of *Chlorella*

Chlorella is a unicellular green microalga that grows in aquatic environments, characterized by a spherical shape and a diameter of less than 10 µm. Due to its photosynthetic capacity, high proliferation rate, and resistance to adverse environmental conditions, it stands out as a promising source of nutrients and bioactive compounds. Widely recognized as both a food and nutritional supplement, *Chlorella* is broadly consumed in East Asian countries such as Korea, Japan, Taiwan, China, and Indonesia (Hosseini et al., 2021).

Among commercially available microalgae, *Chlorella* vulgaris is one of the most valued species, with market projections reaching USD 412.3 million by 2028 and an annual production of approximately 5,000 tons of dry biomass (Maurício et al., 2023). Its composition includes about 51–58% proteins, 12–17% polysaccharides, and 14–22% lipids, along with polyunsaturated fatty acids (PUFAs) such as linoleic acid (ω-6) and oleic acid (ω-9), which contribute to cardiovascular health and epidermal barrier regulation (Grieco et al., 2025).

Chlorella is also rich in vitamins, minerals, and antioxidant compounds, including carotenoids (lutein and zeaxanthin) and chlorophyll. These compounds exhibit properties that help protect against oxidative stress and mitigate age-related diseases. Studies highlight its ability to increase high-density lipoprotein (HDL), reduce low-density lipoprotein (LDL) and triglycerides, prevent inflammation, and improve insulin sensitivity (Jahromi et al., 2022). In vegan diets, *Chlorella* serves as a sustainable alternative for obtaining essential amino acids such as lysine, arginine, and leucine, as well as minerals including potassium, calcium, iron, zinc, and magnesium (Cabrita et al., 2022; Lousada et al., 2023).

Its lipid profile, mainly composed of monounsaturated fatty acids (MUFAs) and polyunsaturated fatty acids (PUFAs), is widely applied in both cosmetic formulations and nutraceutical products. Linoleic acid, essential in infant formulas, also plays a role in regulating the transepidermal water barrier, proving useful in dermatological treatments. Oleic acid, present in high concentrations, is effective in preventing cardiovascular diseases (Davani et al., 2022).

Beyond nutritional and cosmetic applications, *Chlorella* contains phenolic compounds such as caffeic and chlorogenic acids, which contribute to its antioxidant capacity. Innovative applications include its incorporation into foods, such as cheese, where significant increases in protein content and antioxidant activity have been observed in the final product (Lousada et al., 2023). Another key property of *Chlorella*, attributed to its rich nutritional composition, was highlighted in a study by Mahmoud et al. (2020).

This study demonstrated *Chlorella's* ability to protect hematological parameters through its potent bioactive compounds. Furthermore, the results emphasized its mitigating effects on hematological parameters under exposure to various toxic substances, reinforcing its potential as a protective agent in conditions of toxin-induced oxidative stress. With its versatility and growing market acceptance, *Chlorella* represents a strategic resource to meet modern consumer demands, promoting health and sustainability while driving technological innovation.

3.2 Mechanisms of Action

Hemoglobin is a globular protein with a quaternary structure, specialized in oxygen (O_2) transport through the bloodstream. It is composed of four polypeptide subunits, known

as globins, each associated with a heme group. The heme group contains an iron atom, which is responsible for oxygen binding and for the characteristic red color of hemoglobin (Safo et al., 2013).

The iron essential for hemoglobin function is derived from two primary sources: dietary intake and the recycling of senescent erythrocytes (Grotto, 2008). The role of iron in hemoglobin production is critical, as hemoglobin mediates oxygen transport from the lungs to peripheral tissues. Anemia is defined as a reduction in hemoglobin concentration in the blood and may result from pathophysiological conditions or nutritional deficiencies (Colpo, 2022).

The clinical signs and symptoms of iron-deficiency anemia include apathy, fatigue, irritability, and tachycardia. For diagnosis, it is essential to perform laboratory tests such as a complete blood count to assess hemoglobin and hematocrit levels, reticulocyte count to evaluate bone marrow response, and serum ferritin measurement, which reflects the body's iron stores (Yamagishi et al., 2017).

Treatment of iron-deficiency anemia typically involves nutritional interventions with iron-rich foods or the use of supplements to restore hemoglobin levels (Freire et al., 2020). Iron deficiency is the leading global cause of anemia, occurring when the body lacks sufficient iron for normal hemoglobin synthesis (Negreiro & Saenz, 2024).

In addition to iron, other nutrients such as vitamin B12 and folic acid play fundamental roles in heme synthesis and hematopoiesis. These B-complex vitamins are crucial for red blood cell production and for maintaining iron homeostasis. Evidence indicates that folic acid supplementation during pregnancy enhances neurogenesis, synaptogenesis, primitive reflexes, spatial learning, and motor function (McGarel et al., 2014; Wang et al., 2018, 2019, 2021; Harlan et al., 2021).

Specific conditions such as pregnancy, vegetarian diets, gastrectomy, and pancreatic insufficiency can lead to vitamin B12 deficiency, thereby increasing the risk of anemia. Alternative dietary sources, including microalgae, have emerged as valuable options due to their richness in antioxidant pigments such as chlorophylls and carotenoids (Christaki et al., 2011; Um & Kim, 2009).

3.3 Clinical Evidence of the Use of *Chlorella* for the Treatment of Anemia

The use of microalgae as nutritional supplements in human diets has become a reality, with expanding applications due to the presence of various nutrients and antioxidant compounds that offer numerous health benefits. According to Uchiyama-Tanaka et al. (2023), species of the genus *Chlorella* are particularly rich in vitamins, including folate derivatives, vitamins B12 and D, minerals such as iron and magnesium, as well as dietary fibers that help reduce the risk of anemia. *Chlorella* shows great potential as a source of bioavailable iron and other nutrients essential for hematopoiesis.

Moreover, bioactive compounds found in microalgae, such as chelated iron and phycocyanin, have the ability to stimulate hemoglobin production. Uchiyama-Tanaka et al. (2023) investigated the effects of *Chlorella* supplementation in 22 pregnant women with low-grade inflammation. Although not the main focus of the study, the authors monitored iron levels and other anemia-related parameters, but no significant improvements in hemoglobin or ferritin were observed. Additionally, 14 participants required further iron supplementation.

Conversely, studies such as Rzymski and Jaśkiewicz (2017) reported several beneficial effects of microalgae supplementation, including enhanced immunity, increased vitality, improved hair and skin quality, and greater overall well-being. However, these authors highlighted the need for further research to better understand the safety of such supplementation, given the limited data available on adverse events associated with microalgae consumption.

Bito et al. (2020) reinforced the promising potential of *Chlorella* as a dietary supplement, indicating that its proper intake may prevent anemia and hypertension, in addition to providing other health benefits. In animal models, Gao et al. (2019) demonstrated that microalgae may be effective supplements against iron deficiency, although the precise mechanisms remain not fully elucidated.

Clinical evidence suggests that *Chlorella* supplementation is particularly beneficial for the prevention and management of anemia in specific populations, such as pregnant women and young individuals. Its richness in essential

nutrients, including iron, folate, and vitamin B12, contributes to improved hematological indices. However, most studies involve small sample sizes and focus on restricted groups, making larger and more comprehensive clinical trials essential.

Therefore, caution is advised when generalizing these findings, as more robust investigations are required to validate the benefits of microalgae in anemia management. Although recognized for their high iron and nutrient content, there is still a lack of conclusive clinical evidence confirming their specific efficacy in the treatment of anemia in humans.

3.4 Limitations and Controversies

The limitations of studies investigating the use of *Chlorella* in anemia management are varied and often related to the type of research, non-standardized methodological designs, sample size, study duration, generalizability of results, and limited population diversity. According to Bito et al. (2020), further research is needed to determine the optimal dosage of *Chlorella* for the treatment of anemia and other health conditions.

Clinical studies frequently involve small sample sizes, which, according to Soltanifar et al. (2024), reduces statistical robustness. A limited sample can restrict the observations or lead to overgeneralization of the results to larger populations. Regional studies or those focusing on specific populations may fail to capture inter-population variability due to genetic, dietary, cultural, individual factors, and nutritional requirements, introducing regional bias. Similarly, studies limited to healthy individuals, pregnant women, patients with chronic diseases, or elderly populations may influence analytical outcomes.

Another critical factor is study duration. Many of the evaluated articles involved only a few weeks of observation, without assessing potential risks associated with long-term administration, maximum dosage limits, short- and long-term side effects, nutrient and vitamin excess, among other factors. Studies in pregnant women also often omitted information regarding postnatal effects or impacts on infants. In summary, robust data on the long-term safety of *Chlorella* supplementation are lacking.

There is also a scarcity of comparisons with conventional treatments. Few studies compare *Chlorella* supplementation with the various forms of pharmaceutical iron, either alone or in combination with other supplements. Without such comparisons, it is difficult to determine whether *Chlorella* is superior, equivalent, or inferior in terms of efficacy and cost-effectiveness.

Although studies indicate potential benefits of *Chlorella* in anemia management, Gurney and Spendiff (2022) noted that methodological limitations and variability among studied populations underscore the need for larger, multicenter, randomized, and long-term clinical trials to confirm its efficacy and safety. Controversies in the literature regarding Chlorella's role in anemia treatment are primarily related to low sample sizes, methodological challenges, and limitations in data interpretation. Studies often focus on specific populations, such as Japanese pregnant women or malnourished children, which may limit the generalizability of the findings.

Another point of contention concerns the consistency of *Chlorella's* efficacy in improving anemia. The magnitude of observed benefits varies significantly between studies. While some report a substantial reduction in anemia prevalence among pregnant women supplemented with *Chlorella*, others show more modest results or suggest that effects are comparable to traditional iron supplements. This raises questions as to whether the observed benefits are unique to *Chlorella* or achievable with other iron sources.

Focusing on specific nutrients, such as iron in the context of anemia, presents additional challenges. *Chlorella* contains multiple nutrients, making it difficult to determine whether anemia improvements are solely due to iron or result from a combined effect of its nutrient profile. Furthermore, the reviewed studies lack consensus on the precise mechanism by which *Chlorella* improves anemia. Some suggest that iron absorption from this microalga may be more efficient due to bioactive compounds, but detailed investigations are still needed to confirm and clarify these mechanisms.

Despite reported benefits, limited information exists regarding potential adverse effects of *Chlorella* supplementation. The analyzed studies did not document significant adverse events, though this may reflect small sample sizes or short observation periods. Overall, controversies

surrounding *Chlorella's* use in anemia treatment emphasize the need for more rigorous research, including well-designed randomized clinical trials, to resolve discrepancies and address outstanding questions. Science has yet to conclusively determine whether *Chlorella* represents a robust and reliable alternative for anemia management across diverse populations.

Studies comparing the benefits of *Chlorella* with conventional treatments for anemia remain scarce. As a microalga rich in essential nutrients, proteins, and antioxidants, *Chlorella* may offer a natural and multifactorial approach, contributing to anemia improvement while promoting additional benefits for overall health. Bito et al. (2020) highlight that *Chlorella* exhibits various pharmacological activities, including immunomodulatory, antioxidant, antidiabetic, antihypertensive, and antihyperlipidemic effects. The iron naturally present in *Chlorella*, associated with bioactive compounds, has demonstrated greater bioavailability in some studies.

In conventional treatments, synthetic iron, usually administered as ferrous sulfate, is widely used due to its low cost. However, Gao et al. (2019) suggest that *Chlorella* shows comparable efficacy to ferrous sulfate in certain cases. More advanced iron supplements are also available on the market, such as chelated iron alone or combined with vitamins, which provide better absorption, albeit at a higher cost. Furthermore, intravenous iron replacement offers greater bioavailability but involves high costs and risks of adverse effects.

To improve iron absorption in conventional treatments, it is common to combine iron with other nutrients such as folate and vitamin B12, especially in cases of megaloblastic anemia, as described by Vieira et al. (2024). These treatments provide targeted nutrient supplementation, allowing for rapid recovery of hemoglobin levels, but also increase costs. In contrast, the broad nutritional profile of *Chlorella* reduces the need for multiple supplements, thereby minimizing negative interactions.

Regarding side effects, *Chlorella* is generally well tolerated, with few adverse reports, although Tezel Yalçın (2024) notes possible nausea, diarrhea, abdominal cramps, flatulence, green stools, allergic reactions, asthma, and anaphylaxis. Conventional treatments, however, often cause nausea, constipation, or diarrhea, impairing adherence to therapy (Cancelo-Hidalgo et al., 2013). Intravenous iron, in turn, may trigger severe allergic reactions or iron overload.

In terms of efficacy, *Chlorella* has shown promise in the management and prevention of mild to moderate anemia, providing a gradual and sustainable improvement in hemoglobin levels and other hematological indicators. On the other hand, conventional treatments remain the primary choice for moderate to severe anemia due to their rapid and direct response. Nonetheless, conventional therapies are generally more accessible and cost-effective in the short term.

Thus, *Chlorella* emerges as a promising natural alternative for the prevention and treatment of mild anemia, while conventional treatments remain indispensable for severe cases due to their immediate efficacy. Future studies should explore combined approaches to maximize the benefits of both strategies.

The therapeutic potential of *Chlorella* still requires further investigation, particularly in the context of anemia and other health conditions. Comparative studies on the efficacy of *Chlorella*, synthetic iron supplements, and standard therapies may help identify optimal supplementation strategies, therapeutic doses, and treatment duration. Moreover, evaluating cost-effectiveness, tolerability, and patient adherence will help determine whether *Chlorella* can be established as a viable and sustainable alternative in different clinical settings.

Advancing this research will strengthen the scientific evidence regarding the efficacy and safety of *Chlorella*, enabling its integration as a reliable therapeutic option in medical and nutritional treatments. In this way, both science and patients may benefit from new alternatives for the management of anemia and associated conditions.

4. CONCLUSION

Chlorella emerges as a natural and potentially effective alternative for the prevention and treatment of iron-deficiency anemia, particularly due to its comprehensive nutritional profile and high iron bioavailability. The studies reviewed

suggest that its use may promote a gradual and sustained improvement in hemoglobin levels, while also providing additional health benefits attributable to its antioxidant, immunomodulatory, and metabolic properties. Compared to conventional treatments, Chlorella appears to be associated with a lower incidence of gastrointestinal adverse effects and may reduce the need for multiple nutritional supplements. However, the current evidence remains limited, particularly regarding standardized dosing, treatment duration, and direct comparisons with traditional synthetic iron therapies. Therefore, larger and well-controlled clinical studies are essential to confirm its efficacy, safety, and cost-effectiveness across different populations. Based on the available evidence, Chlorella stands out as a promising complementary approach, capable of contributing not only to anemia management but also to overall health promotion.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that generative AI technologies such as Large Language Models, etc. have been used during the writing or editing of manuscripts. This explanation will include the name, version, model, and source of the generative AI technology and as well as all input prompts provided to the generative AI technology

Details of the AI usage are given below:

1. The generative AI technology used was ChatGPT, which is based on large language models (LLMs) developed by OpenAI. The applied version is the most recent in the series, belonging to the GPT-5 (Generative Pre-trained Transformer 5) family. All of the generative artificial intelligence behind ChatGPT was developed and trained by OpenAI.

2. The technology was used strictly to assist in the translation of the manuscript from Brazilian Portuguese to English for the purpose of publication in the current journal. After the translation, the text was reviewed again by team members to identify and correct any potential translation errors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

Benson, C. S., Shah, A., Stanworth, S. J., Frise, C. J., Spiby, H., Lax, S. J., Murray, J., & Klein, A. A. (2021). The effect of iron deficiency and anaemia on women's health. *Anaesthesia*, *76*(S4), 84–95. https://doi.org/10.1111/anae.15405

Bito, T., Okumura, E., Fujishima, M., & Watanabe, F. (2020). Potential of *Chlorella* as a dietary supplement to promote human health. *Nutrients*, *12*(9), 2524. https://doi.org/10.3390/nu12092524

Cabrita, A. R. J., Guilherme-Fernandes, J., Valente, I. M., Almeida, A., Lima, S. A. C., Fonseca, A. J. M., et al. (2022). Nutritional composition and untargeted metabolomics reveal the potential of *Tetradesmus obliquus*, *Chlorella vulgaris* and *Nannochloropsis oceanica* as valuable nutrient sources for dogs. *Animals*, *12*(19), 2643. https://doi.org/10.3390/ani12192643

Camaschella, C. (2015). Iron-deficiency anemia. *New England Journal of Medicine*, *372*(19), 1832–1843. https://doi.org/10.1056/NEJMra1401038

Cancelo-Hidalgo, M. J., Castelo-Branco, C., Palacios, S., Haya-Palazuelos, J., Ciria-Recasens, M., & Manasanch, J. (2013). Tolerability of different oral iron supplements: A systematic review. *Current Medical Research and Opinion*, *29*(4), 291–303. https://doi.org/10.1185/03007995.2012.761599

Christaki, E., Florou-Paneri, P., & Bonos, E. (2011). Microalgae: A novel ingredient in nutrition. *International Journal of Food Sciences and Nutrition*, *62*(8), 794–799. https://doi.org/10.3109/09637486.2011.582460

Colpo, E., da Silva, D. G., dos Santos Araújo, M. D. C., Bevilaqua, L. T., & Colpo, E. (2022). Fatores associados com a presença de anemia em pacientes hospitalizados. *Revista da Associação Médica do Rio Grande do Sul*, 01022105–01022105.

Davani, L., Terenzi, C., Tumiatti, V., De Simone, A., Andrisano, V., & Montanari, S. (2022). Integrated analytical approaches for the characterization of *Spirulina* and *Chlorella* microalgae. *Journal of Pharmaceutical and Biomedical Analysis*, 114943. https://doi.org/10.1016/j.jpba.2022.114943

Falcão, R. L., Pinheiro, V., Ribeiro, C., Sousa, I., Raymundo, A., & Nunes, M. C. (2023). Nutrition improvement of fresh cheese with microalga *Chlorella vulgaris*: Impact on composition, structure and sensory acceptance. *Food Technology and Biotechnology*, *61*(2). https://doi.org/10.17113/ftb.61.02.23.7851

Freire, S. T., Alves, D. B., & Maia, Y. L. M. (2020). Diagnóstico e tratamento da anemia ferropriva. *Referências em Saúde do Centro Universitário Estácio de Goiás*, *3*(01), 124–131. https://estacio.periodicoscientificos.com.br/index.php/rrsfesgo/article/view/209

Gao, F., Guo, W., Zeng, M., Feng, Y., & Feng, G. (2019). Effect of microalgae as iron supplements on iron-deficiency anemia in rats. *Food & Function*, *10*(2), 723–732. https://doi.org/10.1039/c8fo01834k

Grieco, T., Paolino, G., Moliterni, E., Chello, C., Sernicola, A., Brandi, M. L., .. & Calvieri, S. (2025). Non-Skeletal Roles of Vitamin D in Skin, Gut, and Cardiovascular Disease: Focus on Epithelial Barrier Function and Immune Regulation in Chronic Disease. *International Journal of Molecular Sciences*, *26*(17), 8520.

Grotto, H. Z. W. (2008). Metabolismo do ferro: uma revisão sobre os principais mecanismos envolvidos em sua homeostase. *Revista Brasileira de Hematologia e Hemoterapia*, *30*(5). https://doi.org/10.1590/s1516-84842008000500012

Gurney, T., & Spendiff, O. (2022). Algae supplementation for exercise performance: Current perspectives and future directions for *Spirulina* and *Chlorella*. *Frontiers in Nutrition*, *9*. https://doi.org/10.3389/fnut.2022.865741

Harlan De Crescenzo, A., Panoutsopoulos, A. A., Tat, L., Schaaf, Z., Racherla, S., Henderson, L., Leung, K.-Y., Greene, N. D. E., Green, R., & Zarbalis, K. S. (2021). Deficient or excess folic acid supply during pregnancy alter cortical neurodevelopment in mouse offspring. *Cerebral Cortex*, *31*(1), 635–649. https://doi.org/10.1093/cercor/bhaa248

Hosseini, A. M., Keshavarz, S. A., Nasli-Esfahani, E., Amiri, F., & Janani, L. (2021). The effects of *Chlorella* supplementation on glycemic control, lipid profile and anthropometric measures on patients with type 2 diabetes mellitus. *European Journal of Nutrition*, *60*(6), 3131–3141. https://doi.org/10.1007/s00394-021-02492-5

Hurrell, R., & Egli, I. (2010). Iron bioavailability and dietary reference values. *The American Journal of Clinical Nutrition*, *91*(5), 1461S–1467S. https://doi.org/10.3945/ajcn.2010.28674f

Jahromi, K. G., Koochi, Z. H., Kavoosi, G., & Shahsavar, A. (2022). Manipulation of fatty acid profile and nutritional quality of *Chlorella vulgaris* by supplementing with citrus peel fatty acid. *Scientific Reports*, *12*(1). https://doi.org/10.1038/s41598-022-12309-y

Kumar, A., Sharma, E., Marley, A., Samaan, M. A., & Brookes, M. J. (2022). Iron deficiency anaemia: pathophysiology, assessment, practical management. *BMJ Open Gastroenterology*, *9*(1), Artigo e000759. https://doi.org/10.1136/bmjgast-2021-000759

Mahmoud, E. A., El-Sayed, B. M., Mahsoub, Y. H., El-Murr, A. E. I., & Neamat-Allah, A. N. F. (2020). Effect of *Chlorella vulgaris* enriched diet on growth performance, hemato-immunological responses, antioxidant and transcriptomics profile disorders caused by deltamethrin toxicity in Nile tilapia (*Oreochromis niloticus*). *Fish & Shellfish Immunology*, *102*, 422–429. https://doi.org/10.1016/j.fsi.2020.04.061

Maladkar, M., Sankar, S., & Yadav, A. (2020). A novel approach for iron deficiency anaemia with liposomal iron: Concept to clinic. *Journal of Biosciences and Medicines*, *08*(09), 27–41. https://doi.org/10.4236/jbm.2020.89003

Marks, P. W. (2018). *Anemia: Clinical Approach*. In *Concise Guide to Hematology* (pp. 21–27). Springer International Publishing. https://doi.org/10.1007/978-3-319-97873-4_4

Maurício, T., Couto, D., Lopes, D., Conde, T., Pais, R., Batista, J., Melo, T., Pinho, M., Moreira, A. S. P., Trovão, M., Barros, A., Cardoso, H., Silva, J., Domingues, P., & Domingues, M. R. (2023). Differences and similarities in lipid composition, nutritional value, and bioactive potential of four edible

Chlorella vulgaris strains. *Foods*, *12*(8), 1625. https://doi.org/10.3390/foods12081625

McGarel, C., Pentieva, K., Strain, J. J., & McNulty, H. (2014). Emerging roles for folate and related B-vitamins in brain health across the lifecycle. *Proceedings of the Nutrition Society*, *74*(1), 46–55. https://doi.org/10.1017/s0029665114001554

Negreiros, B. R. D., & Saenz, C. C. B. D. (2024). O papel da deficiência de ferro no desenvolvimento da anemia: uma análise das pesquisas mais recentes. *Revista Ibero-Americana de Humanidades, Ciências e Educação*, *10*(11), 7942–7959. https://doi.org/10.51891/rease.v10i11.17343

Rani, K., Sandal, N., & Sahoo, P. K. (2018). A comprehensive review on *Chlorella*—its composition, health benefits, market and regulatory scenario. *The Pharma Innovation Journal*, *7*(7), 584–589.

Ru, I. T. K., Sung, Y. Y., Jusoh, M., Wahid, M. E. A., & Nagappan, T. (2020). *Chlorella vulgaris*: A perspective on its potential for combining high biomass with high value bioproducts. *Applied Phycology*, *1*(1), 2–11. https://doi.org/10.1080/26388081.2020.1715256

Rzymski, P., & Jaśkiewicz, M. (2017). Microalgal food supplements from the perspective of Polish consumers: Patterns of use, adverse events, and beneficial effects. *Journal of Applied Phycology*, *29*(4), 1841–1850. https://doi.org/10.1007/s10811-017-1079-5

Safo, M. K., Ko, T.-P., Abdulmalik, O., He, Z., Wang, A. H. J., Schreiter, E. R., & Russell, J. E. (2013). Structure of fully liganded Hb ζ2β2 strapped in a tense conformation. *Acta Crystallographica Section D Biological Crystallography*, *69*(10), 2061–2071. https://doi.org/10.1107/s0907444913019197

Soltanifar, M., Lee, C. H., Shirazi, A., Behnke, M., Raymond-Loher, I., & Dagne, G. A. (2024). GenTwoArmsTrialSize: An R statistical software package to estimate generalized two arms randomized clinical trial sample size. *arXiv preprint arXiv:2407.11342*. https://doi.org/10.48550/arXiv.2407.11342

Tezel Yalçın, H., Yalçın, N., Ceulemans, M., & Allegaert, K. (2024). Drug safety during breastfeeding: a comparative analysis of FDA adverse event reports and LactMed®. *Pharmaceuticals*, *17*(12), 1654.

Uchiyama-Tanaka, Y., Shimabukuro, F., Okumura, E., & Fujishima, M. (2023). The effect of *Chlorella* supplementation in pregnant women with low-grade inflammation. *Food Science & Nutrition*. https://doi.org/10.1002/fsn3.3759

Um, B.-H., & Kim, Y.-S. (2009). Review: A chance for Korea to advance algal-biodiesel technology. *Journal of Industrial and Engineering Chemistry*, *15*(1), 1–7. https://doi.org/10.1016/j.jiec.2008.08.002

Vieira, G., Vasconcelos, L. H. F., Oliveira, D. F. D., & Duarte, N. L. (2024). Anemia megaloblástica induzida por fármacos. *Revista Eletrônica Acervo Saúde*, *24*(2), Artigo e15897. https://doi.org/10.25248/reas.e15897.2024

Wang, X., Li, W., Li, Z., Ma, Y., Yan, J., Wilson, J. X., & Huang, G. (2018). Maternal folic acid supplementation during pregnancy promotes neurogenesis and synaptogenesis in neonatal rat offspring. *Cerebral Cortex*, *29*(8), 3390–3397. https://doi.org/10.1093/cercor/bhy207

Wang, X., Li, W., Li, Z., Ma, Y., Yan, J., Wilson, J. X., & Huang, G. (2019). Maternal folic acid supplementation during pregnancy promotes neurogenesis and synaptogenesis in neonatal rat offspring. *Cerebral Cortex*, *29*(8), 3390–3397. https://doi.org/10.1093/cercor/bhy207

Wang, X., Li, Z., Zhu, Y., Yan, J., Liu, H., Huang, G., & Li, W. (2021). Maternal folic acid impacts DNA methylation profile in male rat offspring implicated in neurodevelopment and learning/memory abilities. *Genes & Nutrition*, *16*(1). https://doi.org/10.1186/s12263-020-00681-1

Watanabe, F., Yabuta, Y., Bito, T., & Teng, F. (2014). Vitamin B12-containing plant food sources for vegetarians. *Nutrients*, *6*(5), 1861–1873. https://doi.org/10.3390/nu6051861

World Health Organization. (2024, July 27). Anaemia. *World Health Organization*.

Retrieved from https://www.who.int/health-topics/anaemia#tab=tab_1

Yamagishi, J. A., Alves, T. P., Geron, V. L. M. G., & Lima, R. R. O. (2017). Anemia ferropriva: diagnóstico e tratamento. *Revista Científica da Faculdade de Educação e Meio Ambiente*, *8*(1), 99–110. https://doi.org/10.31072/rcf.v8i1.438

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