ISSN: 2536-7153 SJMLS

Sokoto Journal of Medical Laboratory Science 2024; 9(4): 215 - 228

SJMLS - 9(4) - 023

Haemopoeitic Potential of Haematinics, Limitation and Adverse Effects: An Update

Ibrahim Kalle Kwaifa[1*], and Ukashat Almustapha[1]
Department of Haematology, School of Medical Laboratory Sciences, College of Health Sciences, Usmanu Danfodiyo University (UDU), Sokoto, North-Western, 2346, Nigeria

Author for Correspondence*: Ibrahim.kwaifa@udusok.edu.ng/+234-703-548-8394
https://dx.doi.org/10.4314/sokjmls.v9i4.23

Summary
Haematinics are substances that aid in the formation of red blood cells and are commonly used to treat various types of anaemia. Haematinics, which come in a variety, such pills, capsules, syrups, and injections, are frequently used in human health to treat anaemia. Iron and folic acid are essential haematinic that are vital to avoid neural tube malformations and other congenital abnormalities, particularly during pregnancy. Both iron, folic acid are Vitamin B12 contribute significantly to haematopoiesis, and deficiencies in them can result in diseases such as macrocytic anaemia. Furthermore, red blood cell production depends on the regulation of methyl production and cell division, both of which are mediated by vitamin B12. Haematinic deficiencies, including iron, folate, and vitamin B12 deficiencies, can cause disorders like recurrent aphthous stomatitis, which impair the body's capacity to carry oxygen and cause problems with the oral mucosa. Haematinics play a crucial role in many physiological functions other than the formation of blood. Heme, for example, has been connected to thrombosis, suggesting that it plays a part in the coagulation process. Understanding how different types of haematinics work in the body is vital for their effective use in clinical practice. In this review information were sorted from PubMed, Google Scholar, Tailor and Francis, MDPI, Springer, Nature, BMC and some other related data. This review gives detail update on the significant roles played by haematinics in haemopoiesis, their limitation and the side effects associated with haematinics supplementations.

Keywords: Haematinics, iron, folate, vitamin B12, limitations and their side effects

1.0 Introduction

Haematinics play a crucial role in haemopoeisis by supporting processes such as erythropoiesis and haemoglobin synthesis. These substances, including iron, vitamin B12, and folic acid, which have been essential for the production of red blood cells and the prevention of anaemiaH (Hoenemann *et al.,* 2021). Iron deficiency, in particular, is a common cause of anaemia and can lead to increased transfusion needs, morbidity, and mortality (Hoenemann *et al.,* 2021). Haematinics, such as haematin, have also been demonstrated to stimulate the complement system and encourage the accumulation of C3 activation fragments on erythrocytes, which may influence the pathophysiology of anaemia in diseases like malaria (Pawluczkowycz *et al.,* 2007). Anaemia and other health problems can result from haematinic abnormalities, even though they are essential for blood production. Haematinic deficits and anaemia can be caused by several factors, including decreased bone perfusion, inflammation, malnourishment, and adverse medication reactions (Palazzuoli *et al*., 2011). Due to a reduced blood oxygen transport capacity, deficiencies in haematinics, such as haemin, can also cause diseases such recurrent aphthous stomatitis (Nur'aeny, 2024). The complex involvement of haematinics in blood function is further highlighted by the distinct actions of haematin on haemostasis, such as causing platelet aggregation and preventing coagulation (Glueck, 1983). However, because haematinic therapies can have side effects and

limits, caution is necessary. Haematinic therapies require careful dose and monitoring, as demonstrated by the fact that fast haematin administration in patients with acute intermittent porphyria has been linked to temporary renal failure (Dhar *et al.,* 1980). Additionally, haematinics' possible adverse effects, like haemolysis and renal problems, highlight the necessity of carefully evaluating their use in clinical settings (Auparakkitanon *et al*., 2006). Therefore, in this review details update on the significant roles of haematinics in haemopoiesis, their limitation and the side effects associated with haematinics supplementations were discussed.

2.0 Sources of Haematinics

Iron: Although iron absorption varies greatly, foods with a relatively high iron concentration include liver, red meat, beans, nuts, green leafy vegetables, and fortified breakfast cereals (Ross et al., 2020; Hurrell and Egli, 2010). Heme iron, which makes up 10–15% of the daily dietary iron intake of cultures that consume meat, and non-heme iron, which is found in both plant and animal-based foods, including meat, are the two main types of food iron (Intakes *et al.,* 2002). Important sources of non-heme iron include ferritin iron, which is found in relatively high concentrations in liver and legume seeds like beans, as well as the several types of iron utilised for food fortification. Heme iron always absorbs effectively. However, ferritin iron and other non-heme iron absorption are dependent on the iron n (Intakes *et al*., 2002).

Iron as Supplement: Iron deficiency and iron deficiency anaemia can be prevented and treated with iron supplements. Iron supplements should not be taken by people who are not at risk of iron deficiency, such as postmenopausal women and adult men, without a proper medical examination. There are several varieties of iron supplements that offer varying amounts of elemental iron. 20% elemental iron is found in ferrous sulphate heptahydrate, 33% in ferrous sulphate monohydrate, 12% in ferrous gluconate, and 33% in ferrous fumarate. Unless otherwise noted, elemental iron is the type of iron covered in this article n (Intakes *et al.,* 2002).

Natural Folate: Its name comes from the fact that folate is abundant in green leafy foods, or foliage. Although the folate concentration in fortified cereal varies widely, other good sources of folate include citrus fruit juices, legumes, and fortified meals (Nutrients *et al.,* 2000).

Folate as Supplement: Folic acid is the main type of supplementary folate. It is offered as a supplement with only one ingredient as well as in combination products like multivitamins and B-complex vitamins. A prescription is needed for doses of 1 mg or more (Hendler and Rorvik, 2008). 5-A supplement containing methyltetrahydrofolate is also accessible (Health & Health, 2017). Furthermore, several metabolic illnesses are treated using folinic acid, a derivative of tetrahydrofolic acid. Additionally, the addition of folate to oral contraceptives has been authorised by the US FDA. To improve folate status in women of reproductive age, levomefolate calcium (the calcium salt of MeTHF; 451µg/tablet) is added to oral contraceptives. A nationwide poll in the United States found that just 24% of women aged 15 to 44 who were not pregnant (Wiesinger *et al*., 2012).

Vitamin B12: Vitamin B12 can only be synthesised by specific bacteria and archaea (Watanabe and Bito, 2018; Fang *et al.,* 2017). Animal food including meat, poultry, fish (including shellfish), and to a lesser extent, dairy and eggs, contain vitamin B12 (Brody, 1999). Vegans, or strict vegetarians who abstain from all animal products, require extra vitamin B12 to meet their needs. Bioactive vitamin B12 may be present in a few plant-based foods, including some fermented vegetables and beans, as well as edible mushrooms and algae. These foods may help, however somewhat, prevent vitamin B12 deficiency in vegetarians when combined with B-vitamin-fortified meals (such as cereal and nutritional yeast) and pills. People who are over 50 should take supplements to increase their consumption of vitamin B12 (Watanabe *et al*., 2013).

Vitamin B12 as a Supplement: According to Fang *et al*. (2017), vitamin B12 can be purchased over the counter as a single nutritional supplement or as part of multivitamin and vitamin B-complex supplements. While hydroxycobalamin is mostly utilised in Europe, cyanocobalamin is the main

type found in oral supplements in the United States. There are more types, such as adenosylcobalamin and methylcobalamin (Health & Health, 2017). Vitamin B12 can be purchased over the counter and is sublingual, meaning it is inserted under the tongue until it dissolves. Some research indicates that sublingual methylcobalamin (Orhan Kiliç *et al*., 2021; Varkal and Karabocuoglu, 2021) and sublingual cyanocobalamin (Bensky *et al*., 2019; Del Bo *et al*., 2019), are useful for improving vitamin B12 status. Additionally, to treat pernicious anaemia, cyanocobalamin and hydroxocobalamin are prescribed in injectable form. Cyanocobalamin is available as a prescription nasal spray (Bensky *et al*., 2019; Del Bo *et al*., 2019).

3.0 Molecular Mechanisms and the Role of Haematinics in Haemopoeisis

3.1 Iron Participation in Haemoglobin Synthesis

Haemoglobin production, a vital mechanism for the body's oxygen delivery, requires iron. According to Aoto *et al.* (2019), transferrin receptor-1 facilitates the transport of iron into cells, which is essential for erythroblast enucleation during erythroblast development (Fig. 1). Hepcidin controls ferroportin, which affects haemoglobin production and cellular iron levels (Weiss *et al.,* 2019). Hepcidin levels can rise because of inflammatory reactions, which can also lower iron bioavailability and impact haemoglobin synthesis (Lee *et al*., 2019). An essential component of many physiological processes, iron is especially important for oxygen transport and metabolism. According to Ul Hassan *et al*. (2017), iron is necessary for the creation of iron-sulfur proteins, which are involved in important metabolic processes such oxidative respiration, nitrogen fixation, and photosynthesis. These proteins, which include cytochromeb and ferredoxin are crucial parts of electron transport chains, which are necessary for energy production and cellular respiration. Moreover, metabolic functions include microbial defence, cell signalling, and redox reactions require iron (Rochaix, 2011). Iron is essential for haemoglobin, the protein in red blood cells that carries oxygen, in the context of oxygen transport. Iron atoms are found near the centre of haemoglobin, where they attach to oxygen molecules to facilitate their movement throughout the body (Yusuf *et al*., 2023). Iron is also necessary for muscle function, cell respiration, and mitochondrial metabolism, all of which are critical for athletic performance (Buratti *et al*., 2015). Anaemia brought on by iron shortage can disrupt oxygen delivery to tissues and impede metabolic processes in general (Zhang *et al.,* 2019). Furthermore, hepcidin-mediated hypoferremia, which can impair immunological responses to infection and vaccination, provides evidence that iron status can affect immune responses (Frost *et al*., 2021). Reduced immune cell activity and changed expression of important genes have been linked to low iron levels.

According to studies, people with iron deficiency anaemia can effectively raise their haemoglobin levels by taking iron supplements, such as ferric carboxymaltose (Breymann *et al.,* 2017). Degenerative alterations in brain areas such as the putamen have been linked to excessive iron exposure (Dusek *et al.,* 2022). Injections of iron sucrose have been used to promote the development of erythroid precursors into reticulocytes, which helps produce haemoglobin (Kavilapurapu, 2018). Haemoglobin synthesis can be hampered by iron deficiency, especially in situations like sepsis (Czempik and Wiórek, 2023). Real-time information on haemoglobin synthesis can be obtained by tracking metrics like the reticulocyte haemoglobin equivalent (RET-He), particularly in diseases like chronic renal disease (Sahid, 2016). Blood transfusions may be avoided with intravenous iron treatment, which has been studied as a successful method to maintain postoperative haemoglobin levels (Moon *et al.,* 2021). Furthermore, illnesses like type 2 diabetes mellitus have been associated to increased brain iron deposition in areas like the putamen, highlighting iron's intricate role in a variety of physiological processes (Li *et al*., 2020). Anaemia is frequently caused by iron deficiency, and haematinics such ferric citrate, like Auryxia, improves iron parameters in individuals with chronic renal disease by functioning as phosphate binders. This process aids in treating anaemia and hyperphosphataemia brought on by renal failure (Malanda, 2018).

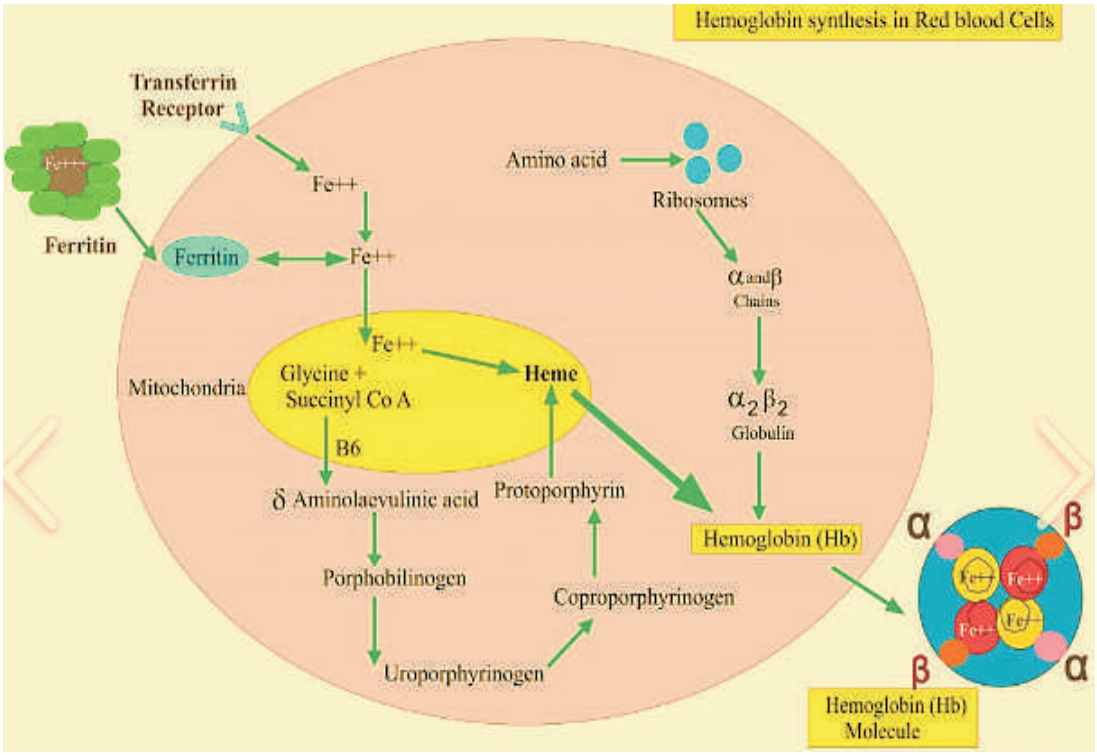

Figure 1: Molecular Mechanisms and Role of Iron in Haemoglobin Synthesis. Haemoglobin synthesis, an essential mechanism for the delivering of oxygen to the body, requires iron. Transferrin receptor-1 promotes the transport of iron into cells, which is vital for erythroblast enucleation during erythroblast development. α; alpha globin, β; beta globin (Modified from Aoto et al., 2019).

3.2 The significance of Vitamin B12 in DNA Synthesis for RBC Production:

Vitamin B12 is essential for DNA synthesis, especially for red blood cell growth. It functions as a coenzyme for enzymes such as methylmalonyl-CoA mutase and methionine synthase, which are essential for nucleotide synthesis, DNA methylation, and the formation of red blood cell precursors (Froese *et al.,* 2019). As a cofactor in metabolic processes, this vitamin is necessary for DNA synthesis, red blood cell creation, and brain function (Andrés *et al.,* 2024). Furthermore, cobalamin, another name for vitamin B12, is essential for the brain, nervous system, and red blood cell production to operate normally (Rizzo and Laganà, 2020). It plays a role in vital bodily chemical processes, including the transformation of homocysteine into methionine, methylmalonic acid into succinyl coenzyme A (Fig. 2) (Rizzo and Laganà, 2020).

The production of red blood cells, known as erythropoiesis, depends on vitamin B12 and folic acid. Methionine regeneration is essential for healthy erythropoiesis, and vitamin B12 functions as a coenzyme in these processes (Nair, 2011). Cell division, myelin synthesis, DNA synthesis, and one-carbon metabolism, which are essential for erythropoiesis, and all depend on it (Jha *et al*., 2021). During their development, erythroblasts require folic acid and vitamin B12 for proliferation (Erdem, 2022). The production of haematopoietic cells, such as red blood cells, white blood cells, and platelets, requires vitamin B12 (Di Costanzo *et al*., 2016). Supplementing with vitamin B12 has been linked to platelet recovery and has been demonstrated to improve haematological parameters, which lowers the requirement for platelet transfusions (Sagar *et al.,* 2022). By restoring DNA synthesis during haemoglobin manufacture, folic acid, like vitamin B12, is essential for erythropoiesis (Aisya *et al.,* 2022). Folic acid deficiency anaemia in individuals with chronic kidney disease can be caused by folic acid deficits, inflammation, and vitamin deficiencies

(including vitamin B12), as well as by factors such as reduced bone marrow response to erythropoietin (Guagnozzi and Lucendo, 2014). Red blood cell formation and DNA synthesis may be significantly impacted by vitamin B12 deficiency. Reduced thymidine and purine synthesis may result from the deficit, impacting the synthesis of DNA and RNA required for cell division, the creation of red blood cells, and general immunity (Green *et al.,* 2017). Furthermore, microcytic anaemia is one sign of vitamin B12 insufficiency that can conceal the underlying deficit (Means and Fairfield, 2022). The significance of vitamin B12 in preventing such haematological consequences is further highlighted by the fact that severe vitamin B12 deficiency can present as chronic atrophic gastritis that result in haemolytic anaemia (Woodford *et al*., 2021). A prevalent treatment for type-2 diabetes, metformin, has been linked to vitamin B12 insufficiency, which can cause haematological problems and neurological symptoms (Tiwari *et al*., 2023).

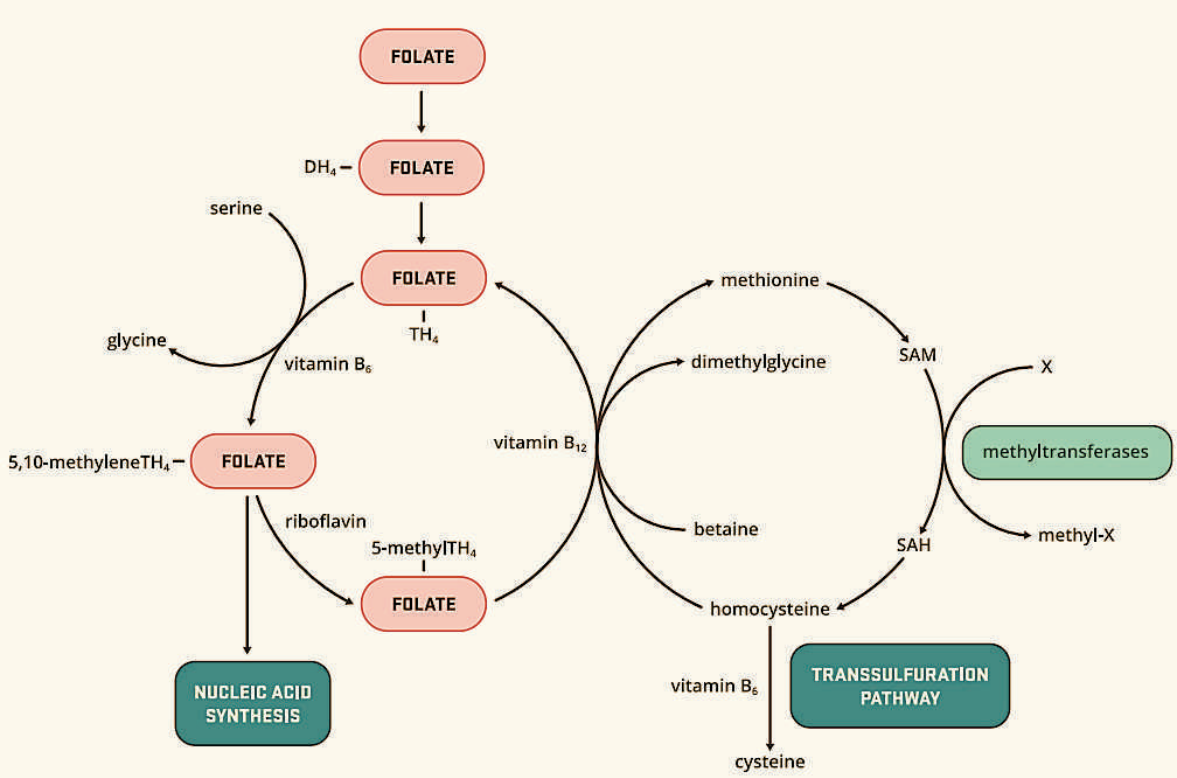

Figure 2: Carbon metabolism during erythropoiesis. The production of red blood cells, known as erythropoiesis, depends on vitamin B12 and folic acid. Methionine regeneration is essential for healthy erythropoiesis, and vitamin B12 functions as a coenzyme in these processes (Modified from Nair, 2011).

3.3 Participation of Folic Acid in DNA synthesis and Cell Division:

Folic acid, sometimes referred to as vitamin B9, is an essential part of many cellular functions, especially those related to amino acid and RNA metabolism, DNA synthesis, repair, and methylation. It is a cofactor for vital biological processes, such as DNA synthesis, which transfers single-carbon units required for cell division (Shulpekova et al., 2021). Because it mediates DNA synthesis, modification, repair, and gene expression control, this vitamin is essential for cell development and division (Rakha et al., 2022). Furthermore, because it promotes the transfer of one-carbon units, which are essential for regular metabolism and regulation of folic acid, very essential for nucleotide synthesis, DNA repair, and epigenetic changes (Liu et al., 2020). Folic acid is important because it plays a role in stem cell and neural

development. Through one-carbon metabolism, folic acid is necessary for DNA synthesis and methylation, which affects oocyte maturation, pre-implantation embryo development, and wound healing (Fig. 2) (Shulpekova *et al.,* 2021). Folic acid is essential for many physiological processes, and a lack of it can also negatively impact neurobehavioral development and cognitive function (Quehl, 2015). By controlling DNA methylation, folic acid affects several biological functions, such as monocyte function and the onset of atherosclerosis (Napiórkowska-Baran *et al.,* 2023). Furthermore, it has been demonstrated that folic acid affects granulosa cell survival via interacting with the AhR pathway (Francis *et al.,* 2019).

4.0 Haematinics Interaction with Enzymes and other Cellular Processes

Haematin, a porphyrin molecule that contains iron, is essential for many biological functions, including the storage and transportation of oxygen and the malarial parasite's ability to operate (Srinivas and Senthil, 2024). Antimalarial drugs, especially those based on quinolines, cause the parasite to die by interfering with its ability to crystallise haematin into hemozoin (Aguiar *et al.,* 2018). To activate enzymes such as galactose oxidase, haematin and copper II have a role in regulating the production of radicals (Chen *et al.,* 2023). Additionally, the antimalarial action of some substances, including tryptanthrin, which interfere with Plasmodium glycolysis enzyme pathways and hinder heme detoxification, depends critically on interactions with haematin (Jampilek, 2017). Furthermore, the malaria parasite uses the detoxification mechanism of hemozoin, also called β-hematin, to transform heme into a harmless crystalline form that facilitates its removal (El Saftawy *et al.,* 2024).

Human erythrocytes undergo spherization and haemolysis due to haematin and haemin, which are unaffected by the amount of calcium outside the cell (Mikhailova *et al.,* 2024).

5.0 Drug Interaction

5.1 Haematinics interaction with other Medications:

Haematin, a key ingredient in the treatment of malaria, interacts in different ways with different drugs. Haematin and antimalarial medications frequently interact, impacting heme aggregation and β-hematin production (de Villiers and Egan, 2021). For example, porphyrins, like modern antimalarial medications, use π-π stacking interactions to prevent the synthesis of β-hematin (Isaac-Lam and Nguyen, 2023). Furthermore, it has been demonstrated that metal-amodiaquine complexes inhibit the production of haematin crystals by interacting with haematin via π-π stacking interactions (Colina-Vegas *et al.,* 2023). Furthermore, a great deal of research has been done on the relationship between antimalarial medications and haematin utilising methods such mass spectrometry, Raman spectroscopy, NMR, and EXAFS spectroscopy (Valadbeigi and Causon, 2024). These investigations have shown that when haematin binds to antimalarial medications, its molecular structure undergoes substantial alterations that result in different peak heights and locations in the spectra (Wolf *et al.,* 2024).

Additionally, it has been proposed that treating haematinic deficiencies with dietary supplements or in conjunction with other medications can improve the therapeutic effects of illnesses such as oral lichen planus (Lucchese *et al.,* 2023). Like chloroquine, transition metal complexes have also been shown to bind with haemin and limit the production of β-haematin (Mandal *et al.,* 2023).

6.0 Clinical Uses

Chronic illnesses, cancers, chronic kidney disease (CKD), and vitamin deficiencies are some of the underlying causes of anaemia. To effectively treat anaemia, the exact cause must be addressed. Iron, folate, and vitamin B12 deficiencies are examples of micronutrient deficient that are used frequently to treat anaemia, to improve patient outcomes (Borgmeier *et al.,* 2022). To diagnose and treat anaemia, especially iron deficient anaemia, serum ferritin levels are essential (Maikap *et al.,* 2024). Hypoxia-inducible factor-prolyl hydroxylase inhibitors have demonstrated potential in the treatment of anaemia in chronic kidney disease (CKD) by promoting the

generation of endogenous erythropoietin (Ogawa *et al.,* 2023). Furthermore, by stabilising the HIF-α subunit and promoting erythropoiesis, medications such as Daprodustat have been successful in treating anaemia in CKD patients (Singh *et al.,* 2021). The link between Helicobacter pylori infection and pernicious anaemia emphasises how crucial it is to take these infections into account while diagnosing and treating autoimmune gastritis and associated anaemia (Allakky, 2023). It has been demonstrated that iron replacement therapy is an effective treatment for anaemia and iron deficiency in individuals suffering from heart failure and atrial fibrillation (Trohman *et al.,* 2023). Men's active participation in sickle cell anaemia management can have a major impact on the quality of life for those who are afflicted (Obeagu & Obeagu, 2024). Blood transfusions, especially donor red blood cell transfusions, are essential for treating anaemia in cancer patients, regardless of the cause (Fischer *et al.,* 2019). Traditional treatments like immunosuppression or therapeutic plasma exchange may not work as well in situations with haemolytic anaemia linked to cancer, thus specialised strategies are needed to address the unique underlying mechanisms (Thomas and Scully, 2021).

Other Conditions Requiring Haematinics Supplementation

Haematinics are necessary to avoid anaemia and maintain normal haemoglobin levels. Supplementing with haematinics may be required to resolve deficits and normalise haematological parameters in some situations, such as pregnancy, recurrent aphthous stomatitis, oral lichen planus, HIV infection, and porphyria (Chiang *et al.,* 2019). A diet high in haematinics and appropriate education can help lower the risk of anaemia in expectant mothers (Siu and Force, 2015). To maximise neurological recovery in cases of severe neuropathies linked to disorders like porphyria, preventive or long-term haematinic dosage may be necessary (Abrahams, 2022). Furthermore, removing triggering factors is essential in acute porphyric attacks (Alqwaifly *et al.,* 2019).

7.0 Limitations of Haematinics

Numerous research has emphasized on the effectiveness, difficulties in diagnosing, and biochemical interactions of haematinics; substances that increase the formation of blood cells or improve the quality of blood:

1. The absence of standardised laboratory assays for evaluating haematinic deficits is a major drawback. Despite their usefulness, current tests frequently fall short of the sensitivity and specificity needed for standard clinical practice. For example, holotranscobalamin II measurement and other indicators like methylmalonic acid and total homocysteine are recommended for additional research, suggesting that current techniques might not fully reflect the complexity of a patient's haematinic state (Bao *et al.,* 2020). This restriction may result in incorrect diagnosis or postponed treatment, especially for diseases like anaemia when prompt action required.
2. The way haematinics interact with other biochemical substances can complicate their effectiveness. For instance, it has been demonstrated that the well-known antimalarial drug chloroquine inhibits the crystallisation of β-hematin, a form of heme that can accumulate in certain diseases like malaria. Chloroquine's effectiveness depends on its concentration and the particular conditions of the environment in which it is used (Ketchum *et al.,* 2023). This suggests that although haematinics can be helpful, aspects like solubility and the presence of competing substances may limit their effectiveness.
3. Methodological restrictions may make it more difficult to use haematinics practically in clinical settings. For example, because of its practical difficulties, the alkaline haematin technique, which is regarded as the gold standard for assessing menstrual blood loss, is mostly limited to research settings (Magnay *et al.,* 2018). This drawback emphasises the necessity of more approachable and trustworthy techniques to assess haematinic levels in a range of groups.
4. Additionally, research has shown that although several haematinics have the potential to improve blood quality, their modes of action might differ greatly. For instance, certain drugs' suppression of β-

haematin production can result in varying treatment effects, making it difficult to determine how beneficial they are overall (Kumar *et al.,* 2011; Manohar *et al.,* 2014). Because of this heterogeneity, the use of haematinics in clinical practice requires a more nuanced approach, as the same substance may provide various results depending on the situation.

8.0 Adverse Effect of Haematinics

Haematopoietic agents, especially haematinics, are used extensively in clinical settings to treat anaemia and other haematological disorders. However, their use is not without potential side effects, which can vary depending on the specific agent used, dosage, and patient condition:

1. One major concern is the toxicity associated with haematin and haemin, especially in pathological states, which emphasises that even though albumin has a high affinity for heme derivatives. Conditions like haemorrhagic stroke can result in elevated concentrations of haematin and haemin that are greater than albumin's scavenging capacity. This can have toxic effects, particularly in severe conditions like sepsis, where albumin levels drop due to increased capillary permeability and accelerated catabolism (Zhang *et al.,* 2024).
2. According to Aich *et al.* (2015), haematin can cause the production of reactive oxygen species that mediate lipid peroxidation, which results in cell damage. This further exacerbates the harmful effects of free haematin and haemin by causing haemolysis in erythrocytes.
3. Haematins interactions with other substances have been investigated in relation to the treatment of malaria. According to studies, haematin contributes to the antimalarial action of several medications, such as quinolines and artemisinins, by preventing the synthesis of haemozoin, which is essential for the malaria parasite's survival (Quadros *et al.,* 2022). Developing successful antimalarial treatments requires an understanding of these mechanisms.
4. The use of haematin in patients with underlying conditions requires careful monitoring and management, as it has been linked to the activation of coagulation parameters in porphyria patients, suggesting a possible impact on the haemostatic balance in these individuals (Conran and De Paula, 2020).

Conclusion

Haematinics are essential for blood production since they support haematopoiesis and correct deficits that might cause anaemia and recurring aphthous stomatitis. It has been demonstrated that haematinics raise haemoglobin levels in fish, highlighting their significance in promoting blood health. Moreover, non-anaemic haematinic deficits can affect postoperative anaemia recovery and preoperative haemoglobin optimisation, underscoring the wider consequences of these deficiencies beyond anaemia. The various ways that haematinics can affect blood cell synthesis are demonstrated that haematinics can promote haematopoiesis by improving progenitor responsiveness. Additionally, the way that iron protoporphyrins, such as heme, interact with antimalarial medications shows the variety of functions these substances have in biological processes other than the creation of blood.

Reference

Abrahams, L. (2022). Hemin, Erythropoietin and Antithrombotics to Treat Covid-19.

Aguiar, A. C., Murce, E., Cortopassi, W. A., Pimentel, A. S., Almeida, M. M., Barros, D. C., Guedes, J. S., Meneghetti, M. R. and Krettli, A. U. (2018). Chloroquine Analogs as Antimalarial Candidates with Potent in Vitro and in Vivo Activity. International Journal for Parasitology: Drugs and Drug Resistance; 8(3): 459-464.

Aich, A., Freundlich, M. and Vekilov, P. G. (2015). The Free Heme Concentration in Healthy Human Erythrocytes. Blood Cells, Molecules, and Diseases; 55(4): 402-409.

Aisya, M., Rachmawati, H., Hasmono, D. and Kusumaningtyas, A. P. (2022). The Use of Folic Acid in Chronic Kidney Disease Patients with Anemia. KnE Medicine: 50–59-50–59.

Allakky, A. (2023). Exploring the Association of Helicobacter Pylori with Anti-Intrinsic

Factor and Anti-Parietal Cell Antibodies in Pernicious Anemia: A Systematic Review. Cureus; 15(9):e45887

Alqwaifly, M., Bril, V. and Dodig, D. (2019). Acute Intermittent Porphyria: A Report of 3 Cases with Neuropathy. Case Reports in Neurology; 11(1): 32-36.

Andrés, C. M. C., Pérez de la Lastra, J. M., Juan, C. A., Plou, F. J. and Pérez-Lebeña, E. (2024). Antioxidant Metabolism Pathways in Vitamins, Polyphenols, and Selenium: Parallels and Divergences. International Journal of Molecular Sciences; 25(5): 2600.

Aoto, P. C., Stanfield, R. L., Wilson, I. A., Dyson, H. J. and Wright, P. E. (2019). A Dynamic Switch in Inactive P38γ Leads to an Excited State on the Pathway to an Active Kinase. Biochemistry; 58(51): 5160-5172.

Auparakkitanon, S., Chapoomram, S., Kuaha, K., Chirachariyavej, T. and Wilairat, P. (2006). Targeting of Hematin by the Antimalarial Pyronaridine. Antimicrobial Agents and Chemotherapy; 50(6): 2197-2200.

Bao, C., Tao, X., Cui, W., Yi, B., Pan, T., Young, K. H. and Qian, W. (2020). Sars-Cov-2 Induced Thrombocytopenia as an Important Biomarker Significantly Correlated with Abnormal Coagulation Function, Increased Intravascular Blood Clot Risk and Mortality in Covid-19 Patients. Experimental Hematology & Oncology; 9: 1-8.

Bensky, M. J., Ayalon-Dangur, I., Ayalon-Dangur, R., Naamany, E., Gafter-Gvili, A., Koren, G. and Shiber, S. (2019). Comparison of Sublingual Vs. Intramuscular Administration of Vitamin B12 for the Treatment of Patients with Vitamin B12 Deficiency. Drug Delivery and Translational Research; 9: 625-630.

Borgmeier, E., Lawrence, H., Morton, C. and McEvoy, M. D. (2022). Perioperative Anemia Management. International Anesthesiology Clinics; 60(1): 1-7.

Breymann, C., Milman, N., Mezzacasa, A., Bernard, R., Dudenhausen, J. and investigators, F.-A. (2017). Ferric Carboxymaltose Vs. Oral Iron in the Treatment of Pregnant Women with Iron Deficiency Anemia: An International, Open-Label, Randomized Controlled Trial (Fer-Asap). Journal of Perinatal Medicine; 45(4): 443-453.

Brody, T. (1999). Classification of Biological Structure. Academic Press: San Diego, CA, USA: 1-56.

Buratti, P., Gammella, E., Rybinska, I., Cairo, G. and Recalcati, S. (2015). Recent Advances in Iron Metabolism: Relevance for Health, Exercise, and Performance. Medical Science Sports and Exercise; 47(8): 1596-1604.

Chen, Y., Zou, J., Ji, P. and Feng, W. (2023). Hematin and Cuii Control Generations of Hydroperoxyl and Superoxide Radicals to Activate Galactose Oxidase for 5-Hydroxymethylfurfural Conversion. Iscience; 26(12):

Chiang, C.-P., Chang, J. Y.-F., Wang, Y.-P., Wu, Y.-H., Wu, Y.-C. and Sun, A. (2019). Recurrent Aphthous Stomatitis–Etiology, Serum Autoantibodies, Anemia, Hematinic Deficiencies, and Management. Journal of the Formosan Medical Association; 118(9): 1279-1289.

Colina-Vegas, L., da Cruz B. Silva, M., de Souza Pereira, C., Isis Barros, A., Araujo Nobrega, J., Navarro, M., Rottmann, M., D'Alessandro, S., Basilico, N. and Azevedo Batista, A. (2023). Antimalarial Agents Derived from Metal-Amodiaquine Complexes with Activity in Multiple Stages of the Plasmodium Life Cycle. Chemistry–A European Journal; 29(55): e202301642.

Conran, N. and De Paula, E. V. (2020). Thromboinflammatory Mechanisms in Sickle Cell Disease–Challenging the Hemostatic Balance. Haematologica; 105(10): 2380.

Czempik, P. F. and Wiórek, A. (2023). Iron Deficiency in Sepsis Patients Managed with Divided Doses of Iron Dextran: A Prospective Cohort Study. Scientific Reports; 13(1): 5264.

de Villiers, K. A. and Egan, T. J. (2021). Heme Detoxification in the Malaria Parasite: A Target for Antimalarial Drug Development. Accounts of Chemical Research; 54(11): 2649-2659.

Del Bo, C., Riso, P., Gardana, C., Brusamolino, A., Battezzati, A. and Ciappellano, S. (2019). Effect of Two Different Sublingual

Dosages of Vitamin B12 on Cobalamin Nutritional Status in Vegans and Vegetarians with a Marginal Deficiency: A Randomized Controlled Trial. Clinical Nutrition; 38(2): 575-583.

Dhar, R., Chanock, R. M. and Lai, C.-J. (1980). Nonviral Oligonucleotides at the 5' Terminus of Cytoplasmic Influenza Viral Mrna Deduced from Cloned Complete Genomic Sequences. Cell; 21(2): 495-500.

Di Costanzo, M., Morelli, M., Malamisura, M., Puoti, M. G. and Berni Canani, R. (2016). Immunodeficiency Disorders Resulting in Malabsorption. Textbook of Pediatric Gastroenterology, Hepatology and Nutrition: A Comprehensive Guide to Practice: 425-436.

Dusek, P., Hofer, T., Alexander, J., Roos, P. M. and Aaseth, J. O. (2022). Cerebral Iron Deposition in Neurodegeneration. Biomolecules; 12(5): 714.

El Saftawy, E., Farag, M. F., Gebreil, H. H., Abdelfatah, M., Aboulhoda, B. E., Alghamdi, M., Albadawi, E. A. and Abd Elkhalek, M. A. (2024). Malaria: Biochemical, Physiological, Diagnostic, and Therapeutic Updates. Peer Journal; 12: e17084.

Erdem, M. G. (2022). Ferric Carboxymaltose Versus Ferrous Glycine Sulfate for Treatment of Iron Deficiency Anemia and Their Effect on Vitamin B12 and Folic Acid: A Retrospective Study. Archives of Clinical and Experimental Medicine; 7(3): 56-60.

Fang, H., Kang, J. and Zhang, D. (2017). Microbial Production of Vitamin B 12: A Review and Future Perspectives. Microbial Cell Factories; 16: 1-14.

Fischer, D., Neb, H., Choorapoikayil, S., Zacharowski, K. and Meybohm, P. (2019). Red Blood Cell Transfusion and Its Alternatives in Oncologic Surgery—a Critical Evaluation. Critical Reviews in Oncology/Hematology; 134: 1-9.

Francis, F., Raji Kanakkaparambil, R. P., Mankuzhy, P. and Vazhur, B. Vitamin B12 and Folic Acid Impact on Tcdd-Treated Granulosa Cell Viability.

Froese, D. S., Fowler, B. and Baumgartner, M. R. (2019). Vitamin B12, Folate, and the Methionine Remethylation Cycle—Biochemistry, Pathways, and Regulation. Journal of Inherited Metabolic Disease; 42(4): 673-685.

Frost, J. N., Tan, T. K., Abbas, M., Wideman, S. K., Bonadonna, M., Stoffel, N. U., Wray, K., Kronsteiner, B., Smits, G. and Campagna, D. R. (2021). Hepcidin-Mediated Hypoferremia Disrupts Immune Responses to Vaccination and Infection. Medicine; 2(2): 164-179. e112.

Glueck, C. J. (1983). Therapy of Familial and Acquired Hyperlipoproteinemia in Children and Adolescents. Preventive Medicine; 12(6): 835-847.

Green, R., Allen, L. H., Bjørke-Monsen, A.-L., Brito, A., Guéant, J.-L., Miller, J. W., Molloy, A. M., Nexo, E., Stabler, S. and Toh, B.-H. (2017). Vitamin B12 Deficiency. Nature reviews Disease Primers; 3(1): 1-20.

Guagnozzi, D. and Lucendo, A. J. (2014). Anemia in Inflammatory Bowel Disease: A Neglected Issue with Relevant Effects. World Journal of Gastroenterology (WJG), 20(13): 3542.

Health, N. I. O. and Health, N. I. O. (2017). Office of Dietary Supplements. Niacin Fact Sheet for Health Professionals. Available online: https://ods. od. nih. gov/factsheets/Niacin-HealthProfessional (Accessed on 24 January 2022):

Hendler, S. and Rorvik, D. (2008). Pdr for Nutritional Supplements. Montvale: Physicians' Desk Reference. In: Inc.

Hoenemann, C., Ostendorf, N., Zarbock, A., Doll, D., Hagemann, O., Zimmermann, M. and Luedi, M. (2021). Reticulocyte and Erythrocyte Hemoglobin Parameters for Iron Deficiency and Anemia Diagnostics in Patient Blood Management. A Narrative Review. Journal of Clinical Medicine; 10(18): 4250.

Hurrell, R. and Egli, I. (2010). Iron Bioavailability and Dietary Reference Values. The American journal of clinical nutrition, 91(5): 1461S-1467S.

Intakes, S. C. O. t. S. E. O. D. R., Interpretation, S.O., Intakes, U. O. D. R., Nutrients, S. o. U. R. L. O. and Micronutrients, P. O. (2002). Dietary Reference Intakes for Vitamin a, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese,

Molybdenum, Nickel, Silicon, Vanadium, and Zinc, National Academies Press.

Isaac-Lam, M. F. and Nguyen, T. (2023). Photodynamic Therapy Applications in Cancer, Infections and Cardiovascular Diseases. TTU Journal of Biomedical Sciences; 2(1): 9-28.

Jampilek, J. (2017). Design of Antimalarial Agents Based on Natural Products. Current Organic Chemistry; 21(18): 1824-1846.

Jha, R. K., Kanyal, D., Devi, R. and Butola, L. K. (2021). Vitamin B12 Deficiency and Psychiatric Manifestations-a Consise Review. Indian Journal of Forensic Medicine & Toxicology; 15(3): 2664-2667.

Kavilapurapu, A. (2018). A Comparative Study of Efficacy of Intravenous Iron Sucrose to Oral Ferrous Sulphate in Moderate Iron Deficiency Anaemia in Paediatric Population. Rajiv Gandhi University of Health Sciences (India),

Ketchum, F. B., Erickson, C. M., Basche, K. E., Chin, N. A., Rosario, H. L., Johnson, S. C. and Clark, L. R. (2023). Informing Disclosure: Efficacy of a Brief Educational Intervention on Research Participants' Knowledge About Alzheimer's Disease Biomarkers. Journal of Alzheimer's Disease,(Preprint): 1-8.

Kumar, A., Srivastava, K., Kumar, S. R., Siddiqi, M., Puri, S. K., Sexana, J. K. and Chauhan, P. M. (2011). 4-Anilinoquinoline Triazines: A Novel Class of Hybrid Antimalarial Agents. European Journal of Medicinal Chemistry; 46(2): 676-690.

Lee, E. H., Otoukesh, S. and Nagaraj, G. (2019). Hemolytic Anemia of Malignancy: A Case Study Involving Signet Ring Cell Metastatic Breast Cancer with Severe Microangiopathic Hemolytic Anemia. Case Reports in Oncology; 12(1): 104-108.

Li, J., Zhang, Q., Zhang, N. and Guo, L. (2020). Increased Brain Iron Deposition in the Putamen in Patients with Type 2 Diabetes Mellitus Detected by Quantitative Susceptibility Mapping. Journal of Diabetes Research; 2020(1): 7242530.

Liu, H.-Y., Liu, S.-M. and Zhang, Y. Z. (2020). Maternal Folic Acid Supplementation Mediates Offspring Health Via DNA Methylation. Reproductive Sciences; 27(4): 963-976.

Lucchese, A., Di Stasio, D., De Stefano, S., Nardone, M. and Carinci, F. (2023). Beyond the Gut: A Systematic Review of Oral Manifestations in Celiac Disease. Journal of Clinical Medicine; 12(12): 3874.

Magnay, J. L., O'Brien, S., Gerlinger, C. and Seitz, C. (2018). A Systematic Review of Methods to Measure Menstrual Blood Loss. BMC Women's Health; 18: 1-13.

Maikap, A., Roy, B., De, N., Samanta, S. and Chakraborty, S. (2024). Paper Strips Functionalized with a Mixture of Zno Nanotubes and Mn3o4 Nanoparticles for Simultaneous Separation of Blood Plasma and Detection of Physiological Iron Levels. ACS Applied Nano Materials:

Malanda, E. M. d. O. (2018). Tradução Para Português De "Chronic Kidney Disease (Ckd): Clinical Practice Recommendations for Primary Care Physicians and Healthcare Providers". Universidade de Évora,

Mandal, A., Kushwaha, R., Mandal, A. A., Bajpai, S., Yadav, A. K. and Banerjee, S. (2023). Transition Metal Complexes as Antimalarial Agents: A Review. ChemMedChem; 18(19): e202300326.

Manohar, S., Tripathi, M. and S Rawat, D. (2014). 4-Aminoquinoline Based Molecular Hybrids as Antimalarials: An Overview. Current Topics in Medicinal Chemistry; 14(14): 1706-1733.

Means, R. and Fairfield, K. M. (2022). Clinical Manifestations and Diagnosis of Vitamin B12 and Folate Deficiency. Up to Date. Available online: https://www. uptodate. com/contents/clinical-manifestations-and-diagnosis-of-vitamin-b12-and-folate-deficiency (accessed on 30 November 2021):

Mikhailova, D. M., Skverchinskaya, E., Sudnitsyna, J., Butov, K. R., Koltsova, E. M., Mindukshev, I. V. and Gambaryan, S. (2024). Hematin-and Hemin-Induced Spherization and Hemolysis of Human Erythrocytes Are Independent of Extracellular Calcium Concentration. Cells; 13(6): 554.

Moon, T., Smith, A., Pak, T., Park, B. H., Beutler, S. S., Brown, T., Kaye, A. D. and Urman, R. D. (2021). Preoperative Anemia Treatment

with Intravenous Iron Therapy in Patients Undergoing Abdominal Surgery: A Systematic Review. Advances in Therapy; 38: 1447-1469.

Mucha, P., Kus, F., Cysewski, D., Smolenski, R. T. and Tomczyk, M. (2024). Vitamin B12 Metabolism: A Network of Multi-Protein Mediated Processes. International Journal of Molecular Sciences; 25(15): 8021.

Nair, K. M. (2011). Metabolism of Iron, Folic Acid and Vitamin B12. the Book 'Public Health Nutrition in Developing Countries'-Part; 2: 607-636.

Napiórkowska-Baran, K., Schmidt, O., Szymczak, B., Lubański, J., Doligalska, A. and Bartuzi, Z. (2023). Molecular Linkage between Immune System Disorders and Atherosclerosis. Current Issues in Molecular Biology; 45(11): 8780-8815.

Nur'aeny, N. (2024). Recurrent Aphthous Stomatitis: A Review of Hematinic Deficiency Factor. European Journal of Theoretical and Applied Sciences; 2(1): 291-297.

Nutrients, S. o. U. R. L. o., Intakes, S. C. o. t. S. E. o. D. R., Folate, i. P. o., Vitamins, O. B. and Choline. (2000). Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B6, Folate, Vitamin B12, Pantothenic Acid, Biotin, and Choline.

Obeagu, E. and Obeagu, G. (2024). The Role of Parents: Strengthening Adolescent Education for Sickle Cell Disease Prevention. Elite Journal of Public Health; 2(1): 15-21.

Ogawa, C., Tsuchiya, K. and Maeda, K. (2023). Hypoxia-Inducible Factor Prolyl Hydroxylase Inhibitors and Iron Metabolism. International Journal of Molecular Sciences; 24(3): 3037.

Orhan Kiliç, B., Kiliç, S., Şahin Eroğlu, E., Gül, E. and Belen Apak, F. B. (2021). Sublingual Methylcobalamin Treatment Is as Effective as Intramuscular and Peroral Cyanocobalamin in Children Age 0–3 Years. Hematology; 26(1): 1013-1017.

Palazzuoli, A., Antonelli, G. and Nuti, R. (2011). Anemia in Cardio-Renal Syndrome: Clinical Impact and Pathophysiologic Mechanisms. Heart Failure Reviews; 16: 603-607.

Pawluczkowycz, A. W., Lindorfer, M. A., Waitumbi, J. N. and Taylor, R. P. (2007). Hematin Promotes Complement Alternative Pathway-Mediated Deposition of C3 Activation Fragments on Human Erythrocytes: Potential Implications for the Pathogenesis of Anemia in Malaria. The Journal of Immunology; 179(8): 5543-5552.

Quadros, H. C., Silva, M. C. and Moreira, D. R. (2022). The Role of the Iron Protoporphyrins Heme and Hematin in the Antimalarial Activity of Endoperoxide Drugs. Pharmaceuticals; 15(1): 60.

Quehl, R. (2015). Food and Mood: An Investigation into the Association between Diet Quality and Depressive Symptoms. University of Guelph,

Rakha, S. I., Elmetwally, M. A., El-Sheikh Ali, H., Balboula, A., Mahmoud, A. M. and Zaabel, S. M. (2022). Importance of Antioxidant Supplementation During in Vitro Maturation of Mammalian Oocytes. Veterinary Sciences; 9(8): 439.

Rizzo, G. and Laganà, A. S. (2020). A Review of Vitamin B12. Molecular nutrition: 105-129.

Rochaix, J.-D. (2011). Regulation of Photosynthetic Electron Transport. Biochimica et Biophysica Acta (BBA)-Bioenergetics; 1807(3): 375-383.

Ross, A. C., Caballero, B., Cousins, R. J. and Tucker, K. L. (2020). Modern Nutrition in Health and Disease, Jones & Bartlett Learning.

Sagar, V., Kumar, M., Rawat, R., Kumar, P., Kumar, G. and Yadav, S. K. (2022). To Determine the Correlation of Severity of Thrombocytopenia, with Vitamin B12 Deficiency in Patients of Dengue Fever. International Journal of Health Sciences;(II): 5579-5590.

Sahid, E. N. M. (2016). Reticulocyte Haemoglobin Equivalent (Ret-He): Establishing Reference Interval and Comparison of Ret-He Cut-Off Value in Iron Deficiency Anaemia and Anaemia in Chronic Kidney Disease. University of Malaya (Malaysia),

Shulpekova, Y., Nechaev, V., Kardasheva, S., Sedova, A., Kurbatova, A., Bueverova, E., Kopylov, A., Malsagova, K., Dlamini, J. C. and Ivashkin, V. (2021). The Concept of

Folic Acid in Health and Disease. Molecules; 26(12): 3731.

Singh, A. K., Carroll, K., McMurray, J. J., Solomon, S., Jha, V., Johansen, K. L., Lopes, R. D., Macdougall, I. C., Obrador, G. T. and Waikar, S. S. (2021). Daprodustat for the Treatment of Anemia in Patients Not Undergoing Dialysis. New England Journal of Medicine; 385(25): 2313-2324.

Siu, A. L. and Force*, U. P. S. T. (2015). Screening for Iron Deficiency Anemia and Iron Supplementation in Pregnant Women to Improve Maternal Health and Birth Outcomes: Us Preventive Services Task Force Recommendation Statement. Annals of Internal Medicine; 163(7): 529-536.

Srinivas, S. and Senthil Kumar, A. (2024). Electrical Wiring of Malarial Parasite Intermediate Hematin on a Tailored N-Doped Carbon Nanomaterial Surface and Its Bioelectrocatalytic Hydrogen Peroxide Reduction and Sensing. Langmuir:

Thomas, M. and Scully, M. (2021). How I Treat Microangiopathic Hemolytic Anemia in Patients with Cancer. Blood, The Journal of the American Society of Hematology; 137(10): 1310-1317.

Tiwari, V., Tiwari, A., Singh, G. and Singh, M. K. (2023). Immune Response against Helminths. Parasitic Infections: Immune Responses and Therapeutics: 100-123.

Trohman, R. G., Huang, H. D. and Sharma, P. S. (2023). Atrial Fibrillation: Primary Prevention, Secondary Prevention, and Prevention of Thromboembolic Complications: Part 1. Frontiers in Cardiovascular Medicine; 10: 1060030.

Ul Hassan, Z., Ali, S., Rizwan, M., Ali, Q., Haider, M. Z., Adrees, M. and Hussain, A. (2017). Role of Iron in Alleviating Heavy Metal Stress. Essential Plant Nutrients: Uptake, Use Efficiency, and Management: 335-350.

Valadbeigi, Y. and Causon, T. (2024). Computational and Experimental Im-Ms Determination of the Protonated Structures of Antimalarial Drugs. Journal of American Society of Mass Spectrometry;35(8):1930-1939.

Varkal, M. A. and Karabocuoglu, M. (2021). Efficiency of the Sublingual Route in Treating B12 Deficiency in Infants. International Journal for Vitamin and Nutrition Research:

Watanabe, F. and Bito, T. (2018). Vitamin B12 Sources and Microbial Interaction. Experimental Biology and Medicine; 243(2): 148-158.

Watanabe, F., Yabuta, Y., Tanioka, Y. and Bito, T. (2013). Biologically Active Vitamin B12 Compounds in Foods for Preventing Deficiency among Vegetarians and Elderly Subjects. Journal of Agricultural and Food Chemistry; 61(28): 6769-6775.

Weiss, G., Ganz, T. and Goodnough, L. T. (2019). Anemia of Inflammation. Blood, The Journal of the American Society of Hematology; 133(1): 40-50.

Wiesinger, H., Eydeler, U., Richard, F., Trummer, D., Blode, H., Rohde, B. and Diefenbach, K. (2012). Bioequivalence Evaluation of a Folate-Supplemented Oral Contraceptive Containing Ethinylestradiol/Drospirenone/Levomefolate Calcium Versus Ethinylestradiol/Drospirenone and Levomefolate Calcium Alone. Clinical Drug Investigation; 32: 673-684.

Wolf, S., Domes, R., Domes, C. and Frosch, T. (2024). Spectrally Resolved and Highly Parallelized Raman Difference Spectroscopy for the Analysis of Drug–Target Interactions between the Antimalarial Drug Chloroquine and Hematin. Analytical Chemistry; 96(8): 3345-3353.

Woodford, A. M., Chaudhry, R., Conte, G. A., Gupta, V. and Anne, M. (2021). Chronic Atrophic Gastritis Presenting as Hemolytic Anemia Due to Severe Vitamin B12 Deficiency. Case Reports in Hematology; 2021(1): 9571072.

Yusuf, A., Almotairy, A. R. Z., Henidi, H., Alshehri, O. Y. and Aldughaim, M. S. (2023). Nanoparticles as Drug Delivery Systems: A Review of the Implication of Nanoparticles' Physicochemical Properties on Responses in Biological Systems. Polymers; 15(7): 1596.

Zhang, H., Zhabyeyev, P., Wang, S. and Oudit, G. Y. (2019). Role of Iron Metabolism in Heart Failure: From Iron Deficiency to Iron

Overload. Biochimica et Biophysica Acta (BBA)-Molecular Basis of Disease; 1865(7): 1925-1937.

Zhang, J., Lin, D., Wu, Y., Chen, L., Ma, Z., Wu, M., Liu, X., Zhang, Y. and Cao, H. (2024). Blood-Supplementing Effect of Low Molecular Weight Peptides of E-Jiao on Chemotherapy-Induced Myelosuppression: Evaluation of Pharmacological Activity and Identification of Bioactive Peptides Released in Vivo. Frontiers in Pharmacology; 15: 1366407.

Citation: Ibrahim Kalle Kwaifa, and Ukashat Almustapha. Haemopoeitic Potential of Haematinics, Limitation and Adverse Effects: An Update. ***Sokoto Journal of Medical Laboratory Science*; 9(4): 215 – 228.** https://dx.doi.org/10.4314/sokjmls.v9i4.23