

CHAPTER 5: DISCUSSION

5.1 Systematic Review

a) Beneficial Effects of Date Palm (*Phoenix dactylifera*) in Iron Deficiency Anaemia

The systematic review focused on the beneficial effects of date palm in IDA. *Phoenix dactylifera* is known to possess numerous medicinal properties (Baliga *et al.*, 2011; Vayalil, 2012). However, there is very limited information reported on the effects of *Phoenix dactylifera* on haematological disorders. This review found a small number of studies that investigated the effects of date palm extract on haemopoietic activity in IDA.

The inclusion of date palm in the animal diet was proven to increase the haemoglobin, red blood cell counts, packed cell volume and platelet counts. The increment in haemoglobin was associated with an increase in red blood cell counts. It is believed that the high iron content in date palm plays a major contribution to this (Onuh *et al.*, 2012; Zen *et al.*, 2013; Abdelsalam *et al.*, 2014). The iron content in various types of date palm such as Kalas date (1.75 mg/ 100 g), Gondaila date (6.48 mg/ 100 g), Madini date (6.91 mg / 100 g), Lulu date (6.8 mg/ 100 g) and Sukkary date (2.3 mg/ 100 g) was discovered and reported by many researchers (Ali-Mohamed & Khamis, 2004; Elleuch *et al.*, 2008). Erythroid precursors need much more iron than any other type of cells in the body. They take up iron through transferrin. Iron is required for the formation of heme that is part of haemoglobin (Waldvogel-Abramowski *et al.*, 2014). The content of protein, carbohydrates and

fat in date palms extract support the hemoglobin synthesis process (Sotolu *et al.*, 2011). Carbohydrates and fats form Succinyl CoA which further along with glycine to form protoporphyrin. Protoporphyrin formation together with heme molecules and globin chain will form haemoglobin. To date, they were no physiological explanations for the significant increase in platelet count in the subjects when given date palm extract (Abdelsalam *et al.*, 2014).

Iron deficiency anaemia treatment usually involves consumption of iron supplements, diet alteration and treatment of the underlying disease such as chronic blood loss due to peptic ulcer, hiatal hernia and colorectal cancer in order to increase iron levels. The most commonly prescribed supplements are ferrous sulphate and ferrous fumarate tablet, commonly taken twice a day. Severe iron-deficiency anaemia may require a blood transfusion, intramuscular iron injections, or intravenous (IV) iron therapy (WHO, 2001).

Supplementing pregnant ewes at the late stage of pregnancy with probiotic cow milk alone and a mixture of cow's milk and dates extract would not increase the haemoglobin concentration in blood as much as treatment with dates extract alone (Abdelsalam *et al.*, 2014). These suggest that treating anaemia with dates extract would be better if it is taken alone without mixing it with probiotic cow's milk. Studies of nutritive components of food have shown that calcium derived from cow's milk strongly inhibits the absorption of iron in the diet (Hallberg *et al.*, 1991). Zen *et al.*, (2013) reported that the increase in haemoglobin level was more remarkable when treated with higher concentration of date palm extract. Therefore, treating anaemia would be more effective when the subject is given dates extract alone with 100% concentration. The result obtained by Onuh *et al.*, (2012) revealed

a significant dosage dependent increase in haemoglobin and red blood cell count in both groups treated with aqueous and methanolic extract when compared with the control. This suggests that the improvement of the haemopoietic activities in IDA when treated with date palm extract is dose related.

We identified several knowledge gaps in the currently available reports. There were very few experimental studies looking at the effects of date palm on IDA. It is noted that the available studies only reported on the effects of improvements in haemoglobin level, red blood cell count and packed cell volume. There were no reports on the effects of date palm on the functional iron and iron storage. There was also no report on the mechanism of iron absorption when IDA subjects were treated with date palm. The experimental studies state that high iron content in the dates extract is responsible for the increase of the haemoglobin level in the blood samples (Onuh *et al.*, 2012; Zen *et al.*, 2013; Abdelsalam *et al.*, 2014). However, none of them provides valid experimental data and design in terms of iron absorption by the animal's digestive system that could support this conclusion.

Date palm contained a lot of other biochemical components such as tannin, folic acid, amino acid, ascorbic acids and phenol (Okwu, 2004; Abdelsalam *et al.*, 2014). Some of these components may be responsible for the increment of haemoglobin. Components like ascorbic acid and fructose are known as enhancers of iron absorption while phytate, tannin, casein and calcium are among the known inhibitors. Further study should be carried out to evaluate the interaction between iron and other components present in date palm extracts.

Many studies focused on the biochemical composition of the date palm such as proteins, carbohydrates, amino acids, fatty acids, minerals, vitamins and dietary

fibre (Ali-Mohamed & Khamis, 2004; Elleuch *et al.*, 2008) and the improvement of the haemopoietic activity (Onuh *et al.*, 2012; Zen *et al.*, 2013; Abdelsalam *et al.*, 2014) with the use of dates. All the experiments were conducted in the regions that have a close relation with dates in term of geographical, religion and culture. Currently, there is no experimental study that utilises this treatment on humans. Many researchers focus on *in vivo* studies by using Sprague- Dawley rats (Park *et al.*, 1986) and albino wistar rats (López- Aliaga *et al.*, 2000; Barrionue vo *et al.*, 2002; Alférez *et al.*, 2006; Diaz- Castro *et al.*, 2014). Therefore, it is crucial to perform human studies in order to understand the precise effect of dates extract as food supplementation in IDA. This is due to several significant physiological and biochemical variations between animals and human.

To get a broader understanding of the effects of date palm in IDA, further studies are needed, which looks into more haematological parameters. Further prospective data are also needed to confirm the iron content in date palm extract as well as other biochemical components that may play a role in increasing the haemoglobin level in IDA. It is also important to identify the optimum concentration dosage of date palm extract that would give an optimum result in treating IDA. Studies on the mechanism of iron absorption associated with date palm consumption would be valuable to enhance our understanding regarding this matter.

b) Beneficial Effects of Goat Milk in Iron Deficiency Anaemia

The systematic review is looking at the effects of goat milk in IDA. This review found a small number of studies that investigated the effects of goat milk on haematological parameters in IDA.

The inclusion of goat milk in animal diet was proven to increase the Fe bioavailability, improves haematological parameters by increasing red blood cell count, serum hepcidin and restore Fe content in liver and spleen (Yangilar, 2013; Diaz-Castro *et al.*, 2014). This fact can be explained due to the nutritional characteristics of goat milk. Goat milk contains a higher proportion of soluble proteins (β -lactoglobulin, α -lactoalbumin, and serum albumin), which favours Fe absorption and a higher amount of dietary components capable of reducing Fe (III) to Fe (II), including ascorbic acid and amino acid such as cysteine, forming chelates with Fe, which remain soluble at a higher pH within the small intestine (Pourghassem *et al.*, 2000). Goat milk also contain high amount of vitamin A which is able to mobilize available Fe stores and use them for haemoglobin formation (Park and Haenlein, 2008). Therefore, combination of high Fe supplement and goat milk does not only increase Fe bioavailability but also counter calcium interference. This might be very useful in treating IDA among pregnant women and infant since intake of high calcium diet is very crucial among these groups of people.

Currently all the experiments were focussing on animal study and no human study ever conducted. Therefore it is crucial to perform human study in order to

understand the precise effect of goat milk on IDA. This is due to several significant physiological and biochemical variations between animals and human.

This review identified several reports on the beneficial effect of goat's milk in iron deficiency anaemia. All the reports supported the hypothesis that goat's milk is beneficial in iron deficiency anaemia. Inclusion of goat milk is recommended in the diet of iron deficient anaemic subjects as it increases the haemoglobin regeneration efficiency as well as the iron store. It was also noted that goat milk does not interfere with iron absorption as compared with cow's milk. It also improves the metabolism and digestive utilization of calcium because goat milk richer in medium-chain triglycerides which are rapidly absorbed and metabolised for energy, increasing the synthesis of carrier proteins and thus iron absorption (Diaz *et al.*, 2015). These findings are very useful to improve the management of iron deficiency anaemia in pregnant women and infants as they usually have concurrent iron deficiency anaemia and increased calcium demand.

5.2 Nutritional Analysis

The nutritional analysis revealed that both types of dates (Mariami and Ajwa) were rich in reducing sugar content and had lower content of non-reducing sugar such as sucrose, galactose, lactose and maltose. The goat milk, however, showed no significant content of reducing and non-reducing sugar compared to date palm. Both dates and goat milk were rich in calcium and magnesium. Goat milk fed Ajwa seed is higher in calcium but has lower magnesium content than regular goat milk. The iron content was higher in dates compared to both goat milk. The copper level was higher in Mariami dates compared to Ajwa dates and goat milk fed with Ajwa seeds has higher zinc content than goat milk. The vitamin C level was higher in dates than in goat milk.

Results showed that both date palm varieties were rich in reducing sugar (glucose and fructose). The values were 31.60g/100g (glucose) and 29.5g/100g (fructose) for ajwa date and 32.90g/100g (glucose) and 31.2g/100g (fructose) for Mariami date. At the same time, they presented a weak content of sucrose, galactose, lactose and maltose (all $< 0.50\text{g}/100\text{g}$). In line with this result, the previous study by Mrabet *et al.* (2008) and Bouabidi *et al.* (1996), also suggested that soft dates are rich in reducing sugar and poor in sucrose. In our study, both Ajwa and Mariami dates are rich in carbohydrates, with two monosaccharides, glucose and fructose, as the main reducing sugars. As fructose is twice as sweet as glucose, it plays an important role in the flavour and desirability of the dates. The sugar content results from our study were higher than those found in the previous study reported by Hamad *et al.* (2015), which reports Ajwa date glucose and fructose were 35.4mg/100g and 39.4mg/100g, respectively. However, the previous

study also detected 13.45mg/100g sucrose which was not detected in this study. Looking at the nutritional value of the two dates (Mariami and Ajwa), the differences in sugar could be related to the degree of ripeness with the highest concentration at the Tamr (fully ripe) stage and the area of cultivation with poor moisture (Parvin *et al.*, 2015). Soft date fruit is mainly composed of inverted sugars (fructose and glucose) with little or no sucrose; meanwhile, dry date fruit has a high proportion of sucrose. Dates are flexible, dry date fruit with a delicate texture. Dates have spiritual significance for Muslims worldwide and are mentioned several times in the Quran. They are generally served to break the fast during the holy month of Ramadan. The characteristics of date fruit vary greatly depending on geographical and climatic conditions. Sugars in dates are the most important components as they are a rich source of energy for humans. Reducing sugars such as glucose are easily absorbed during digestion and lead to a rapid rise in blood sugar levels (Parvin *et al.*, 2015). Fructose is twice as sweet as glucose; therefore, it induces a feeling of fullness and may also reduce total calorie intake compared to high-fat foods.

Minerals and vitamins, in general, are important components in bones, teeth, soft tissues, haemoglobin, muscles and nerve cells. Minerals is very important for human cells metabolism (Sawaya *et al.*, 1983). In the current study, several minerals (e.g; magnesium, calcium, zinc) and vitamin (e.g;vitamin C) were identified. Magnesium and calcium are essential for healthy bone development and for energy metabolism, meanwhile, the high potassium and low sodium contents of dates are suitable to be consumed by people with hypertension (Ali *et al.*, 2012). Previous study by Assirey (2015), showed potassium concentration was the highest in date, followed by calcium, magnesium, phosphorus, and sodium, with the lowest

concentration. In this current study also showed the same result; with calcium content is higher than magnesium in both type of date (Mariami and Ajwa). Ajwa and Mariami date palm was found to contain moderate amount of ascorbic acid of 9.80mg/100g and 5.49mg/100g, respectively. Previous studies demonstrated that Tunisian date variety, contains ascorbic acid ranging between 17.7mg/100g to 31.86 mg/100g while Bahraini varieties ranging from 2.0 mg/100g to 6.7mg/100 (Allaith, 2008; Chaira *et al.*, 2009). Vitamin C acts as an antioxidant, protecting tissues from oxidative stress and can therefore play an important role in preventing disease, apart from being a coenzyme that facilitates the physiological process of every cell in our body (Parvin *et al.*, 2015). The differences in mineral and vitamin content in dates fruits might due to variety of date fruits, soil types, and environmental conditions influence, especially magnesium and sodium (Aslam *et al.*, 2019).

In this study, The amount of lactose contained in goat milk was 3.38g/100ml. Glucose, sucrose, galactose, fructose and maltose were not detected. Fresh goat milk contains trace amounts of iron and zinc of 0.90mg and 0.99mg/L, respectively. These results obtained are lower than those previously reported with 1550mg/L calcium and 142mg/L magnesium were detected in fresh goat milk (Moreno-Rojas *et.al*, 1994). The variation in biochemical composition among goat milk is highly depend on genetic variation, environmental conditions and goat farming practices and feeding diet (Al-Suwiegh, 2016).

Although milk is known to be nutritious and possess many health benefits, they are also linked to a number of human health problems, most notably food allergies, for which cow's milk proteins are the main cause. Cow milk allergy is

considered a common condition with a prevalence of 2.5% in children in the first three years of life. Replacing with goat's milk resolved between 30 and 40 % of problem cases, and in one particular study, 49 out of 55 treated children benefited (Park *et al.*, 2008). There are a variety of genetic polymorphisms of the different caseins and whey proteins, which make the situation in cow's milk allergies even more complex and make it difficult to determine which protein is mainly responsible for an allergic reaction. Since goat's milk contains predominantly smaller fat globules, it is easier to digest than cow's milk. This could be related to the faster lipase activity in smaller fat globules which has a larger surface area. In addition, fatty acids such as caproic acid, caprylic acid and capric acid are believed to have great medicinal value for patients suffering from malabsorption disorders, childhood epilepsy, cystic fibrosis and gallstones (Park *et al.*, 2017). Previous studies have shown that goat's milk's mineral content is higher than cow's milk (Turck, 2013). Overall, goat's milk contains more calcium, phosphorus, potassium and magnesium. However, the iron content in goat's and cow's milk is significantly lower than in human milk (Turck, 2013). As the current recommendations for infants are based on the iron content of human milk, the milk needs to be studied more closely. Human breast milk contains very little iron (0.4 mg/L). Since humans developed breast milk for humans, it can be concluded that the iron content of breast milk is optimal for infant development. While it is undisputed that the iron content in breast milk is low, it is currently assumed that the low amount must be sufficient in some way. In fact, breast milk is thought to contain "a special form" of iron, often referred to as "highly bioavailable." The Fe content in human breast milk is considered low compared to maternal serum Fe. The Fe concentration in human colostrum is about 0.8 µg/ml; in mature breast milk, it is 0.2-0.4 µg/ml. In contrast,

Fe concentrations in the milk of other animal species are much higher (Lonnerdal *et al.*, 1981). The iron concentration in mature rat milk is 5-10 µg/mL, which is about 25 times higher than the iron concentration in human milk. Although the iron concentration in human milk is low, it is thought to be independent of maternal iron status and cannot be increased by maternal diet or iron supplementation (Friel *et al.*, 2018).

A study by AL-Suwaiegh (2016) shows that goats fed a diet containing 20% date seed contain higher total protein levels and triglyceride levels in their milk production. In our study, we found that goats fed Ajwa seed diet had higher levels of lactose, calcium, zinc, and manganese in their milk compared to regular goat milk, which is important for optimal growth and maintenance of the human body. Date seeds can be considered a low-cost source of dietary fibre, natural antioxidants and a good alternative feed ingredient that can be utilized efficiently by ruminants. Date seeds are mainly used as animal feed, while most of it is considered as waste. Date seeds can be efficiently utilized by animals as non-traditional feed. However, the nutritional value of date kernels is lower than traditionally concentrated feed because date kernels have a hard seed coat that makes it difficult to digest the seed components. To increase their nutritional value, the kernels must therefore be processed before being fed to ruminants. Grinding the date kernels makes the nutrients more available to the animals as the seed coat is broken and removed (Al-Suwaiegh, 2016). Date seeds contain relatively high protein compared to date flesh and are a rich source of fibre and antioxidants (Nadeem *et al.*, 2019).

5.3 Iron bioavailability

Cytotoxicity assay was used to examine the Caco-2 cell viability and maximum non-toxic dose prior to the uptake experiment as well as following completion to examine any detrimental effects of the treatment on the Caco-2 cells. The cell viability analysis showed the same trend for both dates as they exhibited high cytotoxicity to the cell at 1000mg/ml, and the maximum non-toxicity was exhibited at 100mg/ml for both dates. Hence, the safest concentration level for iron bioavailability study is set at 100mg/ml. In goat milk, however, the cell viability was directly proportional to goat milk. Hence, the concentration level for iron bioavailability study is set at 100ml/ml.

In this current study, Caco-2 cell line was used to measure iron bioavailability. This cell model has been used in a wide variety of nutritional studies, particularly in the study of mechanisms and regulation of iron absorption and iron bioavailability (Au *et al.*, 2000). It differentiates post-confluence into a polarised cell layer with a phenotype comparable to human small intestine enterocytes. The results of the previous study indicate that these differentiated Caco-2 cells have an endocytic, apical uptake pathway for the uptake of luminal hydrolyzed (polyoxo-hydroxide) dietary Iron (III). This pathway apparently relies on endocytic uptake of small clusters of LM-Fe(III) polyoxohydroxide nanoparticles that agglomerate at the cell membrane (Marziano *et al.*, 2019). The application of a Caco-2 cell model appears to be promising as a physiological means of measuring mucosal cell iron uptake. A model in which in vitro gastric and intestinal digestion is combined

with cultured Caco-2 cells to simulate digestion and absorption in the human intestine (Glahn *et al.*, 1998).

The bioavailability study of iron is an important measure to identify the absorption of iron from dates and goat milk. Both types of date palm (Mariami and Ajwa) shows high iron bioavailability when compared to goat milk. This is because of the high iron and vitamin C content in date palm when compared to goat milk. This statement is supported by Khalid *et al.* (2016) that shows date palm possesses anti-anaemic properties attributable to the high level of iron and vitamin C. It contains approximately 0.15 - 0.5 mg/100g of iron (Khalid *et al.* 2016) and 2.4 - 17.5mg/100g of ascorbic acid (Al-Shahib and Marshall, 2003). Vitamin C which is also known as ascorbic acid, acts as a reductant and cofactor in iron haemostasis. It enhances the absorption of non-heme iron in the small intestine, and stimulates the synthesis of ferritin.

In this study, goat milk shows lower iron bioavailability than date palm. This is because goat milk has a low iron content (Park, 2006). According to Park *et al.* (1986), the bioavailability of iron from whole goat milk in iron-deficient rats had negative net increases in haemoglobin concentrations, showing that goat milk's iron content was insufficient. However, the haemoglobin regeneration efficiencies for groups fed with whole goat and cow milk were 50.6% and 13.1%, respectively, showing that goat milk had higher iron bioavailability than cow milk.

High iron bioavailability was found in a mixture of the date fruits with goat milk for both types of date (Mariami and Ajwa). This finding suggests that consuming date palms along with goat milk may help to enhance iron absorption. Those with iron deficiency anaemia who regularly consume goat milk recover more

quickly because it maximizes the nutritional utilization of iron in the food and promotes haemoglobin regeneration, which reduces calcium and iron interactions (Alférez *et al.*, 2019).

In the current study, a mixture of date palm (Mariami and Ajwa) with goat milk fed with Ajwa seed shows high iron bioavailability compared to a mixture of date palm (Mariami and Ajwa) with regular goat milk. This suggests that the Ajwa seed used as goat's feed has an effect on the quality of the milk. The volume and composition of milk produced by goats are greatly influenced by the diet consumed. Date seed can provide many essential nutrients and potential health benefits. The chemical composition of date seed includes dietary fiber, fat, protein, minerals, sugar, antioxidants, and phytosterols. The nutritional and medicinal activities of date seeds are related to their chemical composition (Shi *et al.*, 2014). Date seeds contain relatively high protein compared to date flesh and are a rich source of fibre and antioxidants (Nadeem *et al.*, 2019). A study by AL-Suwaiegh (2016) shows that goats fed with a diet containing 20% date seed produced higher total protein and triglyceride levels in their milk. Protein and triglyceride help promote iron bioavailability by increasing the synthesis of carrier proteins and, thus, iron absorption.

From this study, iron bioavailability of Mariami date with goat milk fed Ajwa seed is higher compared to Ajwa date with goat milk fed Ajwa seed. This result may be related to higher fructose content in the Mariami date (31.2g/100g) compared to the Ajwa date (29.5g/100g). Fructose is well known for increasing the ferrous iron synthesis and thereby improving iron bioavailability (O'Dell, 1993).

Fructose dramatically increases iron bioavailability in human intestinal epithelial

cells by increasing ferrous iron production, according to a study by Christides and Sharp (2013) employing *in vitro* cell models of the gut and liver. Results demonstrated a 300 per cent rise in ferrozine-chelatable ferrous iron levels when fructose and FeCl₃ are mixed. Besides, the calcium content in the Mariami date (482.00 mg/kg) is lower than the Ajwa date (536.00 mg/kg). Calcium can inhibit iron absorption. However, it is still unclear how calcium interacts with iron absorption. According to Lynch (2000), the inhibitory effect of calcium on iron absorption is caused by the interaction of calcium and dietary components that affect iron bioavailability.

Impaired erythropoiesis underlies the pathophysiology of anaemia in chronic diseases, although other mechanisms such as suppressed erythropoiesis and poor response to erythropoietin also contribute to this form of anaemia (Poggiali *et al.*, 2014). Diet rarely contributes to iron deficiency anaemia without severe malnutrition or concomitant disease (Aspuru *et al.*, 2011). A balanced diet is usually sufficient to prevent anaemia. However, nutrition plays a much greater role when iron stores are inadequate or anaemia has already developed, and the host needs additional iron absorption from the gut to recover (Johnson & Graham, 2011). This is particularly the case with chronic blood loss, rapid growth in infancy, malaria and hookworm infestation. In these cases, diet and iron supplements are crucial for maintaining iron availability (Miller, 2013). Besides the iron content itself, the bioavailability of iron depends largely on the dietary component. Diet containing iron in the form of haem is particularly bioavailable, and vitamin C improves the bioavailability (Pasricha *et al.*, 2021). The better iron utilisation from goat's milk could be due to several nutritional factors. Goat milk fat is richer in

medium-chain triglycerides compared to fat from cow's milk. The medium-chain triglycerides in the diet are oxidised and provide a rapid energy discharge that can be utilised in various metabolic pathways, thus contributing to an increase in the synthesis of carrier proteins and thus iron absorption (Diaz *et al.*, 2015). The digestion and metabolic utilisation of copper is increased in iron deficiency anaemia, as a deficiency of divalent iron cations in the intestine can increase the absorption of other divalent cations, including copper (Diaz *et al.*, 2015).

The interaction between calcium and iron is well known. The divalent metals transporter-1 (DMT1), the major transporter for uptake of non-haem iron at the intestinal brush border, is also used by calcium (Li *et al.*, 2017). Therefore, calcium acts as a non-competitive inhibitor with low affinity (but not as a transport substrate) for the DMT1, which explains the inhibitory effect of dietary calcium on the bioavailability of iron (Li *et al.*, 2017). Goat milk improves the bioavailability of iron in anaemic rats, increases iron deposition in target organs and promotes recovery of haematological parameters (Diaz *et al.*, 2015). Goat milk fat is richer in medium-chain triglycerides, which are rapidly absorbed and metabolised for energy, increasing the synthesis of carrier proteins and thus iron absorption. Goat's milk has a higher content of vitamins A and C, which further promotes iron absorption. In addition, consumption of goat's milk improves the digestion and metabolic utilisation of calcium and phosphorus and their deposition in the appropriate target organs, minimising Ca-iron interactions (Diaz *et al.*, 2015).

Calcium intake can have a negative effect on the absorption of non-haem iron and haem iron. As a rich source of protein and minerals, cow's milk plays an important role in the overall nutrition of infants and young children nowadays.

Despite the fact that cow's milk is the most common in infant formulas, there has been an increase in parental demand for goat milk infant formulas. In some countries, the government provides cow's milk at subsidised prices or free of charge to low-income groups. The adverse effects of cow's milk on iron status diminish the value of cow's milk as a staple food. Fortifying cow's milk with iron offsets the adverse effects of cow's milk on iron metabolism. In addition, fortification takes advantage of the widespread use of cow's milk by using it as a vehicle for general iron supplementation as part of efforts to combat ID. Fortification of cow's milk with iron is technically feasible and has no impact on the organoleptic properties of the milk (Ziegler, 2011).

5.4 Human Study

In the current study, improvement in haemoglobin concentration, reticulocyte count, red blood cell and packed cell volume was observed in date palm groups of treatment. This result is supported by studies conducted by Irandegani *et al.* (2019), who found that all participants with IDA among primary school girls at the start of the trial showed an increase in blood indices. It may be assumed that this is because of the iron present in dates and its function in the formation of haemoglobin. Yossef and Khedr (2015) also discovered that children in the orphanage between the ages of 9 and 11 who consumed dates for two months had higher levels of haemoglobin. Moreover, Abdul Rahman *et al.* (2008) noted that pregnant Egyptian women's haemoglobin levels increased after consuming 100 g of dates every day for seven weeks. The results from previous studies suggest that date palm, regardless of variety and method of extraction, is rich in beneficial

nutrients that support haemoglobin and erythropoiesis synthesis (Majid *et al.*, 2020;). Another study also stated that the inclusion of date palm was proven to increase the haemoglobin, red blood cell counts, reticulocyte count and packed cell volume (Onuh *et al.*, 2012; Zen *et al.*, 2013; Abdelsalam *et al.*, 2014). The increment in haemoglobin was associated with an increase in red blood cell counts. It is believed that the high iron content in date palms plays a major contribution to this (Onuh *et al.*, 2012; Zen *et al.*, 2013; Abdelsalam *et al.*, 2014).

The current study also observed improvement in haemoglobin, reticulocyte count, red blood cell and packed cell volume after consuming goat milk. This finding is supported by Majid *et al.* (2020) that goat milk improved haemoglobin, red blood cell and packed cell volume in anemic rats. Besides that, a study by Park *et al.* (1986) and Alférez *et al.* (2006) also reported that iron deficient rats treated with goat's milk showed increased serum haemoglobin level, red blood cell count and packed cell volume. Consumption of goat's milk has been reported to increase iron metabolism, which promotes the cure of iron deficiency anaemia (Moreno *et al.*, 2020). In addition, Diaz *et al.* (2014) found that the divalent metaltransporter-1 (DMT-1) receptor which plays an important role in iron absorption in the small intestine, was significantly up-regulated in anaemic rats treated with goat's milk compared with cow's milk or normal diet. This indicates an early induction of erythropoiesis by goat's milk. The inclusion of goat milk in animal diet was proven to increase the iron bioavailability and improves haematological parameters (Yangilar, 2013;Diaz-Castro *et al.*, 2014). This fact can be explained by the nutritional characteristics of goat milk. Goat milk contains a higher proportion of soluble proteins (β -lactoglobulin, α -lactoalbumin, and serum albumin), which

favours Fe absorption and a higher amount of dietary components capable of reducing Fe (III) to Fe (II), including ascorbic acid and amino acid such as cysteine, forming chelates with Fe, which remain soluble at a higher pH within the small intestine (Pourghassem *et al.*, 2000). Goat milk also contain high amount of vitamin A which is able to mobilize available iron stores and use them for haemoglobin formation (Park and Haenlein, 2008). Currently, all the experiments regarding goat milk were focused on animal study and no such study on the human was conducted (Zahir *et al.*, 2017).

In the current study, a subject who consume date palm together with goat milk shows improvement in reticulocyte count, red blood cell, haemoglobin, packed cell volume and mean corpuscular hemoglobin concentration. These findings are in line with the previous report by Majid *et al.* (2020)) that date palm + goat milk consumption in anaemic rats improved haemoglobin, red blood cells and packed cell volume. Therefore, a combination of date palm and goat milk does not only increase iron bioavailability but also counter calcium interference.

Serum ferritin concentration, an indicator of iron storage in the body, indicates a lack of iron stores when the level is below 11 µg/l for normal adult women (Mayo clinic, 2023). In the current study, the subject treated with date palm, goat milk and date palm + goat milk shows an increase in serum ferritin level from week to week. This indicates that date palm and goat milk have proven to increase serum ferritin levels. These findings are supported by the previous results (Nestares *et al.* 2008) that show an increase in serum ferritin in anaemic rats fed a goat milk diet. Besides that, studies by Irandegani *et al.* (2019) also proved that serum ferritin levels in female elementary school children increased following date palm

consumption. Yossef and Khedr (2015) also discovered that children in the orphanage between the ages of 9 and 11 who consumed dates for two months had higher levels serum ferritin. Ferritin concentration is increased in inflammatory diseases such as rheumatoid arthritis, chronic kidney disease and malignant diseases (Khan *et al.*, 2016).

The haemoglobin regeneration efficiency (HRE) index is commonly used to estimate the percentage of ingested iron absorbed and utilized for haemoglobin regeneration (Majid *et al.*, 2015). Recycled iron from macrophages and senescent erythrocytes is normally used for haemoglobin production. However, when the supply of iron is insufficient to meet physiological needs, iron absorption is enhanced in the intestine. In the case of iron deficiency, more iron is absorbed from the small intestine, but when iron stores in the body are high, iron absorption in the small intestine decreases. The efficiency of haemoglobin restoration in anaemic individuals reflects the absorption of dietary iron into haemoglobin during the treatment period (Majid *et al.*, 2015). In the present study, haematological parameter and iron profile were analyzed to assess the absorption of dietary iron in subjects with mild iron deficiency anaemia.

Numerous nutritional factors can influence the bioavailability of minerals in the small intestine, as they depend on the presence or absence of enhancers and inhibitors in the diet and, thus in the nutritional matrix (Zhang *et al.*, 2021). From this current study, serum iron and transferrin saturation in a subject treated with date palm, goat milk and date palm + goat milk were lower than the normal range as compared with iron tablet treated subjects that showed the improvement in serum iron and transferrin saturation. This shows the increasing iron absorption activity

by the cells. This is further confirmed by the slight increase in total iron binding capacity from week to week. Transferrin saturation is lower in all the treatment group indicating the activity of transporting iron to the cell. In addition, there is an early induction of erythropoiesis had occurred. This is supported by the increase in reticulocyte counts in all the treatments group in the present study. The iron profile with reduced serum iron concentration and transferrin saturation is consistent with the state of iron deficiency (Elsayed *et al.*, 2016). The subject still has mild iron deficiency anaemia despite receiving date palm and goat milk treatment. Probably a longer period of treatment is needed with date palm and goat milk to counter iron deficiency anaemia. Serum iron concentration and transferrin saturation are often used as indicators of iron status in the body. In iron deficiency, reduced serum iron concentration and transferrin saturation resulted in limited iron availability for erythropoiesis (Khan *et al.*, 2016).

The total iron binding capacity is equal to the amount of transferrin in the blood. The unsaturated or latent iron binding capacity (UIBC) can be easily measured by spectrophotometric methods. The sum of UIBC and serum iron is the total iron binding capacity (TIBC). In iron deficiency anaemia, both the UIBC and the TIBC are increased, and the serum iron concentration is decreased, so that the transferrin saturation is reduced (Faruqi & Mukkamalla, 2021). Transferrin receptors are abundant in erythroid cells. The concentration of circulating transferrin receptor correlates with the number of cellular receptors, which is proportional to the number of erythroblasts expressing the receptor (Yoon *et al.*, 2015). When cells are deficient in iron, transferrin receptor synthesis is enhanced, resulting in increased circulating receptor levels. In inflammatory anaemia, transferrin receptor synthesis

is suppressed by cytokines. The circulating transferrin receptor is a soluble form of the membrane receptor that is produced by proteolytic cleavage. Both the expression of TfR on the cell surface and the concentration of soluble transferrin receptor are inversely related to the intracellular iron content. The concentration of serum transferrin receptor is therefore a reliable indicator of functional iron deficiency and increased red cell production. Serum transferrin receptor levels have been reported to be significantly elevated at stages of iron deficiency and are a reliable index of early tissue iron deficiency (Speeckaert *et al.*, 2010). This current study shows that all the treatment group shows normal level of serum transferrin receptor. The serum transferrin receptor offers an advantage in the assessment of iron status, as it can distinguish iron deficiency anaemia from inflammation-related anaemia and detect iron depletion and functional iron deficiency in patients with concurrent inflammation (Speeckaert *et al.*, 2010). The measurement of serum transferrin receptor provides additional information for the assessment of iron status. Several studies have shown that serum transferrin receptor levels in IDA also increase in the presence of inflammatory disease and are a reliable indicator of iron deficiency (Lee, 2020). Unlike serum iron, transferrin serum percentage and serum ferritin, the serum transferrin receptor level is not affected by the acute phase reaction and should be more reliable in the differential diagnosis of iron status. The serum transferrin receptor value not only provides information about the level of intracellular iron but is also proportional to the total mass of the erythrocytes and reflects the speed of erythropoiesis (Speeckaert *et al.*, 2010). This value helps to determine iron deficiency in human.

The significant variability in the severity of iron deficiency and the assessment parameters, when analysed separately, creates the issue of needing to combine multiple parameters, thus offering a broad spectrum that includes atransferrinemia, body iron reserves and anaemia. According to Chaudhry & Kasarla (2022) iron deficiency could be defined by a significant decrease in transferrin saturation content in association with microcytosis and hypochromia. From this point of view, the inclusion of haematological parameters assessing erythrocyte morphology (MCV and RDW) and mean corpuscular haemoglobin concentration (MCHC) would be essential for the correct interpretation of the biochemical indicators (Daniel *et al.*, 2012).

The significant correlation between the parameters assessing endogenous iron reserves, atransferrinemia and the availability of iron for erythropoiesis shows that this association is compatible with the links in the metabolic chain that form the iron cycle in the body (Abbaspour *et al.*, 2014). In relation to atransferrinemia, the observed inverse relationship between serum iron and TIBC levels can be explained theoretically, since when circulating mineral levels are reduced, serum transferrin concentration, as measured by total iron binding capacity, increases.

Laboratory measurements commonly used to assess iron status, such as serum iron, ferritin, transferrin saturation, mean cell volume and zinc protoporphyrin, cannot clearly distinguish iron deficiency anaemia from inflammatory anaemia (Thomas *et al.*, 2013). Identifying the stages of iron deficiency, iron-deficient erythropoiesis, iron-deficient stores and iron-deficiency anaemia with these conventional laboratory tests is complex (Peng & Uprichard, 2017).

Iron is one of the key elements for basic human cells metabolism. Iron which is an important component of the haem (Dev & Babitt, 2017) acts as an active site for electron transport in the cytochromes and cytochrome oxidase, which is involved in the production of energy production in the mitochondria. The haem component in haemoglobin and myoglobin binds with oxygen and thereby transfers oxygen from the lungs to the tissues and stores it (Dev & Babitt, 2017). Dates, which are rich in vitamins and minerals such as folic acid, vitamin C, vitamin B1, vitamin B2, vitamin A, calcium, iron, potassium and vitamin B12, are very good at promoting iron absorption and the formation of red blood cells, which contain haemoglobin (Al-Shahib, 2013). The iron content in dates can be used to treat anaemia. The iron contained in dates is absorbed by the intestine and transported by the blood to haemopoiesis (blood formation). The iron binds to haem and globin, which in turn form a whole to haemoglobin. Thus, dates can indirectly help raise haemoglobin levels to normal in people with anaemia. The potential for dates is very high in the health field, one of which is to increase haemoglobin levels in the blood. Dates are a good source of antioxidants and fibre and are high in mineral vitamins which can be very helpful in the formation of haemoglobin. Many studies show that dates have the potential to increase haemoglobin levels (Onuh *et al.*, 2012; Zen *et al.*, 2013; Abdelsalam *et al.*, 2014), so they can be used as supportive therapy for anaemia alongside iron tablets. Iron is an essential microelement for the body. This substance is particularly needed in haemopoiesis (blood formation). Some iron is contained in haemoglobin, a protein molecule that transports oxygen in the blood to the cells that need it to convert glucose, fat and protein into energy. Dates are fruits that contain iron, protein, carbohydrates and fats that can increase haemoglobin levels and thus prevent anaemia (Dahlan *et al.*, 2021). Heme is the

active site in peroxidases activities, the enzymes involved in protecting cells from oxidative damage by reducing peroxides to water and microbicidal hypochlorite in granulocytes. Iron is distributed in haemoglobin, ferritin and transferrin (Dev & Babitt, 2017).

Iron metabolism is unlike other metals; it differs from the metabolism of other metals in that there is no physiological mechanism for iron excretion and nearly 90 % of daily iron requirements are derived from an endogenous source, namely the breakdown of circulating red blood cells. However, there are regular iron losses, which include mandatory losses in shedding of the cells (skin, intestinal, urinary and respiratory) and menstrual blood losses in women of childbearing age. To maintain iron balance, the sum of these losses plus the iron needed for growth in infants, children and adolescents, body requirement during pregnancy and lactation must be supplied through the diet. There are two types of dietary iron: non-haem iron, which is found in both plant foods and animal tissues, and haem iron, which comes from haemoglobin and myoglobin in foods of animal origin. Heme iron is estimated to contribute 10-15% of total iron intake in meat-eating populations but could account for $\geq 40\%$ of total ingested iron due to its higher and more consistent absorption (estimated at 15-35%). Non-haem iron is generally absorbed much more poorly than haem iron. All non-haem iron from the diet that enters the common pool of iron in the digestive tract is absorbed at the same rate, which depends on the balance between absorption inhibitors and enhancers and the iron status of the individual. However, it is important to note that not all fortified iron enters the common pool.

5.5 Implication of Study

Numerous components in a healthy diet help to boost iron absorption in the human body. There are many studies that convincingly show the dose-dependent effect of native or added ascorbic acid on iron absorption. The enhancing effect is largely due to ascorbic acid's ability to reduce iron(III) to iron(II), but also to its potential to chelate iron. Ascorbic acid overcomes the negative effects of all inhibitors on iron absorption, which include, calcium, polyphenols, phytate and proteins in dairy products, and increases the absorption of both fortified and native iron. In fruits and vegetables, the absorption-enhancing effect of ascorbic acid is often offset by the inhibitory effect of polyphenols. Ascorbic acid is the only major absorption enhancer in vegetarian diets, and iron absorption from vegetarian and vegan meals can best be optimised by the intake of ascorbic acid-containing vegetables. This study implies the importance of identifying natural supplementary to fight against anaemia in human.

The improved utilisation of iron in date palm and goat milk feeds may be due to many nutritional factors. Rich in carbohydrates, minerals, vitamins and fibre, date palm can be considered as an ideal food providing a wide range of essential nutrients with many health benefits. The date palm contains large amounts of carbohydrates in the form of reducing sugars, namely glucose and fructose, which are easily absorbed during digestion and provide immediate energy. Dietary fibre provides satiety and has a laxative effect and can thus prevent gastrointestinal disorders. Date palm also contains minerals such as magnesium, calcium, iron and zinc, which are important for optimal growth and maintenance of the human body.

Date palms are rich in ascorbic acid, which improves iron absorption by reducing

iron(III) (Fe^{3+}) to iron(II) (Fe^{2+}). Ascorbic acid is also able to chelate iron and stimulate ferritin synthesis. In addition, date palm fruit is rich in phytochemicals such as, phenolic acids, phytosterols, carotenoids, flavonoids, sterols and tannins, which may have health benefits when taken as an alternative medicine or as part of the daily diet. Identification and quantification of different classes of phytochemicals as well as pharmacological studies (*in vitro* and *in vivo*) have shown that date palm has therapeutic effects on health, as its consumption is associated with antifungal activity, anti-inflammatory activity, anti-cancer activity antibacterial activity and protective effect against toxicity. Goat's milk, on the other hand, contains a higher amount of soluble proteins such as β -lactoglobulin, serum albumin and α -lactoalbumin, which promote iron absorption in the small intestine. Goat's milk also contains a high content of medium-chain triglycerides (MCTs), a form of saturated fatty acids with 6-10 carbon atoms that are easily absorbed by intestinal cells and contribute to easier and more efficient digestion. MCTs are rapidly hydrolysed and converted to energy with less fat accumulation. It increases the synthesis of protein carriers leading to increased absorption of nutrients.

Different methods to improve the bioavailability of iron from plant-based complementary foods, through enzymatic degradation of phytic acid and through increased consumption of ascorbic acid-rich fruits and vegetables, should be analyzed and adapted to local requirements. Also, it is advisable to assess whether adding foods with a high iron content and high bioavailability to the diet might be beneficial. Oral iron supplements, although effective in restoring iron levels in ID and IDA patients, are poorly tolerated by a large proportion of patients, including inflammatory bowel disease patients. Their frequent gastrointestinal side effects

can lead to treatment non-adherence and delayed restoration of iron levels, leading to inflammation in the gastrointestinal tract. However, the mechanism by which oral iron supplements cause these adverse gastrointestinal effects is unknown (Bloor *et al.*, 2021). The search for alternatives and substitutes may help to address iron deficiency in patients and target groups such as infants, children and pregnant women.

There is lack of valid experimental data and scientific design of efficacy of alternative medicine towards human health. These gaps arise mainly due to lack of interest on therapeutic properties hidden in traditional herbs, foods and medicine among researchers and main industries. However, several issues involving side effects of conventional treatment involving modern drugs have initiated efforts to find better treatments that involving usage of more effective methods and alternative medicine. Therefore, modern researchers and scientist comes up with the idea of disease prevention through foods or plant based and healthy lifestyle. The release of the WHO Traditional Medicine Strategy 2002–2005 also plays a major role in the significant advances in research regarding the effect of traditional and complementary medicine products on health (WHO, 2013). This highlight attracts many researchers in developing countries to get involves in this sector supported by development of biotechnology sectors. Traditional and complementary medicine sector now plays a significant role in the economic development of a number of countries (WHO, 2013). Dates have gained popularity in recent years due to their multiple health benefits; as a result, numerous *in vitro* and animal studies, as well as the identification and quantification of several classes of phytochemicals, are being conducted worldwide (Vayalil, 2012). The high value

of nutritional in goat milk has also drawn attention to its use as a crucial component of human nutrition, according to Clark & Garca (2017).

5.6 Limitation and future of the study

There is a limitation in the human study. The iron content in 5 pieces of Ajwa date palm and 250 ml goat milk is not equal to the standard amount of 100mg found in ferrous fumarate. The specific iron content in 5 Ajwa dates and 250 ml goat milk is currently unknown. Besides that, there is no comparison between groups of treatment in this current study, therefore in future studies the comparison between group of treatment should be analyse. There is only 11 to 12 subject in each group. It is considered a bit small for comprehensive analysis of the parameters. As the number of subjects increases, the greater confidence in the accuracy and validity of the findings. While larger sample sizes may involve more time, resources, cost and effort, contribute to the robustness and credibility of research outcomes. Therefore, future studies should aim to increase the number of subjects to ensure comprehensive analysis of the parameters.

A constraint of the current study lies in the challenge of controlling human subjects' dietary habits and food consumption. The study relied on the monitoring of participants' food diaries, which introduces a level of uncertainty due to potential inaccuracies and variations in reporting. In future investigations, a more rigorous approach could involve daily analysis of participants' food intake. This longitudinal assessment would allow for a comprehensive understanding of how daily dietary patterns influence iron absorption. This would likely results in more accurate into the

effects of the date and goat milk in conjunction on iron absorption, as it would encompass a broader spectrum of real dietary habits and their potential impact on the observed outcomes.



5.7 Recommendation and suggestions

There is an urgent need for effective strategies to overcome iron deficiency, the most prevalent micronutrient deficiency in the world, particularly for newborns and young children in underdeveloped nations. It is important to assess the efficacy and efficiency of various strategies under realistic circumstances in order to increase the iron content and bioavailability of iron in complementary meals through food fortification and dietary habits. Traditional food fortification programmes are not an option because many settings for newborns and young children do not have access to industrially manufactured foods. It is necessary to investigate novel strategies, such as the potential for fortifying supplementary foods at the household level. To counteract the inhibitory impact of phytic acid and adjust them to local conditions, it is also important to investigate the potential to breakdown phytic acid in complementary foods made from grain and to enhance consumption of foods high in ascorbic acid. In order to improve the iron status of infants and children, it is necessary to assess the role of animal products in the diet, particularly whether small, reasonable amounts of meat may be incorporated into plant-based diets.

To prevent and manage anaemia and iron deficiency anaemia, the World Health Organization (WHO) suggests a combination of four fundamental strategies: iron supplementation, adequate nutrition education, food fortification with iron compounds, and control of parasitic and viral illnesses. Regular intake of date fruits can help control IDA considering the prevalence of the disease and the impact that nutrition education has on IDA prevention and management. Dates, a fruit with the scientific name *Phoenix dactylifera*, are one of the fruits consumed by humans and

have a significant nutritional value. Dates provide 314 calories per 100 g. Ten minerals are discovered, including selenium, copper, potassium, and magnesium. 100 g of dates can provide more than 15% of the daily required amount of these minerals. Dates also provide 0.3 to 10.4 mg of iron per 100 g. Thus, the body gets all the iron it needs each day from a few dates. Vitamin C contain in dates also can improve iron absorption. At a certain stage of development, dates are one of the few foods that are both high in potassium and low in sugar. Additionally, according to Swider *et al.* (2020), there are five stages of date pre-ripening, ripening, and maturation: Hababauk, Kimri, Khalal, Rutab, and Tamer. Date fruits are available in the market with a variety of products. These products have several health benefits. These products include, date paste, dried dates, date syrup and juice, date oils, date fibre concentrates and date powder. There are changes in the ripening stage of dates at different stages of their sugar profile. After the Khalal stage, the fruit becomes high in sugar, and at the Tamar stage, the fruit shows a sharp increase in sucrose content and a dramatic decrease in moisture content. In the first stages of growth, the sucrose content exceeds the glucose and fructose content, and then the conversion of sucrose into monosaccharides begins until the sucrose content is less than 5% in the tamar stage (Musthafa & Sandhu, 2022). Therefore, dates can be recommended as a snack for children with iron deficiency.

The administration of iron supplements is the most widely used method of treating anaemia. The iron tablet administration programme, which starts after the first trimester of pregnancy, has been used in many developing countries. However, the positive effects fall far short of expectations and the programme is considered unsuccessful because women hardly comply the intake of iron tablets.

Gastrointestinal side effects have generally led to poor compliance of women to take iron tablets. The most common complaints after taking iron tablets are nausea and constipation. This condition is made worse when they are taken by pregnant women, as the body adjusts to the pregnancy hormone. Women who have not had bowel problems in the past may suffer from constipation in early pregnancy, while women who have suffered from constipation in the past may have more severe symptoms during pregnancy due to taking iron tablets. Moreover, pregnancy is a short period of time to treat pre-existing anaemia. Therefore, correction of iron deficiency should be done in the teenage years or before pregnancy. Iron can be absorbed from foods and beverages. Dates are an example of iron-rich nutrients that are commonly consumed and preferred by the Muslim community. Dates are the best source of dietary fibre. High fibre consumption not only reduces the risk of constipation but also improves iron absorption. Indrayani *et al* (2018) reported that 100 g of dates contain 6.4 to 11.5% dietary fibre, including 0.84 g of soluble fibre, 5.76 g of insoluble fibre and 8 g of total fibre. Insoluble dietary fibres play a very important role in the human body. They can protect the body from many diseases, such as diverticular diseases and colon cancer, by increasing the weight of faeces and having a laxative effect.

The future research recommendation can be diverted to exploring the estimated dose level in different formulas. Also, the study can include into clinical trials and better comparison with various other parameters involving actual patient samples. The most common cause of anaemia in admitted patients is anaemia of chronic disease (ACD). It can be difficult to assess the prevalence rate of this disease because it is frequently confused with IDA and is usually a diagnosis of

exclusion. Age-related increases in the prevalence of ACD are known to occur; 77% of older adults with undetermined causes of anaemia are affected, which indicates to a multifactorial aetiology. ACD occurs in patients whose current disease causes an active immunological/inflammatory response resulting in decreased iron uptake at various sites, but not in patients whose disease or its treatment directly causes anaemia, as is the case with some malignancies and the use of cytotoxic drugs. In patients diagnosed with other chronic diseases that are not necessarily purely inflammatory, mild to moderate anaemia is usually observed. It occurs in various disease states such as malignancies, chronic infections and autoimmune diseases. Differentiating between iron deficiency anaemia (IDA) and anaemia of chronic disease/inflammatory anaemia (ACD/AI) can be difficult. IDA is an anaemia caused by low iron stores in the body, while ACD/AI is a functional anaemia caused by impaired erythropoiesis due to diseases such as infections, autoimmune diseases, cancer and end organ failure. After a complete blood count indicating anaemia, testing to differentiate between IDA and ACD/AI includes determination of serum ferritin, iron and iron binding capacity, and soluble transferrin receptor. Erythropoiesis is suppressed as a result of the actions of several pro- and anti-inflammatory cytokines and hormones. Ferroportin regulates iron release from the intestinal mucosa and bone marrow macrophages.

5.8 Conclusion

Findings supports the hypothesis that date palm and goat milk is beneficial in iron deficiency anaemia. Mixture of dates and goat milk proved to increase iron bioavailability *in vitro*. Inclusion of date palm and goat milk is recommended in the diet of mild iron deficiency anaemia people as it can improve the haematological parameters as well as the iron store. High nutritional value in date palm and goat milk play a role in increasing the haemoglobin and ferritin in IDA. It was also noted that goat's milk does not interfere with iron absorption as compared to cow's milk. But both date palm and goat milk cannot be used to totally replace the standard treatment involving oral iron supplements.