ABSTRACT: Iron deficiency anaemia (IDA) is a global health problem. It is an indicator of poor nutrition and poor health. Based on the Al-Quran and prophetic Sunnah, dates are mentioned as a superfood that helps in the preservation of health. Therefore, we are evaluating the potential of using dates as a treatment for IDA from data published in various reports. The search was conducted for relevant articles published in four electronic indexed databases namely Medline, Ovid, Scopus, Biomed Central, and PubMed. Bibliographies of the screened studies and relevant reviews and manuscripts were also searched using Google scholar. The data reported involved systematic reviews and reports of studies that are according to the PRISMA guidelines. There were only three articles that discussed the effects of the use of dates in IDA. A significant increase was shown (p<0.05) in haematological parameters such as haemoglobin level, red blood cell count, packed cell volume and platelet count while no effect was shown on total white blood cell count, differential white blood cell and bone marrow (p>0.05). This systematic review identified limited reports that reported on the beneficial effects of dates in reducing IDA. There are several gaps in the available evidence, hence, further studies are needed to provide a comprehensive understanding on this matter.

KEYWORDS: Anaemia, Date palm, Haemoglobin, Phoenix dactylifera, Systematic review

INTRODUCTION

Anaemia is a pathological condition in which the haemoglobin concentration in red blood cell is abnormally low. Iron Deficiency Anaemia (IDA) is the most common cause of anaemia in the world (Alferetz et al., 2006). It is characterised by the reduction or absence of iron stores, low serum iron concentration, poor haemoglobin concentration, haematocrit reduction and increased platelet count. It commonly affects pregnant women, pre-school and school-age children, infants with low birth weight and women of childbearing age (WHO, 2008). IDA is a major public health problem affecting both developing and developed countries (Viteri, 1993; Pourghassem et al., 2000) including Malaysia (Tee et al., 1999). In Malaysia, a moderately high prevalence of anaemia has been reported amongst the vulnerable group (Foo et al., 2004). The prevalence of IDA among urban Malaysian women is 10.3%, and marked differences were found among the ethnic groups with higher prevalence of IDA among the Indians (Loh and Khor, 2010). It appears that the main reason for the poor iron status is the inadequate intake and poor bioavailability of dietary iron as well as poor intake of other nutrients (Foo et al., 2004). IDA affects children development and growth, lowers resistance to infections and is also associated with mortality of infants younger than 2 years. Grantham-McGregor and Ani (2001) also reported that IDA affects fertility, as well as mortality in...
Pregnant women and the elderly.

Iron is an important component of haemoglobin and intake of iron from fruits and vegetables is necessary for health (Eldaim and Elnadi, 2014) and reduces chances of developing IDA. Vulnerable populations should be encouraged to consume iron-rich food and infants should be breast-fed or supplemented with iron-fortified formula, to help reduce the risk of developing IDA.

Date palm (Phoenix dactylifera) is considered by Al-Quran and prophetic Sunnah as the ultimate superfood for the preservation of good health. This is clearly stated in Surah An-Nahl: “And from the fruits of the palm trees and grapevines, you take intoxicant and good provision. Indeed, in that is a sign for a people who reason.” (Al-Quran 16:66). Besides that, a hadith narrated by Aisha reported that the prophet SAW as saying, “The Ajwah dates of al-aliya contains healing effects and are a remedy when taken first thing in the morning” (Sahih Muslim 23/5083). Numerous scientific studies also reported that date is a rich source of many nutrients and are able to alleviate symptoms of IDA (Alfe´reza et al., 2006; Abdel Rahman, 2006; Onuh et al., 2012).

The date palm has been shown to be rich in iron (Suliman, 2012; Eldaim and Elnadi, 2014) and was reported to increase the haemoglobin level in rats (Onuh et al., 2012; Zen et al., 2013). Date palm also has been described as a major source of iron among fruits and berries (Sahari et al., 2007). As an energy-rich food and a source of a variety of nutrients such as carbohydrates, the date has huge potentials in maintaining human health (Al Farsi et al., 2005). It is also a significant source of dietary fibres, essential vitamins and minerals (Al Shahib and Marshall, 2003). Moderate concentrations of manganese, iron, phosphorus and calcium per 100 g of dates provide over 7% of the daily requirements RDA/AI (Al Farsi et al., 2005). Consumption of date palm would contribute significantly to the daily requirement of many of these components such as carbohydrates and minerals (Fe, Mg, Ca, Zn, P, Cu, Se, I, etc.) and provides reasonable amounts of vitamins (niacin, B6, and folate) (Vayalil, 2012). Therefore, daily consumption of dates may be a good alternative for the treatment of deficiency-related diseases such as anaemia, goitre, rickets and osteomalacia.

We performed a systematic review to determine whether date palm consumption improves relevant blood parameters in IDA.

**METHODS**

**Data Sources and Search Strategy**

Studies eligible for inclusion in the review were located from the Medline, Biomed Central, Ovid, PubMed and Scopus with no limitation on the publication date. Our search strategy involved using a combination or broad indexing terms for each database. The following keywords were used for dates palm (dactylifera, palm* and date*) and anaemia (h*moglobin, an*mia, iron, iron deficiency and blood) respectively. The Medline search strategy was developed and adapted for other databases as required. These are available in supplementary information from the authors upon request. Bibliographies of screened studies and relevant reviews and manuscripts were also searched for eligible studies and a search was conducted by using Google scholar.

**Criteria Included in the Review**

Only experimental studies were eligible for inclusion; only studies that used date palm fruit or seed were chosen while studies on other parts of date palm such as leaves, shoot and root were excluded and the subjects of interest selected were only human or animal population. To be eligible for the review, a study must report validated measures of blood parameters in reducing anaemia after treatment with date palm. This systematic review focused on the contributions of iron in date palm towards significantly increasing the haemoglobin level and reducing anaemia. Besides that, chemical compositions in date palm other than iron (Fe) or that are irrelevant to IDA were ruled out from the database search.

**Identification of Relevant Studies and Data Extraction**

All manuscripts from the searches were downloaded into an Endnote library. Potentially relevant papers were selected by screening the titles (first step), abstracts (second step) and the entire article (third step) and are then retrieved from the database searches. Two researchers independently conducted this screening. Disagreement about eligibility between the reviewers was solved through discussion with a third author. Records of the reasons for rejections were kept.

Data was extracted from the included studies into a table by one author. Each study’s details include study design, sample size, outcomes, parameters, extraction method, duration of exposure, sample collection and details of the study design were listed in the Table 1. Data entry was checked for each study after completion of data extraction.

**Data Reporting**

Data reporting involved a descriptive summary. Report of the study was done according to PRISMA guidelines.

**RESULTS**

The database search identified 3630 titles of potentially relevant articles. A total of 11 titles were located through hand search from the reference section of earlier reviews. A total of 2533 articles were retrieved for abstract review (Figure 1). Screening of the titles and abstracts resulted in the selection of 52 articles for full-text review. Forty-nine of these articles did not meet the inclusion criteria resulting in a final inclusion of only 3 articles. The characteristics of the included studies are shown in Table 1.
<table>
<thead>
<tr>
<th>First Author &amp; Year</th>
<th>Extracts Of Dates</th>
<th>Animals</th>
<th>Types Of Study</th>
<th>Experimental design</th>
<th>Duration of exposure</th>
<th>Sample collection</th>
<th>Parameters</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onuh et al., 2012</td>
<td>Canolic extract of dates</td>
<td>50 Wistar rats weighing between 100 to 200 grammes and aged between 2 to 3 months from Animal House of College of Medicine, University of Nigeria Enugu Campus</td>
<td>Experimental study</td>
<td>2 groups were orally administered with DMSO (n = 10) 4 groups were orally administered with graded doses of the crude aqueous extract of dates (n = 20) 4 groups were orally administered with graded doses of the crude methanolic extract of dates (n = 20)</td>
<td>112 days</td>
<td>Blood samples were collected from retrobulbar plexus of the median canthus of the eye</td>
<td>Red blood cell count, haemoglobin, packed cell volume, reticulocyte, platelet count, total white blood cell count, differential white blood cell count and bone marrow count</td>
<td>Significant increase (p&lt;0.001), in red blood cell count, haemoglobin packed cell volume, reticulocyte and platelet count Total white blood cell count, differential white blood cell count and bone marrow count did not differ significantly (p&gt;0.05)</td>
</tr>
<tr>
<td>Zen et al., 2013</td>
<td>Aqueous extract of dates</td>
<td>24 Wistar rats weighing 200 grammes from Laboratory Study Center for Food and Nutrition, University of Gadjah Mada Yogyakarta</td>
<td>Experimental study</td>
<td>Group 1 was orally administered with standard diet and distilled water (n = 6) Group 2 were orally administered with low Fe diet and distilled water (n = 6) Group 3 were orally administered with low Fe diet and distilled water plus date juice at concentration 50% (n = 6) Group 4 were orally administered with low Fe diet and distilled water plus date juice at concentration 100% (n = 6)</td>
<td>14 days</td>
<td>Blood samples collected from retro-orbital plexus</td>
<td>Haemoglobin level</td>
<td>Date extract increases the haemoglobin level (9.25±0.15 g/dL, 10.35±0.14 g/dL) significantly (p&lt;0.05) as compared to low iron diet group (7.72±0.17 g/dL)</td>
</tr>
<tr>
<td>Abdelsalam et al., 2014</td>
<td>Aqueous extract of dates</td>
<td>20 mature late-pregnant (~60 days prepartum) Najdi ewes.</td>
<td>Experimental study</td>
<td>Group 1 was orally administered with regular commercial pellet plus alfalfa hay (n = 5) Group 2 were orally administered with palm Sukkary dates aqueous extract (n = 5) Group 3 were orally administered with probiotic stirred yoghurt (n = 5) Group 4 were orally administered with palm Sukkary dates aqueous extract and probiotic stirred yoghurt (n = 5)</td>
<td>30 days</td>
<td>Blood sample taken via jugular vein</td>
<td>Red blood cell count, haemoglobin, packed cell volume, reticulocyte, platelet count, total white blood cell count, differential white blood cell count</td>
<td>Dates extract significantly (p&lt;0.01) increase haemoglobin concentration (10.74±0.2 g/dL) No significant (p&gt;0.05) change in red blood cell count, packed cell volume and platelet count Total white blood cell count did not differ significantly (p&gt;0.05)</td>
</tr>
</tbody>
</table>
**Characteristics of Included Studies**

All of the selected experimental studies involved the usage of date palm extract (Onuh et al., 2012; Zen et al., 2013; Abdelsalam et al., 2014). Only one study stated the type of date palm being used which is dried Sukkary Dates (Abdelsalam et al., 2014). Aqueous date palm extract has been used in all of these studies which are prepared by removing the seeds and blending it with distilled water. One of the studies used two types of date palm extract simultaneously which were the aqueous extract and methanolic extract (Onuh et al., 2012). Two studies used only date palm extract in the experiment (Onuh et al., 2012; Zen et al., 2013) while the other study used a combination of date palm extract with probiotic stirred yoghurt from cow's milk in the experiment (Abdelsalam et al., 2014).

Two of the studies used Wistar rats weighing between 100 to 200 g and aged between two to three months as subjects (Onuh et al., 2012; Zen et al., 2013). While the other study involved the use of mature late-pregnant (≈60 days prepartum) Najdi ewes as subjects (Abdelsalam et al., 2014). Red blood cell count, haemoglobin, packed cell volume, reticulocyte, platelet count, total white blood cell count and differential white blood cell count were measured as stated by Abdelsalam et al., (2014). Onuh et al., (2012) included the same parameters with an addition of bone marrow count. The third study only involved haemoglobin level measurement using cyanmethemoglobin method (Zen et al., 2013). All of the selected studies clearly stated the positive effects of date palm towards increasing haemoglobin level and reducing anaemia.

**Effects of Date Palm on IDA**

Abdelsalam et al., (2014) demonstrated that date palm extract significantly increases the haemoglobin level by 13% as compared to the control. Zen et al., (2013) and Onuh et
Iron deficiency anaemia treatment usually involves consumption of iron supplements, diet alteration and treat 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 prescribed supplements are ferrous sulfate and ferrous fumarate tablet, commonly taken twice a day. Severe iron-deficiency anemia may require a blood transfusion, 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 dosage dependent significant increase in haemoglobin and red blood cell in both aqueous and methanolic extract when compared with the control. This suggests that the improvement of the haemopoietic activities in IDA is dose related when treated with date palm extract.

We identified several gaps in the currently available evidence. There were very few experimental studies looking at the effects of date palm in IDA. It is noted that the available studies only reported on the effects of improvements on haemopoietic activity in haemoglobin, red blood cell and packed cell volume. There are 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. These gaps arose mainly due to lack of interest on therapeutic properties hidden in traditional herbs, foods and medicine among researchers and playing industries. However, several issues involving side effects of conventional treatment involving modern drugs have initiate 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). However, one decade is still not enough to discover throughout the potentials of foods in improving public health and researchers all over the world still working on it.

DISCUSSION

The present systematic review looks at the effects of date palm in IDA. Phoenix dactylifera is known to possess numerous medicinal properties (Baliga et al., 2011; Vayalil, 2012; Mallhi et al., 2014; Ruvera et al., 2014). There is very limited information reported on the effects of Phoenix dactylifera on haematological diseases. 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, packed cell volume and platelet counts. The increment in haemoglobin was coincided with an increase in red blood cell. It is believed that the high iron content in date palm plays major contribution to this (Onuh et al., 2012; Zen et al., 2013; Abdelsalam et al., 2014). Iron plays an important role in forming complexes with molecular oxygen in hemoglobin and myoglobin. Erythroid precursors need much more iron than any other type of cells in the body. They take up iron through transferrin. Iron can synthesize the formation of heme that can increase haemoglobin level (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. Up to the knowledge of the researchers, they were no physiological explanations for the significant increase in platelet count when given date palm extract (Abdelsalam et al., 2014). The iron content in various types of date palm such as Kalas date (1.75 mg/ 100 g), Gondala 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 (Salim and Hegazi, 1971; Imad et al., 1995; Ali-Mohamed and Khrais, 2004; Elleuch et al., 2008; Habib and Ibrahim, 2011).

Iron deficiency anaemia treatment usually involves iron supplements, diet alteration and treat 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 prescribed supplements are ferrous sulfate and ferrous fumarate tablet, commonly taken twice a day. Severe iron-deficiency anemia may require a blood transfusion, iron injections, or intravenous (IV) iron therapy (WHO, 2001).
Recent years dates have drawn greater attention owing to their numerous health benefits and consequently many in vitro and animal studies besides the identification and quantification of various classes of phytochemicals are being pursued worldwide (Vayalil, 2012).

Date palm contained a lot of other biochemical components such as tannin, folic acid, amino acids, ascobic acids and phenol (Matol et al., 1985; Okwu, 2004; Abdelsalam et al., 2014). Some of these components may be responsible for the increment of haemoglobin. Components like ascobic acid, vitamin C and fructose are known as enhancers of iron absorption while phyate, 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.

Most studies focused on the biochemical composition of the date palm such as proteins, carbohydrates, amino acids, fatty acids, minerals, vitamins and dietary fibre (Salim and Hegazi, 1971; Imad et al., 1995; Ali-Mohamed and Khamis, 2004; Elleuch et al., 2008; Habib and Ibrahim, 2011) 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. Therefore, it is crucial to use humans as the subject of study in order to understand the precise effect of dates extract in the treatment. This is due to several significant physiological and biochemical variations between animals and human.

Production and cultivation of date palm has long been the most important agricultural activity in arid regions of Arabian Peninsula, North Africa, and the Middle East (Zohary and Hopf, 2000). It is believed that date palm is one of the oldest fruit crops and has been cultivated for at least 5000 years (Zohary and Hopf, 2000). The ability of this crops to survive the arid condition make it the most suitable crops to be use in improving public health. In facts, date palm has been successfully introduced outside of its origin such as Australia, Asia, Mexico, United State, India and Pakistan (Chao and Krueger 2007). Since public health closely related to malnutrition and climate issues, dates can be the main income sources and staple food for local populations in many countries in which suffering from malnutrition due to limited sources of foods coursed by arid climate. Date cultivation can play significant roles in the economy, society, and environment of those countries. Dates are cheap to produce and preserve, and are also very rich in nutrition. Dates contain a high percentage of carbohydrate, fat comprising 14 types of fatty acids, 15 salts and minerals, protein with 23 different amino acids, six vitamins and a high percentage of dietary fibre (Al Shahib and Marshall, 2003). Hence it provides more nutrient even being consumed in less amount than normal food. This could help improving the health problems seen in poor countries where food sources are limited. Promotions of the health-giving benefits of dates in the developed countries also aid governments in meeting nutrition targets. Education about the importance of dates could bring significant health benefits. Besides that, improving the packaging and labelling of dates also can help in promoting public to consume date. Creative innovation via research and development in terms of processing and presentation of dates also can help in improving the dates market value.

CONCLUSION

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.

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CONFLICT OF INTEREST DISCLOSURE

The authors declare that there is no conflict of interest regarding the publication of this paper.

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