A review on chemistry and pharmacology of Ajwa date fruit and pit

Article *in* Trends in Food Science & Technology · March 2017

DOI: 10.1016/j.tifs.2017.02.009.

CITATIONS
72

READS
15,889

5 authors, including:

Rao Sanaullah Khan
Universiti Sultan Zainal Abidin | UniSZA
31 PUBLICATIONS **781** CITATIONS
SEE PROFILE

Asif Ahmad
PMAS - Arid Agriculture University
145 PUBLICATIONS **3,419** CITATIONS
SEE PROFILE

Trends in Food Science & Technology 63 (2017) 60–69

Contents lists available at ScienceDirect

Trends in Food Science & Technology

journal homepage: http://www.journals.elsevier.com/trends-in-food-science-and-technology

Review

A review on chemistry and pharmacology of Ajwa date fruit and pit

Sumaira Khalid [a], Nauman Khalid [b, c], Rao Sanaullah Khan [b], Haroon Ahmed [d], Asif Ahmad [e, f, *]

[a] Institute of Food and Nutritional Sciences, Pir Mehr Ali Shah Arid Agriculture University, Rawalpindi, Pakistan
[b] School of Food and Agricultural Sciences, University of Management and Technology, Lahore 54000, Pakistan
[c] Centre for Chemistry and Biotechnology, School of Life and Environmental Sciences, Deakin University, Waurn Ponds, Victoria, 3216, Australia
[d] Department of Biosciences, COMSATS Institute of Information Technology, Islamabad 45550, Pakistan
[e] Department for Management of Science and Technology Development & Faculty of Applied Sciences, Ton Duc Thang University, Ho Chi Minh City, Viet Nam
[f] Department of Food Technology, PMAS-Arid Agriculture University, Rawalpindi 46300, Pakistan

ARTICLE INFO

Article history:
Received 6 October 2016
Received in revised form
12 December 2016
Accepted 21 February 2017
Available online 10 March 2017

Keywords:
Ajwa
Flesh
Pit
Phytochemicals
Flavonoids
Antioxidant
Nephroprotective

ABSTRACT

Background: *Phoenix dactylifera* is an instinctive plant, cultivated worldwide especially in Arab regions being an edible nutritious fruit. For this plant, **Ajwa** date fruit variety is distinguished among all varieties due to its richness of sugar, dietary fiber, essential mineral and vitamin contents. The unique phytochemical profile of Ajwa dates have potential to cure different diseases.
Scope and Approach: This manuscript provides an overview on pharmacological and nutritional aspects exclusively for Ajwa dates. The excellent **phytochemicals** profile placed Ajwa dates at top among other date varieties. Recently, new *in vitro* and *in vivo* studies prove the effectiveness of Ajwa dates. However, quantitative studies are need to understand the protective actions of Ajwa dates.
Key Findings and Conclusions: Ajwa fruit pits are also enriched with **dietary fibers**, lipids, minerals, and proteins. Ajwa dates are consumed not only for dietary purposes but also used for their medicinal effects against different ailments. Phytochemical studies have showed that Ajwa **flesh** and **pits** are enriched with certain phenolic and **flavonoids**, which have multiple effects on human health due to their strong antioxidant properties. Preclinical studies revealed that Ajwa dates have strong **antioxidant**, anti-inflammatory, anti-mutagenic, hepato-protective, **nephroprotective** and anti-cancer activities.

1. Introduction

Traditionally fruits constitute a major part of human diet from ancient time. Certain fruits acquire a special attention in daily routine of certain population owing to their religious practices. Fruits and vegetables have been recommended strongly by WHO and other nutritional societies around the world for improving general health and wellness of masses. In the wake of health and wellness awareness from last two decades a significant progress has been made on the studies of bioactive compounds in plants foods to find their direct effects on human health and wellbeing (Vayalil, 2012). In this regard date fruit is well-regarded for its nutraceutical properties in Middle East and Africa. However, its significance in Western countries has not been explored yet owing different culture and eating habits. Scientific community now has realized its nutritional value in diet and has started to explore more avenues for development in this category of fruits.

Date palm commonly known as *Phoenix dactylifera* is one of the oldest (5500–3000 BCE) cultivated variety of date palm trees having nutritional, environmental, economic and ornamental, benefits (Barreveld, 1993). Cultivation of date palm is thought to be merged with cultural, environmental, religious and social development of people living in hot and arid areas especially in Middle East and Africa (Terral et al., 2012). Therefore, till now date palm is a major cultivating crop of above described areas and these regions are leading producers and exporters of date products worldwide (Assirey, 2015). Date palm is monocotyledon tree that can grow to an altitude of 1500 m in well-drained soils. Currently, date palm tree is being cultivated mainly in areas of Iraq, Iran, Saudi Arabia, Algeria, Egypt, Libya, Pakistan, Morocco, Sudan and Oman (FAO, 2003). One of the major characteristics of date fruit is to be

* Corresponding author. Department for Management of Science and Technology Development & Faculty of Applied Sciences, Ton Duc Thang University, Ho Chi Minh City, Viet Nam.
E-mail address: asif.ahmad@tdt.edu.vn (A. Ahmad).

http://dx.doi.org/10.1016/j.tifs.2017.02.009
0924-2244/

consumed as staple dietary food in different regions of the world such as Arabian, Asian and some African countries (Barreveld, 1993). Another distinguishing characteristic of date fruit is that it can be consumed at three different maturity stages such as Khalal, Rutab and Tamar. However, newly ripened fresh dates are preferred in many date producing countries. Dates are also commercially available in dehydrated form, but dehydrated dates are prepared by drying processing techniques to increase their shelf life but it reduces the nutritional value of these dates (Abdul-Hamid, Abas, Ismail, Shaari, & Lajis, 2015). Taste, nutritional and phytochemical properties of the dates vary depending upon its maturity stage and the variety of dates. There are approximately 5000 date varieties that are grown in different regions of the world. The most common ones are Aseel, Zahidi, Majdool, Mabrook, Dhakki, Halawi, Lasht, Deggla and Bamy (Eid, Al-Awadi, Vauzour, Oruna-Concha, & Spencer, J. P., 2013; Eid, Al-Awadi, Vauzour, Oruna-Concha, & Spencer, J. P.E., 2013).

Ajwa date fruits (Fig. 1) are soft and dry and this date fruit is cultivated in the Al Madinah region of western Saudi Arabia. The Ajwa date variety has great medicinal properties. The old testaments, "Hadith" and Islamic literature pointed the beneficial properties of this date variety and it is believed that eating this date variety will cure many chronic diseases and ailments. The Ajwa date the most popular and expensive fruit that belongs only to the holy city of Al Madinah Al Munawara and its adjoining areas in Saudi Arabia (Zhang, Adosari, Vidyasagar, P. S. P. V., Nair, & Nair, 2013; Zhang, Aldosari, Vidyasagar, P. S., Nair, & Nair, 2013). Ajwa dates contain ample amount of dietary fiber and have potential to correct the digestion problems. Ajwa date works as natural roughage to the body and stimulate the bowl movement and provide effective relief from constipation (Al-Shahib & Marshall, 2003). Similarly, these dates contain high amounts of potassium and plays an effective role in muscle contraction. The Ajwa fruit shape is ovoid elongated and medium in size. The color is dark red in the rutab stage and turns to dark brown in the tamer stage with wrinkles (Fig. 1). The weights of Ajwa flesh and seed increase during the rutab stage and then decrease during the tamer stage (Gasim, 1994). Ajwa date has a sugar content of 77% (0.5% sucrose, 34.5% glucose and 25.6% fructose) and high proportion of minerals (3%) compared to other varieties of dates (1.5–2.7%), especially calcium (1.22 g/100 g dry matter) (Gasim, 1994).

Ajwa dates are effective for lactating women, since they assist in enriching breast milk with many effective nutrients. Furthermore, several studies have shown that kids of mothers who eat Ajwa dates regularly are less susceptible to diseases and infections (Al-Farsi & Lee, 2008). The other huge advantage of consuming Ajwa dates is that they comprise of high iron content. Iron is vital in red blood cell production and they may also assist to treat and prevent anemia (N. S. Hasan et al., 2010). Ajwa dates due to its high nutritional and health benefit properties can be considered as a potential bioactive ingredient for developing health oriented food products (Al-Farsi & Lee, 2008). Therefore, this review is focused on summarizing the current research studies on nutritional importance, phytochemical composition and health benefits of Ajwa dates.

Fig. 1. Ajwa date fruit together with different ripening stages. The picture is obtained with permission from Eid, Al-Awadi, Vauzour, Oruna-Concha, & Spencer, J. P. (2013); Eid, Al-Awadi, Vauzour, Oruna-Concha, & Spencer, J. P.E. (2013), Copyright by ACS © 2013 America Chemical Society.

2. Nutritional significance of Ajwa date fruit parts

It was suggested in the second American Institute for Cancer Research (AICR) and World Cancer Research Fund International (WCRF) expert committee report that people should overcome their nutritional requirements through routine diet rather than using dietary supplements for preventing cancer and other chronic diseases (Stewart & Wild, 2015). Ajwa date fruit being a staple food has provided nutrition to millions of people worldwide since ancient times till now. Therefore, it is important to characterize the nutritional profile of Ajwa dates in order to enhance its consumption for preventing the onset of various diet related diseases. The nutritional composition of Ajwa date flesh and pit has been reported by various researchers (Assirey, 2015; Hamad et al., 2015). It was found that Ajwa flesh contains 80% reducing sugars (Assirey, 2015; Khalid, Ahmad, Masud, Asad, & Sandhu, 2016) along with other amino acids (Assirey, 2015), proteins and fats. While, Ajwa date pits have higher percentage of proteins, crude fat and crude fiber in comparison to Ajwa flesh (Khalid et al., 2016). Recently, Khalid, et al. (2016) studied the proximate composition of Ajwa date flesh and pits (Table 1) and pointed richness of Ajwa flesh in moisture, ash, glucose, fructose, galactose and maltose. While, the Ajwa pits are enriched with crude fat and fiber and protein (Khalid et al., 2016). Moreover, their study showed a positive correlation (0.90 and 0.94) between crude fiber and fat with crude protein in Ajwa pits. Ajwa dates are also enriched with variety of minerals especially potassium together with zinc and calcium (Assirey, 2015; Gasim, 1994; Khalid et al., 2016). In this section, we briefly highlight the nutrient composition of Ajwa dates.

2.1. Sugars

Ajwa date flesh is a high-energy food due to rich sugar contents that varies between 33.2 and 74.2%. Glucose and fructose (Table 2) are the major reducing sugars, while sucrose as non-reducing share the minor percentage in composition. The Ajwa pits contain low amount of sugars varying between 7.2 and 7.6% (Assirey, 2015; Khalid et al., 2016; C.-R.; Zhang, Aldosari, Vidyasagar, Shukla, & Nair, 2015). The detail sugar contents of Ajwa flesh and pit is presented in Table 1. The bulk of the soluble compounds in Ajwa date fruit comprises of sugars both in aqueous and organic extracts. Recently, proton and carbon NMR studies showed different monosaccharides as mixture of β–D- and α-D-glucopyranose, and as well as mixtures of β-D-fructopyranose and β-D-fructofuranose. These different monosaccharides were identified both in aqueous

Table 1
Carbohydrate found in Ajwa date flesh and pits. The values are reported as %age dry matter.

Ajwa date fruit	Sugars	Assirey, 2015	Khalid et al., 2016	Gasim, 1994
Flesh	Glucose	51.3	54.5	51.2
	Fructose	48.5	52.0	48.7
	Maltose	–	22.5	–
	Galactose	–	12.2	–
	Sucrose	3.2	–	3.1
Pits	Glucose	–	20.1	–
	Fructose	–	16.1	–
	Maltose	–	6.1	–
	Galactose	–	3.4	–
	Sucrose	–	2.8	

Table 2
Amino acids and mineral composition of Ajwa dates. (a) Amino acid composition of Ajwa date flesh from different studies. Ajwa date flesh is rich in both essential and non-essential amino acids. (b) Mineral contents of Ajwa date fruit and pit. The values are reported in %age dry matter.

a

Amino acids	Assirey, 2015 (mg/100 g) DW[a]	Hamad et al., 2015 (μmol/g) FW[a]	Ali et al., 2014 (mg/g) DM[a]
Alanine	82	9.2	0.75–1.16
Arginine	93	1.42	0.45–1.23
Asparagine	186	0.26	1.29–2.80
Cysteine	–	0.001	0.89–1.38
Glutamate	205	0.8	1.76–3.79
Glycine	83	65	1.04–1.98
Histidine	26	0.99	0.36–0.54
Isoleucine	44	0.15	0.55–0.80
Leucine	57	0.02	0.89–1.32
Lysine	73	7.3	0.75–1.14
Methionine	27	0.021	0.03–0.23
Phenylalanine	45	0.99	0.62–0.87
Proline	86	16	1.04–1.98
Serine	59	0.19	0.48–0.74
Threonine	53	–	0.59–0.81
Tryptophan	44	0.027	–
Tyrosine	–	0.80	0.22–0.51
Valine	65	3.13	0.66–0.95

b

Ajwa Date	Minerals	Khalid et al., 2016 (mg/100 g)	Assirey, 2015 (mg/100 g)	Hamad et al., 2015 (mg/100 g)
Flesh	Manganese	0.36–0.5	–	0.31
	Magnesium	1.5	–	35.94
	Sodium	7.5–8.1	7.5	7.01
	Potassium	6.45	476.3	290.02
	Zinc	0.46–0.52	–	1.20
	Phosphorus	1.9–2.3	27.0	53.82
	Calcium	2.0	187.0	0.339
	Iron	0.15–0.5	–	0.15
	Cadmium	0.001–0.005	–	0.001
	Copper	0.37–0.5	–	0.37
Pits	Zinc	1.91	–	
	Potassium	4.60	–	
	Phosphorus	–	–	
	Calcium	2.0	–	

[a] DM = Dry matter, FW = Fresh weight.

and methanolic extracts (Zhang et al., 2015). The reducing sugars tend to increase in Ajwa date with different ripening stages. The % age reducing sugars increased from 41.2 to 81.1 and sucrose content increased from 1.3 to 3.1 during shift from Kimri to Tamre stage (Gasim, 1994). In a recent study by Hamad et al. (2015) they noticed high sucrose content of 25.6% that deviated the results from previous studies.

2.2. Amino acids

The amino acids analysis (Table 2a) Ajwa flesh showed a higher percentage of essential amino acids (Assirey, 2015; Hamad et al., 2015). Among the variations, the major essential amino acids reported were proline (86 mg/100 g), histidine (26 mg/100 g), leucine (57 mg/100 g), glycine (83 mg/100 g), aspartic acid (186 mg/100 g), glutathione (205 mg/100 g) and lysine (73 mg/100 g). Recently, Ali, Alhaj, Al-Khalifa, and Brückner (2014) investigated the proteinogenic and non-proteinogenic amino acids in Ajwa dates using ion-exchange chromatography and found ample amount of both proteinogenic and non-proteinogenic amino acids in Ajwa date fruit. The Ajwa date contains large of non-proteinogenic amino acids like (2S,5R)-5-hydroxypipecolic acid, 1-aminocyclopropane-1-carboxylic acid, γ-amino-*n*-butyric acid, (2S,4R)-4-hydroxyproline, L-pipecolic acid and 2-aminoethanol. Traces of 5-hydroxylysine, L-ornithine, β-alanine, (*S*)-β-aminoisobutyric acid and L-allo-isoleucine was also presented in Ajwa dates (Ali et al., 2014). These non-proteinogenic amino acids bind with the antibodies and produce T lymphocytes, detoxify harmful chemicals in liver and results in reduction of creatinine in the human body. However, no literature was available on amino acid composition of Ajwa date pits.

2.3. Minerals and vitamins

Dietary minerals are essential chemicals that are needed by the human body for maintaining skeleton structure, cellular functioning and biochemical reactions. Therefore, a certain amount of these minerals is essential for optimum growth and maintenance of human body. In this regards Ajwa date fruit (both flesh and pits) can be considered as the richest source of dietary minerals (Table 2b) among all other date varieties (Assirey, 2015; Khalid et al., 2016). It has been reported that variation among Ajwa date parts may come as a result of variation in genetic makeup, soil mineral contents and fertilizers effect. The date flesh was found to be enriched in manganese (0.4 mg/100 g), magnesium (1.5 mg/100 g), sodium (7.5 mg/100 g) and potassium (4.8 mg/100 g). Whereas, Ajwa pits have maximum concentrations of zinc (1.9 mg/100 g), potassium (4.7 mg/100 g), phosphorous (2.7 mg/100 g) and calcium (2.3 mg/100 g). The maturity stages effect the composition of minerals in Ajwa date, mostly from Kimri to the Tamre stage (Gasim, 1994). The

nitrogen content decreases from 1.23% to 0.82%, phosphorus (0.21–0.09%), potassium (1.30–0.65%), calcium (0.32–0.18%), magnesium (0.27–0.20%), similar is the trend with other trace of iron copper and zinc during shifting from Kimri to the Tamre stage. However, the concentration of these minerals are high in comparison to other cultivars like Beid, Burni, Rabeia and Safawi (Gasim, 1994).

Vitamins, such as β-carotene (provitamin A), L-ascorbic acid (vitamin C), thiamine (vitamin B_1), riboflavin (vitamin B_2) and nicotinic acid (niacin) are known to be present in dates (M. A. Al-Farsi & Lee, 2008; Al-Shahib & Marshall, 2003). Ajwa dates contain high contents of provitamin A and vitamin C (Sawaya, Safi, Black, Mashadi, & Al Muhammad, 1983).

2.4. Dietary fiber

Dietary fibers play an important role in human health. Low amount of dietary fiber can cause severe health problems such as constipation, cancer and lowers cholesterol contents in human body. Based on published reports Ajwa date flesh and pits are enriched source of total dietary fiber (TDF), soluble dietary fiber (SDF) and insoluble dietary fiber (IDF) (Assirey, 2015; Khalid et al., 2016). Ajwa date flesh has TDF contents ranging from 6.2 to 8.9% while Ajwa pits have TDF contents in the range between 26.4 and 33.9%. Similarly, Ajwa flesh has SDF varying from 6.2 to 13.5% while pits have a range between 13.5 and 22.5%. In the same context Ajwa flesh has IDF varying from 3.2 to 4.6% whereas Ajwa pits have variation between 11.2 and 12.8% (Khalid et al., 2016). The roasted Ajwa date pit have SDF of 7.0%, IDF 72.1% and TDF of 79.2%, these values are relative high in comparison to Ajwa date flesh (Ahmed, Arshad, Saeed, Ahmed, & Chatha, 2016).

2.5. Lipids

The Ajwa date lipids are regarded as oleic-linoleic lipids. The total lipid yield is about 8.9% and dominating triacylglycerol (TAG) species include dilinoleoyl-1-oleoylsn-glycerol (OLL) and 1,2-dioleoyl-3-linoleoyl-*sn*-glycerol (OOL) (Galeb et al., 2012). Ajwa date has good lipid quality indices with acid value of 1.5 mg KOH/g, iodine value of 59.9 g I_2/100 g. The free fatty acid %age of Ajwa date is about 3.1% (Galeb et al., 2012). The total saturated fatty acid (SFAs) constitutes about 21.2% while the total unsaturated fatty acid constitutes 75.26% of Ajwa date seed. Palmitic acid (10.3%), myristic acid (5.6%), lauric acid (3.2%) and steric acid (2.1%) are the dominant SFAs in Ajwa date seeds. USFAs comprises oleic acid (66.1%), linoleic acid (8.3%) and linoleic acid (0.86%) (Galeb et al., 2012). The Ajwa seed oil composition is of superior quality in comparison to other date varieties like Barni and can be used as vehicle for transversal enhancer in pharmaceutical industry (Galeb et al., 2012).

3. Phytochemicals in Ajwa date fruit

Phytochemicals having strong antioxidant activities are intercellular plant metabolites which have potential health benefits such as prevention of cancer, diabetes and cardiovascular maladies (M. Al-Farsi & Lee, 2008). Ajwa date fruit is enriched with polyphenols, flavonoids including rutin, catechins, iso-flavonoids, sterols, lignans which are important for lowering cholesterol level and thus reducing cardiovascular related illnesses (Hamad et al., 2015; Samad, Hashim, Simarani, & Yaacob, 2016). The quantities of these phenolic and antioxidant compounds may vary in different Ajwa fruit parts depending on genetic makeup, experimental conditions for analysis and extent of hydration (Al-Laith, 2009; Al-Turki, Shahba, & Stushnoff, 2010; Amorós et al., 2009). Similarly, extraction procedure, status of fruit (Fresh or dried) and the solvent used for extraction can affect the quality and quantity of phytochemicals in dates (Al-Farsi, Alasalvar, Morris, Baron, & Shahidi, 2005). This section reviews the phytochemical contents of Ajwa dates.

3.1. Phenolic compounds

The phenolic compounds are secondary metabolites, categorized by the presence of monophenolic or polyphenolic aromatic carbon rings with hydroxyl group attached to functional carbon. However, their nature, formulation and distribution in date palm fruit is dependent on date palm variety, growing conditions and extraction procedures (Al-Laith, 2009; Al-Turki et al., 2010; Amorós et al., 2009). The total phenolic content of Ajwa fruit varied between 245 and 455 mg/100 g. However, the extraction solvent plays a significant role. The contents are always higher in aqueous extract in comparison to alcoholic extracts (Hamad et al., 2015; Saleh, Tawfik, & Abu-Tarboush, 2011). The higher phenolic contents in aqueous solution might be due to polarity of aqueous solution and further depends on method of extraction. The phenolic composition of Ajwa dates include rutin (0.65–0.85 mg/100 g), catechin (0.73 mg/100 g) and caffeic acid (0.57–1.84 mg/100) (Ahmed et al., 2016; Hamad et al., 2015; Saleh et al., 2011). The phenolic content of Ajwa date(10 mg/100 g-290 mg/100 g) also varied according to the ripening stage. The Ajwa date contain higher polyphenol content at kimri stage (290 mg/100 g) followed by khalal (150 mg/100 g), rutab (20 mg/100 g) and tamr (10 mg/100 g) stage (Eid, Al-Awadi, Vauzour, Oruna-Concha, & Spencer, J. P., 2013; Eid, Al-Awadi, Vauzour, Oruna-Concha, & Spencer, J. P.E., 2013).

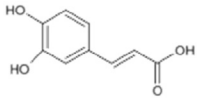
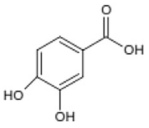
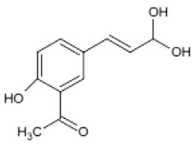
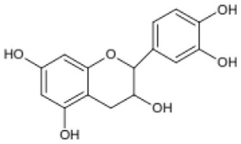
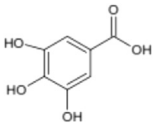
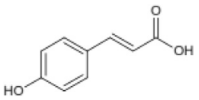
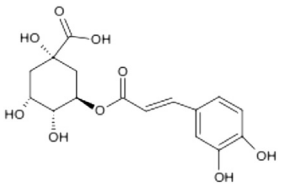
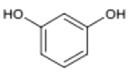
Hamad, et al. (2015) found *p*-coumaric acid, gallic acid and ferulic acid derivatives were the most dominant phenolic compounds in Ajwa dates. Similarly, Eid, Al-Awadi, Vauzour, Oruna-Concha, & Spencer, J. P. (2013); Eid, Al-Awadi, Vauzour, Oruna-Concha, & Spencer, J. P.E. (2013) found protocatechuic acid, hydroxybenzoic acid, vanillic acid, gallic acid, isovanillic acid, chlorogenic acid, ferulic acid, isoferulic acid, caffeic acid, hydroxycinnamic acid and chlorogenic acid as the main phenolic compounds and acid with different ripening stages of Ajwa date. Ahmed et al. (2016) pointed gallic acid, caffeic acid, chlorogenic acid, syringic acid, *p*-coumeric acid, *m*-coumeric acid and ferulic acid as dominant phenols and acids in roasted Ajwa pits. Table 3a shows composition of different phenolic compounds present in Ajwa date.

3.2. Flavonoids and minor components

Polyphenolic flavonoids are the most abundant phenolic compounds found in Ajwa dates with pervasive dispersal. These polyphenolic compounds are mainly present within fruit skins in high concentrations with immense health benefits such as antioxidant and free radical scavenging activities. These are effective in minimizing chronic and cardiovascular diseases with positive effect against proliferation of damaged cells (Eid et al., 2014). These flavonoids can be classified in different sub-classes such as flavones, flavonols, iso-flavones and anthocyanins. Ajwa date fruit is enriched with active flavonoids including quercetin, isoquercetin, luteolin, apgenin, and rutin (Hamad et al., 2015; Ragab, Elkablawy, Sheik, & Baraka, 2013). Hamad et al. (2015) determined total flavonoid content of Ajwa date fruit around 2.79 mg/100 g. The detailed flavonoid composition of Ajwa date is presented in Table 3b. The Ajwa date pit contains quercetin (1.35 mg/100 g) as the dominant flavonoid (Ahmed et al., 2016). The most common flavonoids found in plantae kingdom are flavonols. Ajwa date flesh and pits are enriched with flavonols which occur commonly as *O*-glycosides. However, concentrations of these compounds

Table 3
Phenolic and flavonoids composition of Ajwa dates. (a) Phenolic composition of Ajwa date fruit and pit from different literature. (b) Flavonoids composition of Ajwa date fruit from different literature.

a

Phenolic acid	Structure	Quantity (mg/100 g DW)	Reference
Caffeic acid		0.026–0.050	Hamad et al. (2015) Saleh et al. (2011) Ragab et al. (2013) Ahmed et al. (2016)
Ferullic acid		2.52–3.20	Hamad et al. (2015) Ahmed et al. (2016)
Protocatechuic acid		1.27–2.20	Hamad et al. (2015) Saleh et al. (2011)
Catechin		0.50–0.80	Hamad et al. (2015) Saleh et al. (2011) Ragab et al. (2013)
Gallic acid		13.90–14.10	Hamad et al. (2015) Ahmed et al. (2016)
p-coumanic acid		3.08–3.50	Hamad et al. (2015) Ahmed et al. (2016)
Chlorogenic acid		0.18–0.20	Hamad et al. (2015) Ahmed et al. (2016)
Resorcinol acid		0.03–0.05	Hamad et al. (2015)
Total phenols		22.10–455.80	Hamad et al. (2015) Saleh et al. (2011)

b

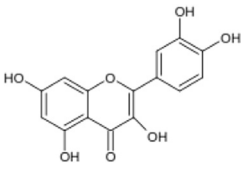
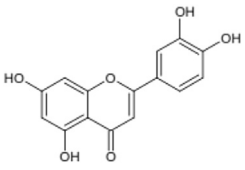
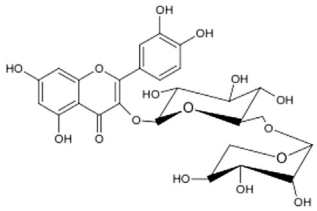
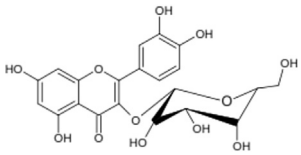
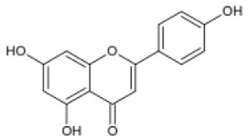
Flavonoids	Structure	Quantity (mg/100 g DW)	References
Quercetin		1.21	Hamad et al. (2015) Ahmed et al. (2016)
Luteolin		0.04	Hamad et al. (2015) Ahmed et al. (2016)

Table 3 (*continued*)

b

Flavonoids	Structure	Quantity (mg/100 g DW)	References
Rutin		0.86	Hamad et al. (2015) Ahmed et al. (2016) Saleh et al. (2011)
Iso-quercetin		0.41	Hamad et al. (2015) Ahmed et al. (2016)
Apigenin		0.26	Hamad et al. (2015) Ahmed et al. (2016)
Total Flavonoids		2.78	Hamad et al. (2015) (Ahmed et al. (2016))

extensively varied between flesh and pits of Ajwa fruit (Ahmed et al., 2016; Hamad et al., 2015). Recently, chrysoeriol-7-*O*-(2,6-dirhamnosyl)-glucoside (Fig. 2a) have been identified in Ajwa date fruit (Zhang, Adosari, Vidyasagar, P. S. P. V., 2013; Zhang, Aldosari, Vidyasagar, P. S., 2013). Eid, Al-Awadi, Vauzour, Oruna-Concha, & Spencer, J. P. (2013); Eid, Al-Awadi, Vauzour, Oruna-Concha, & Spencer, J. P.E. (2013) studied the flavonoid composition of Ajwa dates at different ripening stages and found significant quantities of quercetin, myricetin, naringenin, apigenin, luteolin and kaempferol using LC-MS/MS techniques.

The other minor components in Ajwa date fruit include triterpenoids like lupeol and lup-20(29)-en-3-one (Fig. 2b and c) and steroids like β-sitosterol, β-sitosteryl-3-*O*-β-glucoside and β-sitosteryl-3β-glucopyranoside6′-*O*-palmitate (Fig. 2d–f) and phthalates like bis(2-ethylheptyl) phthalate, bis(2-ethylhexyl) terephthalate (Fig. 2g and h) (Zhang, Adosari, Vidyasagar, P. S. P. V., 2013; Zhang, Aldosari, Vidyasagar, P. S., 2013). These bioactive compounds of Ajwa date contribute towards anti-inflammatory and antioxidant properties. The Ajwa date also contain significant amount of anthocyanidins and are present mostly in kimri stage (Eid, Al-Awadi, Vauzour, Oruna-Concha, & Spencer, J. P., 2013; Eid, Al-Awadi, Vauzour, Oruna-Concha, & Spencer, J. P.E., 2013). The Ajwa date contain few important organic acids like succinic acid, oxalic acid, malic acid, citric acid, isobutyric acid and formic acid. These acids further improves the functionality of Ajwa dates (Hamad et al., 2015).

4. Biological and pharmacological activities of Ajwa date

The efficacy of drugs usage has been decreased due to the emergence of resistance and tolerance in the existing drugs. Therefore, an increasing trend to replace the synthetic drugs with natural products (plants sources) has been observed in pharmaceutical industry. These natural sources are enriched with phytochemicals which have higher disease preventing characteristics (Chirumbolo, 2012). Ajwa date is used traditionally and historically against different diseases due to its anti-inflammatory, hepa-toxic, anti-cancer and most importantly against cardiac function improvement (Table 4) (Al-Yahya et al., 2015; Hussain Mallhi, Qadir, Ali, Ahmad, & Khan, 2014; Ragab et al., 2013). In the following sections pharmacological properties of Ajwa flesh and pit is reviewed.

4.1. Antioxidant activity

Ajwa date fruits are widely consumed in the Arabian countries and the strong antioxidant activity is due to higher phenolics, melatonin, carotenoids and vitamins contents (Al-Farsi et al., 2005; Al-Farsi & Lee, 2008; Chaira et al., 2009). The antioxidant activity of Ajwa fruit have mostly been evaluated in aqueous and alcoholic extracts. The antioxidants in Ajwa fruit are mostly hydrophilic and poses strong antioxidant activity in lipid membrane system (Al-Farsi et al., 2005). Saleh et al. (2011) pointed strong antioxidant activity of Ajwa fruit aqueous extract in comparison to alcoholic extracts. The MTT (3-(4,5-Dimethylthiazol-2-yl)-2,5-Diphenyltetrazolium Bromide) assay with ethyl acetate, methanolic, and water extracts of Ajwa dates at 250 μg/mL inhibited lipid peroxidation by 88, 70, and 91% (Zhang, Adosari, Vidyasagar, P. S. P. V., 2013; Zhang, Aldosari, Vidyasagar, P. S., 2013). The rabbit experimental modeling with ethanolic extract of Ajwa dates showed increased levels of serum antioxidant enzymes together with reduction in lipid hydroperoxides in lead intoxicated rabbits (Ragab et al., 2013). The possible pathway through which Ajwa dates exert antioxidant effect is the suppression of free radicals, that in turn reduces the proliferation of disease. Other studies have confirmed these strong antioxidant effect of Ajwa dates (Ahmed et al., 2016; Al-Yahya et al., 2015; Zhang et al., 2015). Recently, Al-Yahya et al. (2015) evaluated that Ajwa date extracts prevents the depletion of vital antioxidants like glutathione peroxidase, superoxide dismutase and carnitine acyltransferase. In a recent study with different extracts of Ajwa fruit and pit by Arshad, Jelani, Haroon, and Masood (2015) showed strong antioxidant with 74.19 μg/mL of gallic acid equivalents in methanolic extracts. Moreover, they pointed strong radical scavenging activity in DPPH and lipid peroxidation assays in acetone

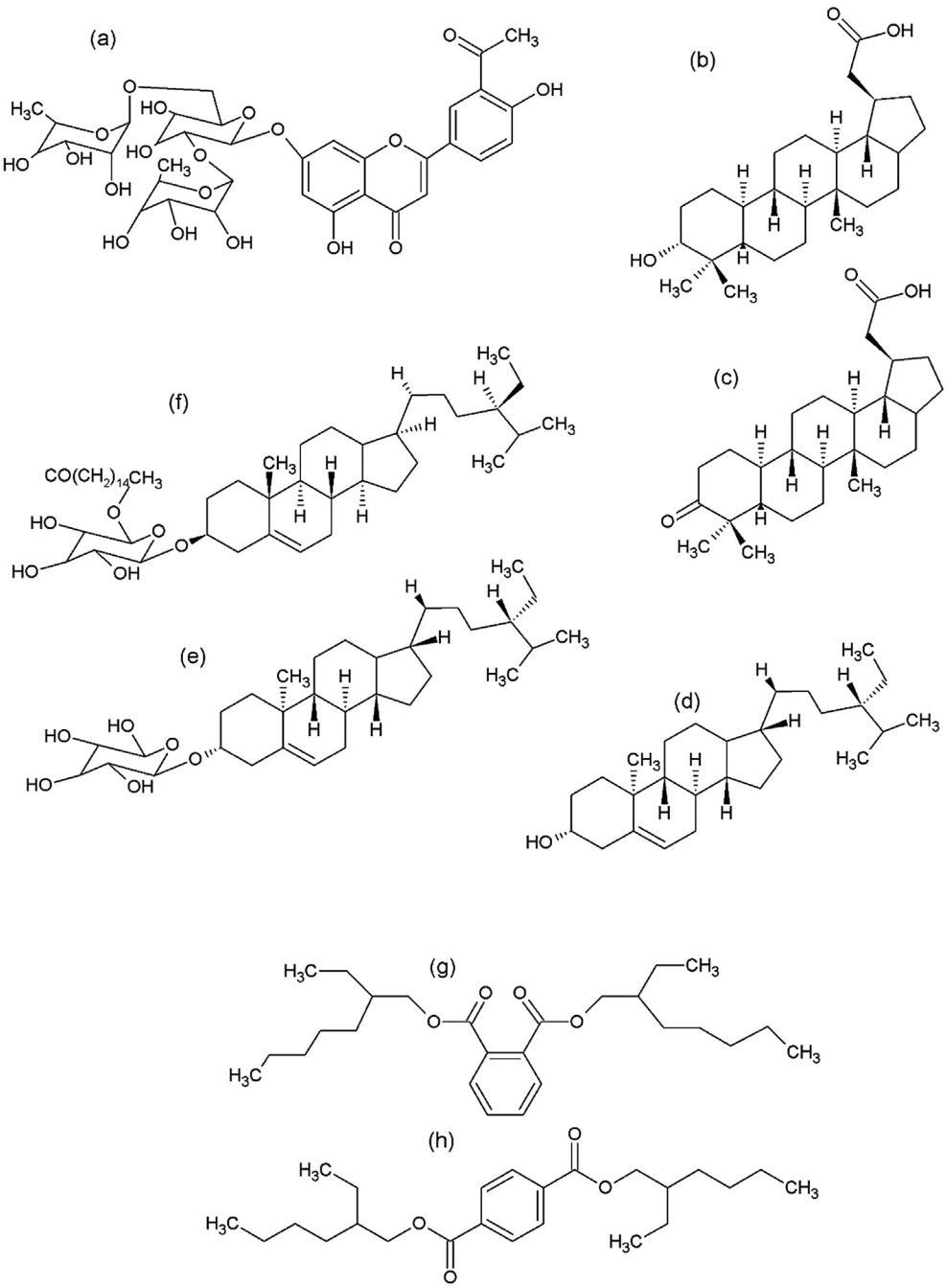


Fig. 2. Different phytochemicals present in Ajwa date fruit. The phytochemicals diversity ranged from triterpenoids to steroids and to phthalates.

extracts of Ajwa dates. However, they mentioned remarkable radical scavenging activity of aqueous extracts of Ajwa pits in comparison to other solvents (Arshad et al., 2015).

4.2. Antiviral, antifungal and antibacterial activities

Jassim and Naji (2010) investigated the antiviral activity of acetone extracted ajwa date pit against *Pseudomonas* phage. The results showed antiviral activity with MIC <10 μg/mL. The factors like concentration exponent, phage inactivation kinetics and decimal reduction time strongly depicting antiviral potential of pit extract. The Ajwa date extract might be an inexpensive way to protect patient from viral infections by inhibiting the infectivity of phage lysis and future reserach should be carried out to determine the potenial of extracts for HIV treatment (Jassim & Naji, 2010).

It was reported that aqeuous, methanol and acetone extracts of leaves and pits of Ajwa dates inhibited the growth of *F. solani, F. oxysporum, Alternaria* spp., *A. alternata, Fusarium* sp., *A. flavus* and *Trichoderma* sp. The leave extract showed inhibitory activity of 51.5% against *A. Alternata*, while the inhibitory activity of 29.4%, 38.5% and 6.3% was observed against *F. solani, F. Fusarium* and *F. oxysporium*. The Ajwa pits also showed inhibitory activity of 40.9% against *A. Alternata* and 38.5% against *F. Fusarium*, mild activity was also observed against *F. solani* and *F. oxysporium*. Moreover, the trend of activity was as methanolic pits extract > methanolic leaves extract > acetone pits extract > acetone leaves extract (Bokhari &

Table 4
Health benefits of Ajwa date fruit and pit from different literatures. The activities were observed in different extraction solvents and using both *in vitro* and *in vivo* approaches.

Pharmacological property	Observations and references
Antioxidant activity	Scavenges free radical activity and reduces lipid peroxidation and prevented depletion of CAT, SOD, NP-SH antioxidants (Al-Yahya et al., 2015; Saleh et al., 2011; Zhang, Adosari, Vidyasagar, P. S. P. V., 2013; Zhang, Aldosari, Vidyasagar, P. S., 2013; Zhang et al., 2015).
Anti-microbial activity	Methanolic extract of Ajwa dates inhibits the growth of *E.coli*, *S. marcescens*, *B. cereus* and *S. aureus* (Samad et al., 2016).
Anti-inflammatory activity	Methanolic Ajwa extracts have showed 22–41% inhibition to COX-I enzyme and 48–52% inhibition to Cox-II enzyme in albino rats (Zhang, Adosari, Vidyasagar, P. S. P. V., 2013; Zhang, Aldosari, Vidyasagar, P. S., 2013).
Antitoxic effect	Strong inhibitory effect against lead acetate toxicity in rabbits with significant restoration of SGPT, SGOT, ALP,TD, SOD and GPx levels (Ragab et al., 2013). Protection against ochratoxin A-toxicity in albino rats with decreased levels of serum creatinine and urea levels in kidney (Ali et al., 2011b, 2011a).
Effect on male fertility	Increased progressive sperms motility and decreased non-progressive immortal sperms morphology (Wahyudi, Retno, & Andi, 2015).
Effect on nephrotoxicity	Protective effect and ameliorated lesions of Ochratoxin nephrotoxicity (Ali et al., 2011b, 2011a; Ali et al., 2011b, 2011a).
Antitumor activity	Methanolic Ajwa extracts showed marginal cells proliferation inhibitory effect against gastric, prostrate, colon, breast and lung tumor cell lines (Zhang, Adosari, Vidyasagar, P. S. P. V., 2013; Zhang, Aldosari, Vidyasagar, P. S., 2013).
Hypolipidemic effect	Ajwa liquid extracts reduced total cholesterol, triglycerides, LDL and increased HDL-C levels in Wister rats (Al-Yahya et al., 2015).
Antidiabetic effect	Ajwa pits showed restoration of liver and kidney functions and significantly reduces glucose levels in induced diabetic a rats (Hasan & Mohieldein, 2016).
Hepatoprotective effect	Positive effects by lowering hepatic marker enzymes (SGPT and SGOT) and correct albumin levels (Sheikh et al., 2014).
Effect on gastric system	Significant increase in bowl movement and stool frequency while reduction in human fecal water and colon cancer risk (Eid et al., 2014; Eid et al., 2015).

Perveen, 2012). The antifungal activity of Ajwa date in dichloromethanalic extract was also reported by Boulenouar, Marouf, and Cheriti (2011).

Bacterial resistance is one of the major challenge against antimicrobial drugs. To overcome the problem of resistance, the use of natural products and their constituents is a good approach to control the infection as they are inexpensive and also having no side effects (Al-Daihan & Bhat, 2010). The Ajwa date and its constituents play a significant effect in the treatment of bacterial diseases. The methanol and acetone extracts of the Ajwa dates pits reasonably inhibited the growth of Gram positive and Gram negative bacteria (Aamir, Kumari, Khan, & Medam, 2013; Jassim & Naji, 2010). Ajwa dates inhibits the activity of *Escherichia coli* and *Klebsiella pneumonia* and also inhibit the reducing effect of methylprednisolone (Aamir et al., 2013). Methanolic extract of Ajwa dates are also effective against enteric diseases, since it suppresses the activity of *Enterococcus fecalis* (Aamir et al., 2013). The methanolic extract of Ajwa date is effective against *Escherichia coli*, *Bacillus cereus*, *Staphylococcus aureus* and *Serratia marcescens* (Samad et al., 2016).

4.3. Anti-inflammatory activity

Inflammation is one of the important physiological defense mechanisms against various factors such as infection, burn, toxic chemicals, allergens and other stimuli (Sharma, Dubey, Sati, & Sanadya, 2011). Excessive production of free radicals from activated inflammatory leukocytes causes many problems like diabetes and arthritis (Zhang et al., 2015). The disturbance in inflammatory mechanism results in development and progression of various disorders. Transcription factors (LOX and NF-kB) play an important role in the inflammation, diabetes, cancer and other diseases. So the critical step in the prevention of disease is the proper regulation of transcription factors. Previous studies have shown that constituents of plants such as flavonoids and phenolics act as excellent anti-inflammatory agents (Talhouk, Karam, Fostok, El-Jouni, & Barbour, 2007). It was investigated that methanolic and aqueous extract Ajwa date possess anti-inflammatory properties in albino rats by increasing levels of COX 1 and 2 enzymes. The ethyl acetate, methanolic, and water extracts of Ajwa dates inhibit the lipid peroxidation cyclooxygenase enzymes COX-1 and COX2. These studies have also shown that Ajwa date constituents such as polyphenols, fiber, steroids and minerals possess anti-inflammatory effects (Zhang, Adosari, Vidyasagar, P. S. P. V., 2013; Zhang, Aldosari, Vidyasagar, P. S., 2013; Zhang et al., 2015; C. Zhang, Aldosari, Vidyasagar, Shukla, & Nair, 2014). lyophilized extract of Ajwa dates at concentration of 250 μg/mL downregulates the expression of pro-inflammatory cytokines like IL-6, IL-10 and TNFα together with apoptotic markers like caspase-3 and Bax in both *ex vivo* and *in vivo* models (Al-Yahya et al., 2015). Similarly, lyophilized extract of Ajwa dates at concentration of 250 μg/mL (Fig. 1) reduces edema, myonecrosis and infiltration of inflammatory cells in cardiomyocytes architecture and shows strong cardioprotective effects in rodent model (Al-Yahya et al., 2015). Abdul-Hamid et al. (2015) showed strong nitric oxide (NO) inhibiting activity of different extracts of Ajwa dates using NMR approach. Their study demonstrated that extraction solvent is the critical factor that affects the NO inhibiting activity of Ajwa date extract. Moreover, freeze dried and methanol extracts of Ajwa dates shows the remarkable NO inhibiting activity in comparison to other extracts (Abdul-Hamid et al., 2015).

4.4. Nephrotoxic and hepatoprotective activities

Nephrotoxicity is a usual side effect of many antibiotic drugs whose amelioration is necessary. Ochratoxin is a mycotoxin generated by these antibiotics can affect the human kidney leading to kidney failure (Kalantaripour, Shekaari, Basiri, & Najar, 2012). Awatef Ali, Susan Abdu, and Sasha Alansari (2011a, b) investigated the potential anti-toxic effect of Ajwa dates in rabbits against ochratoxin. Oral dosage of ochratoxin significantly increased the serum creatinine and urea level in rabbits and damaged the proximal tubules. On the other hand, Ajwa date extracts reduced the serum creatinine and urea levels. However, combination of Ajwa date extract with ochratoxin reduces the severity of lesions (Ali et al., 2011a; Ali et al., 2011b). Bakr Abdu (2011) demonstrated the therapeutic effect of Ajwa date aqueous extract against the hepatotoxicity induced by ochratoxin A in rats. The treatment significantly reduces the bilirubin and ALT enzyme activity in rats pretreated with Ajwa date aqueous extract. Another study reported the positive effects of Ajwa fruit and pit in gentamicin treated nephrotoxicity rat model. The in-cooperation of Ajwa fruit with

food (50% (w/w)) or pit with water (2:1 (w/v)) significantly decrease the plasma creatinine and urea concentrations (Al-Qarawi, Abdel-Rahman, Mousa, Ali, & El-Mougy, 2008). Feeding Ajwa date extract (300 mg/kg/day for 14 days) significantly inhibited the depletion of antioxidants in albino rats when induced with lead acetate toxicity (Ragab et al., 2013). Similar results are also reported with carbon tetrachloride (CCl_4) induced toxicity in rat model by Sheikh, Elsaed, Samman, Sheikh, and Ladin (2014).

4.5. Antidiabetic activity

The plants play a major role to treat the diabetes and its complication including diabetic retinopathy via modulation of metabolic and molecular pathways (Gupta et al., 2011). The phytochemicals have ability to control the functions of pancreatic tissues by enhancing the production of insulin and reduce the absorption of glucose in the intestinal wall. The antidiabetic activity in Ajwa extracts might be due to saponins, phenol, steroids and flavonoids, which play a major role in stopping diabetes (Hussain Mallhi et al., 2014). The phenolic compounds reducing effect of α-glucosidase enzymes, that effect the absorption of glucose in small intestine and kidneys. Moreover, the phenolic compounds also modulate the secretion of insulin in human body. The strong antioxidant profile of Ajwa fruit can plays a strong antidiabetic role by scavenging the free radicals (Zhang et al., 2015). Aqueous Ajwa seed extract in concentration of 100 g/L brings a reduction in blood glucose level in streptozotocin induced diabetic rats. Moreover, prolong use of Ajwa seed extract restores the function of liver and kidneys and balance the oxidative stress conditions in streptozotocin induced diabetic rats (Hasan & Mohieldein, 2016).

4.6. Anticancer activity

It has been reported that aqueous and methanolic extracts of Ajwa dates at concentration of 100 μg/mL inhibited the marginal cell proliferation against human gastric, lung, breast and colon cell lines (. Zhang et al., 2015). These beneficial anti-tumor effect of Ajwa dates are due to the presence of flavonoids especially quercetin, steroids and polyphenols (Hussain Mallhi et al., 2014). The bioactives of Ajwa dates increase the activities of antioxidant enzymes such as SOD, GST, and catalase in body which inhibits the proliferation of damaged cells there by reducing the chances of mutagenesis. Ajwa dates have a cyclo-oxygenase inhibitory effect (Zhang, Adosari, Vidyasagar, P. S. P. V., 2013; Zhang, Aldosari, Vidyasagar, P. S., 2013) that is similar to commercial anti-inflammatory drugs like aspirin, ibuprofen, celebrex and naproxen. Ajwa date extract and Ajwa polyphenols are effective on inhibiting the growth of colon adenocarcinoma cell growth and also maintain bowel health (Eid et al., 2014). Moreover, Ajwa date extract also maintain and resist changes in microbiota (Eid et al., 2015).

5. Conclusion

The data analysis from the last few decades suggests that ajwa date fruit has a potential to become an essential food ingredient for developing new bioactive functional food products targeted at various physiological functions of human body. This review has provided a guideline to proceed further in establishing the efficacy of various observed medicinal effects including anti-cancer, gastro-protective, hepato-protective and nephro-protective activities. These observed pharmacological properties are attributed to the presence of high concentrations of phtyochemicals and minerals stangled diverse chemical structures. These pharmacological effects can be tried and tested in neutraceuticals and functional foods development in pharmaceuticals and food manufacturing industry. This will provide an opportunity for the food companies to develop radically innovative functional food products. This will further enable the food companies to compete in the global health and wellness market by introducing these bioactive functional food products.

References

Aamir, J., Kumari, A., Khan, M. N., & Medam, S. K. (2013). Evaluation of the combinational antimicrobial effect of Annona Squamosa and Phoenix Dactylifera seeds methanolic extract on standard microbial strains. *International Research Journal of Biological Sciences, 2*, 68–73.

Abdul-Hamid, N. A., Abas, F., Ismail, I. S., Shaari, K., & Lajis, N. H. (2015). Influence of different drying treatments and extraction solvents on the metabolite profile and nitric oxide inhibitory activity of Ajwa Dates. *Journal of Food Science, 80*, H2603–H2611.

Ahmed, A., Arshad, M. U., Saeed, F., Ahmed, R. S., & Chatha, S. A. S. (2016). Nutritional probing and HPLC profiling of roasted date pit powder. *Pakistan Journal of Nutrition, 15*, 229.

Al-Daihan, S., & Bhat, R. S. (2010). Antibacterial activities of extracts of leaf, fruit, seed and bark of phoenix dactylifera. *African Journal of Biotechnology, 11*(42), 10021–10025.

Al-Farsi, M., Alasalvar, C., Morris, A., Baron, M., & Shahidi, F. (2005). Comparison of antioxidant activity, anthocyanins, carotenoids, and phenolics of three native fresh and sun-dried date (Phoenix dactylifera L.) varieties grown in Oman. *Journal of Agricultural and Food Chemistry, 53*, 7592–7599.

Al-Farsi, M. A., & Lee, C. Y. (2008). Nutritional and functional properties of dates: A review. *Critical Reviews in Food Science and Nutrition, 48*, 877–887.

Al-Laith, A. A. (2009). Degradation kinetics of the antioxidant activity in date palm (Phoenix dactylifera L.) fruit as affected by maturity stages. *Arab Gulf Journal of Scientific Research, 27*, 16–25.

Al-Qarawi, A., Abdel-Rahman, H., Mousa, H., Ali, B., & El-Mougy, S. (2008). Nephroprotective action of Phoenix dactylifera. in gentamicin-induced nephrotoxicity. *Pharmaceutical Biology, 46*, 227–230.

Al-Shahib, W., & Marshall, R. J. (2003). The fruit of the date palm: Its possible use as the best food for the future? *Int J Food Sci Nutr, 54*, 247–259.

Al-Turki, S., Shahba, M. A., & Stushnoff, C. (2010). Diversity of antioxidant properties and phenolic content of date palm (Phoenix dactylifera L.) fruits as affected by cultivar and location. *Journal of Food Agriculture and Environment, 8*, 253–260.

Al-Yahya, M., Raish, M., AlSaid, M. S., Ahmad, A., Mothana, R. A., Al-Sohaibani, M., et al. (2015). 'Ajwa'dates (Phoenix dactylifera L.) extract ameliorates isoproterenol-induced cardiomyopathy through downregulation of oxidative, inflammatory and apoptotic molecules in rodent model. *Phytomedicine*. http://dx.doi.org/10.1016/j.phymed.2015.1010.1019.

Ali, A., Abdu, S., & Alansari, S. (2011a). Biosafty of ajwa date against biotoxicty of ochratoxin (A) on proximal renal tubules of male rat. *Kidney Research Journal, 1*, 1–12.

Ali, A., Abdu, S., & Alansari, S. (2011b). Renoprotective effect of date fruit extract on ochratoxin (a) induced-oxidative stress in distal tubules of rat: A light and electron microscopic study. *Kidney Research Journal, 1*, 13–23.

Ali, H. S. M., Alhaj, O. A., Al-Khalifa, A. S., & Brückner, H. (2014). Determination and stereochemistry of proteinogenic and non-proteinogenic amino acids in Saudi Arabian date fruits. *Amino acids, 46*, 2241–2257.

Amorós, A., Pretel, M., Almansa, M., Botella, M., Zapata, P., & Serrano, M. (2009). Antioxidant and nutritional properties of date fruit from Elche grove as affected by maturation and phenotypic variability of date palm. *Food Science and Technology International, 15*, 65–72.

Arshad, F. K., Jelani, S., Haroon, R., & Masood, H. b. (2015). A relative in vitro evaluation of antioxidant potential profile of extracts from pits of Phoenix dactylifera L. (Ajwa and Zahedi Dates). *International Journal of Advanced Information Science and Technology, 35*, 28–37.

Assirey, E. A. R. (2015). Nutritional composition of fruit of 10 date palm (*Phoenix dactylifera* L.) cultivars grown in Saudi Arabia. *Journal of Taibah University for Science, 9*, 75–79.

Bakr Abdu, S. (2011). The protective role of ajwa date against the hepatotoxicity induced by ochratoxin a. *Egyptian Journal of Natural Toxins, 8*, 1–15.

Barreveld, W. (1993). *Date palm products. Agricultural services bulletin no. 101*. Rome: FAO.

Bokhari, N. A., & Perveen, K. (2012). In vitro inhibition potential of Phoenix dactylifera L. extracts on the growth of pathogenic fungi. *Journal of Medicinal Plants Research, 6*, 1083–1088.

Boulenouar, N., Marouf, A., & Cheriti, A. (2011). Antifungal activity and phytochemical screening of extracts from Phoenix dactylifera L. cultivars. *Natural Product Research, 25*, 1999–2002.

Chaira, N., Smaali, M. I., Martinez-Tomé, M., Mrabet, A., Murcia, M. A., & Ferchichi, A. (2009). Simple phenolic composition, flavonoid contents and antioxidant capacities in water-methanol extracts of Tunisian common date cultivars (Phoenix dactylifera L.). *International Journal of Food Science and Nutrition, 60*, 316–329.

Chirumbolo, S. (2012). Plant phytochemicals as new potential drugs for immune disorders and cancer therapy: Really a promising path? *Journal of the Science of*

Food and Agriculture, 92, 1573–1577.
Eid, N. M., Al-Awadi, B., Vauzour, D., Oruna-Concha, M. J., & Spencer, J. P. (2013a). Effect of cultivar type and ripening on the polyphenol content of date palm fruit. *Journal of Agricultural and Food Chemistry, 61*, 2453–2460.
Eid, N. M. S., Al-Awadi, B., Vauzour, D., Oruna-Concha, M. J., & Spencer, J. P. E. (2013b). Effect of cultivar type and ripening on the polyphenol content of date palm fruit. *Journal of agricultural and food chemistry, 61*, 2453–2460.
Eid, N., Enani, S., Walton, G., Corona, G., Costabile, A., Gibson, G., et al. (2014). The impact of date palm fruits and their component polyphenols, on gut microbial ecology, bacterial metabolites and colon cancer cell proliferation. *Journal of Nutritional Science, 3*, e46.
Eid, N., Osmanova, H., Natchez, C., Walton, G., Costabile, A., Gibson, G., et al. (2015). Impact of palm date consumption on microbiota growth and large intestinal health: A randomised, controlled, cross-over, human intervention study. *British Journal of Nutrition, 114*, 1226–1236.
FAO. (2003). The marketing potential of date palm fruits in the European market. FAO Commodity and Trade Policy Research Working Paper No. 6. In Pascal Liu (Ed.), *Raw materials, tropical and horticultural products service commodities and trade division*. Rome, Italy: FAO.
Galeb, H. A., Salimon, J., Eid, E. E. M., Nacer, N. E., Saari, N., & Saadi, S. (2012). The impact of single and double hydrogen bonds on crystallization and melting regimes of Ajwa and Barni lipids. *Food Research International, 48*, 657–666.
Gasim, A. A. A. (1994). Changes in sugar quality and mineral elements during fruit development in five date palm cultivars in AI-Madinah AI-Munawwarah. *Journal of King Abdul Aziz University, Science, 6*, 29–36.
Gupta, S. K., Kumar, B., Nag, T. C., Agrawal, S. S., Agrawal, R., Agrawal, P., et al. (2011). Curcumin prevents experimental diabetic retinopathy in rats through its hypoglycemic, antioxidant, and anti-inflammatory mechanisms. *Journal of Ocular Pharmacology and Therapeutics, 27*, 123–130.
Hamad, I., AbdElgawad, H., Al Jaouni, S., Zinta, G., Asard, H., Hassan, S., et al. (2015). Metabolic analysis of various date palm fruit (Phoenix dactylifera L.) cultivars from Saudi Arabia to assess their nutritional quality. *Molecules, 20*, 13620–13641.
Hasan, N. S., Amom, Z. H., Nor, A. I., Mokhtarrudin, N., Esa, N. M., & Azlan, A. (2010). Nutritional composition and in vitro evaluation of the antioxidant properties of various dates extracts (*Phoenix dactylifera* L.) from Libya. *Asian Journal of Clinical Nutrition, 2*, 208–214.
Hasan, M., & Mohieldein, A. (2016). In vivo evaluation of anti diabetic, hypolipidemic, antioxidative activities of Saudi date seed extract on streptozotocin induced diabetic rats. *Journal of clinical and diagnostic research: JCDR, 10*, FF06.
Hussain Mallhi, T., Qadir, M. I., Ali, M., Ahmad, B., & Khan, Y. H. (2014). Ajwa date (Phoenix dactylifera): An emerging plant in pharmacological research. *Pakistan Journal of Pharmaceutical Sciences, 27*.
Jassim, S. A., & Naji, M. A. (2010). In vitro evaluation of the antiviral activity of an extract of date palm (Phoenix dactylifera L.) pits on a Pseudomonas phage. *Evidence-Based Complementary and Alternative Medicine, 7*, 57–62.
Kalantaripour, T. P., Shekaari, M. S., Basiri, M., & Najar, A. G. (2012). Cerebroprotective effect of date seed extract (Phoenix dactylifera) on focal cerebral ischemia in male rats. *Journal of Biological Sciences*, 1–6.
Khalid, S., Ahmad, A., Masud, T., Asad, M. J., & Sandhu, M. (2016). Nutritional assessment of ajwa date flesh and pits in comparison to local varieties. *Journal of Plant and Animal Sciences, 26*(4), 1072–1080.
Ragab, A. R., Elkablawy, M. A., Sheik, B. Y., & Baraka, H. N. (2013). Antioxidant and tissue-protective studies on ajwa Extract: Dates from Al-Madinah Al-Monwarah, Saudia Arabia. *Journal of Environmental & Analytical Toxicology, 2013*.
Saleh, E. A., Tawfik, M. S., & Abu-Tarboush, H. M. (2011). Phenolic contents and antioxidant activity of various date palm (Phoenix dactylifera L.) fruits from Saudi Arabia. *Food and Nutrition Sciences, 2*, 1134–1141.
Samad, M. A., Hashim, S. H., Simarani, K., & Yaacob, J. S. (2016). Antibacterial properties and effects of fruit chilling and extract storage on antioxidant activity, total phenolic and anthocyanin content of four Date Palm (Phoenix dactylifera) Cultivars. *Molecules, 21*, 419.
Sawaya, W., Safi, W., Black, L., Mashadi, A., & Al Muhammad, M. (1983). Physical and chemical characterisation of the major date varieties grown in Saudi Arabia, 2: Sugars, tannins, vitamins A and C. *Date Palm Journal, 2*, 183–196.
Sharma, G. N., Dubey, S. K., Sati, N., & Sanadya, J. (2011). Anti-inflammatory activity and total flavonoid content of Aegle marmelos seeds. *International Journal of Pharmaceutical Sciences and Drug Research, 3*, 214–218.
Sheikh, B. Y., Elsaed, W. M., Samman, A. H., Sheikh, B. Y., & Ladin, A.-M. M. B. (2014). Ajwa dates as a protective agent against liver toxicity in rat. *European Scientific Journal, 3*, 258–368.
Stewart, B., & Wild, C. P. (2015). *World cancer report 2014*. International Agency for Research on Cancer, WHO.
Talhouk, R., Karam, C., Fostok, S., El-Jouni, W., & Barbour, E. (2007). Anti-inflammatory bioactivities in plant extracts. *Journal of medicinal food, 10*, 1–10.
Terral, J. F., Newton, C., Ivorra, S., Gros-Balthazard, M., de Morais, C. T., Picq, S., et al. (2012). Insights into the historical biogeography of the date palm (*Phoenix dactylifera* L.) using geometric morphometry of modern and ancient seeds. *Journal of Biogeography, 39*, 929–941.
Vayalil, P. K. (2012). Date fruits (*Phoenix dactylifera* Linn): An emerging medicinal food. *Critical reviews in food science and nutrition, 52*, 249–271.
Wahyudi, S., Retno, R. A., & Andi, R. (2015). Effect of Dates (*Phoenix Dactilyfera L*) on male infertility. *Althea Medical Journal, 2*(1), 82–86.
Zhang, C.-R., Adosari, S. A., Vidyasagar, P. S. P. V., Nair, K. M., & Nair, M. G. (2013a). Antioxidant and anti-inflammatory assays confirm bioactive compounds in ajwa date fruit. *Journal of agricultural and food chemistry, 61*, 5834–5840.
Zhang, C.-R., Aldosari, S. A., Vidyasagar, P. S., Nair, K. M., & Nair, M. G. (2013b). Antioxidant and anti-inflammatory assays confirm bioactive compounds in Ajwa date fruit. *Journal of Agricultural and Food Chemistry, 61*, 5834–5840.
Zhang, C., Aldosari, S., Vidyasagar, P., Shukla, P., & Nair, M. (2014). Antioxidant, antiinflammatory and antitumor activities of 29 varieties of date fruits. *Planta Medica, 80*, PE11.
Zhang, C.-R., Aldosari, S. A., Vidyasagar, P. S. P. V., Shukla, P., & Nair, M. G. (2015). Health-benefits of date fruits produced in Saudi Arabia based on in vitro antioxidant, anti-inflammatory and human tumor cell proliferation inhibitory assays. *Journal of the Saudi Society of Agricultural Sciences*. http://dx.doi.org/10.1016/j.jssas.2015.09.004.