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REVIEW ARTICLE

Phytotherapeutic potential and pharmaceutical impact of *Phoenix dactylifera* (date palm): current research and future prospects

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Abstract *Phoenix dactylifera* (date palm) is a member of the genus *Phoenix* belonging to family Arecaceae. It is widely cultivated for its edible fruits and kernels. Dates have been used for both dietary purposes as well as for their phytomedicinal impacts against the variety of diseases. Date fruits are rich in alkaloids, protein, carbohydrate, fatty acid (linoleic, lauric, palmitic, and stearic acid), carotenoids, vitamins, polyphenolic compounds, flavonoids, and tannins along with different types of nutrients like potassium, calcium, magnesium, and phosphorus. Due to the presence of the variety of phytochemicals, they have greater impact on human health. They have strong antioxidant potential. It has been proposed now as a potential source of several unique medical and industrial products. In literature, much information is available on botanical descriptions, agriculture technology, and utilization in therapeutic intervention, but a little description is accessible on phytochemical relevance, formulation strategies, nutritional impact, and bioprocess technology. Therefore, the present review provides comprehensive information on the phytochemical relevance, pharmacology/bioactivity, pharmaceutical impact, their scope in bioprocess technology and nutraceutical values of date palm. According to all collected information, every portion of the plant has some beneficial properties that can serve as a source of medicine and nutraceutical.

Keywords *Phoenix dactylifera* (date palm) · Phytochemical constituents · Pharmaceutical impact · Pharmacological action · Bioactivity

Abbreviations

PD	*Phoenix dactylifera*
DP	Date palm
DSO	Date seed oil
DM	Diabetes mellitus
FAO	Food and agriculture organization
GCC	Gulf cooperation council
HPLC–DAD-ESI-MS	High performance liquid chromatography-diode array detection-electrospray ionization-mass spectrometry
SmF	Submerged fermentation
SSF	Solid state fermentation
SLF	Slurry state fermentation
UV	Ultra violet spectroscopy
ZnO-NPs	Zinc oxide nanoparticles
USFDA	United States Food and drug administration

Introduction

Date palms (DPs) are obtained from *Phoenix dactylifera* which belong to family "Arecaceae". It is one of the oldest (5500–3000 BCE) variety of DP trees which had

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"nutritional, environmental, economic, and ornamental values" (Habib and Ibrahim 2009). Cultivation of DP has been related with "cultural, environmental, religious, and social development" of human beings those belong to hot and arid regions such as "Middle East and Africa" (Nehdi et al. 2018). It serves as food for Arabs and is commercially grown throughout the desert regions of the Arabian Peninsula including other gulf regions. Different parts of plant like fruit, leaves, bark, and root are used in the treatment of various diseases and are famed for its medicinal and nutraceutical values. In Ayurveda, it is known as 'Kharjura' and have long been used in various traditional and folk medicine as nutritive and sweetener. About 17 species of dioecious DP is originated from western Asia and northern Africa. Arabian DPs have played a greater role in everyday life of human beings since long time (Saleh et al. 2011). The global production, use, and industrialization of DPs are increasing significantly. According to report proposed by Food and Agricultural Organization (FAO), the production of DP fruits is increasing in major countries including "Egypt (1,352,950 metric tons), Saudi Arabia (1,078,300 metric tons), Iran (1,023,130 metric tons), UAE (775,000 metric tons), and Algeria (710,000 metric tons)" (Zaid and de Wet 1999). DP fruit is marketed around the globe but it has been produced mainly in hot arid regions especially in Gulf Cooperation Council (GCC) countries. Among various GCC countries, Saudi Arabia is considered as one of the world's major producer of DPs. Date seeds are commonly considered as a waste product that is either discarded or used in animal feed (Habib and Ibrahim 2011).

Nowadays, there is a paradigm shift in pharmaceuticals from synthetic to natural sources which are obtained from plants, animals or minerals to control the diseases. Management of illness through medication has entered an era of rapid growth. In past time, every medicine used was from the plants. The plant kingdom still holds many species, containing chemical constituents of medicinal and nutraceutical value, which have yet to be discovered. Fruits and vegetables are a treasure house for a repertoire of nutritional compounds (Mohamed and Al-Okbi 2004). The modern pharmaceutical industries require a large quantity of authentic plants for the manufacture of drugs. Extraction of active constituents and manufacture of drug formulations is sophisticated technology and capital intensive with attractive remuneration. The methanolic extracts of DP fruit as well as kernels have been found to have strong antioxidant activity due to the presence of phenolics and other active phytoconstituents (Mohamed and Al-Okbi 2004). Phenolic compounds are one of the classes of phytoconstituents which are responsible for their antioxidant activities (Vayalil 2002). The plant has also been investigated experimentally to confirm its curative properties (Vayalil 2002). Due to certain biopharmaceutical problems, phytochemicals of DP fruit have been delivered into the body via novel formulation strategies. Techniques like targeted drug delivery systems (Hussain et al. 2011; Khalid et al. 2009) or nanotechnology (Faiyazuddin et al. 2010; Qadir et al. 2016) or synthesis of novel phytopharmaceuticals (Gantait et al. 2018; Javed et al. 2011; Masood et al. 2011) have been tried and reported elsewhere for human intake of these compounds.

The present review highlights the recent studies on the active compounds, pharmacology/bioactivity of phtyoconstituents, therapeutic effects of the plant and their various parts, drug delivery impact, and their scope in bioprocess technology. The information provided here may serve as a useful reference tool for the users of *P. dactylifera* products.

Botanical description

DP is a monocotyledon plant which can grow to an altitude of 1500 m in well drained soils (Masood et al. 2011). It had pinnate with spines on the petiole. The color of its flowers is yellowish which develop into fruits. A taxonomical property of *P. dactylifera* is as follows:

Kingdom:	Plantae
Subkingdom:	Tracheobionta
Super division:	Spermatophyta
Division:	Magnoliophyta
Class:	Liliopsida
Subclass:	Arecidae
Order:	Arecales
Family:	Arecales
Genus:	*Phoenix*
Species:	*Phoenix dactylifera* L.

The fruits of *P. dactylifera* are known as dates which ranged from bright red to bright yellow in color when unripe depending on the variety (Fig. 1). Presently these fruits are cultivated in many countries including "Middle East, North Africa, Central and South America, Southern Europe, Iraq, Iran, Saudi Arabia, Algeria, Egypt, Libya, Morocco, Sudan, Oman and some parts of India and Pakistan" (Ahmed et al. 1995; Al-Shahib and Marshall 2003). Some varieties of DP such as "Ajwa, Medjool, Khalas, and Deglet Noor" are considered as the best varieties (Ahmed et al. 1995). The major uniqueness of DP fruit is that it can be consumed as staple dietary food in various parts of the world including "Arabian, Asian, and some African countries" (Zaid and de Wet 1999). Another distinguished feature of DP fruit is that it can be consumed at three different stages of maturity such as "*Khalal, Rutab, and Tamar*" (AlFarsi and Lee 2008). These fruits are also

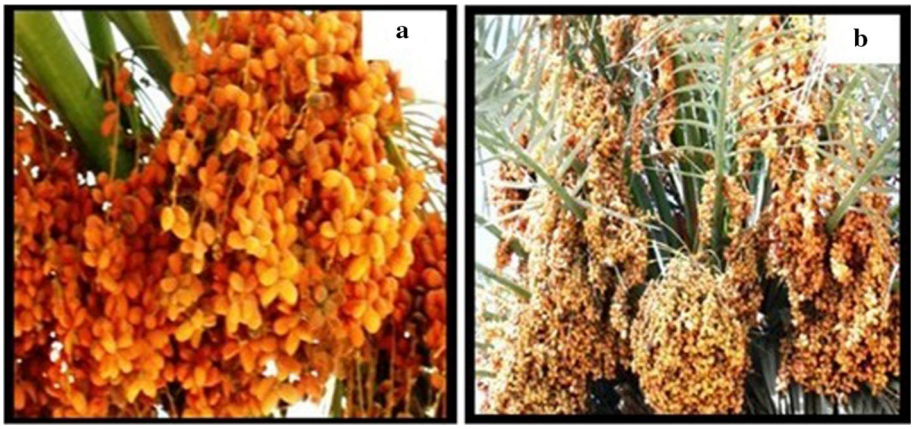


Fig. 1 Photograph of a date palm fruits **a** one single bunch, **b** on the palm

commercially available in dehydrated form but the processing method used to produce dehydrated fruits increase their shelf life and decrease nutritional value (AlFarsi and Lee 2008). Various characteristics features of DP fruits may vary depending upon their maturity stage and variety. About 5000 different varieties of DP fruits are grown in various parts of the world (Hashempoori et al. 2003). United States had highest export price for dates in the world (AlFarsi and Lee 2008). There are three main cultivar groups of DP: "dry (*'Dayri', 'Nabati', 'Ashrasi'*), semi-dry (*'Khadrawi', 'Zahdi', 'Rani'*), and soft (*'Chip-chap', 'Mazafati'*)" (Hashempoori et al. 2003).

DP variety

More than 600 different varieties of DP are existing depending on the shape and organoleptic properties (Al-Alawi et al. 2017; Ashraf and Hamidi-Esfahani 2011). Some of the important varieties of DP are "Aabel, Ajwah, Al-Barakah, Amir Hajj, Abid Rahim, Barhe, Baht, Bekreri, Bomaan, Bouhattam, Barakawi, Bireir, Deglet Noor, Dabbas, Dayri, Empress, Fard, Ftimi, Garn ghzal, Halawi, Haleema, Hayany, Iteema, Jabri, Kenta, Khadrawy, Khlas, Kenta, Kodary, Korkobbi, Khusatawi, Lulu, Maktoomi, Maghool, Manakbir, Mermilla, Medjool, Mejraf, Mishriq, Nabtat-seyf, NaptitSaif, Nefzaoui, Raziz, Rotab, Rotbi, Sagai, Smiti, Shikatalkahlas, Sagay, Shishi, Shikatalkahlas, Sokkery, Saidi, Sayir, Sekkeri, Shabebe, Sellaj, Sultana, Tagyat, Tamej, Thoory, Umeljwary, Umelkhashab, Zahidi and Bericcha Pazham" (Al-Shahib and Marshall 2003; Chaira et al. 2009; Habib and Ibrahim 2009). The quality of DP has been found to be changed with environmental conditions (Fadel et al. 2006).

The developmental stages of date fruits

Five different stages for the development of DP fruits are known to grasp full maturity. The ripening of fruits occurs after 7 months and the color of fruit ranges from yellow to reddish brown (Fig. 1a). These fruits are available in clusters and the weight of each bunch is around 10 kg. A fully productive DP tree is capable to produce ten bunches with around 100 kg of yield (Fig. 1b). The sweetness and texture of DP fruits depend on the maturity and ripeness stage (Zaid and de Wet 1999). The color and chemical compositions of DP fruits are changed during its growth and development. Arabic DP fruits are categorized into five different stages including "Hababouk, Kimri, Khalal, Rutab, and Tamar" which are accepted globally (Al-Shahib and Marshall 2003; Fadel et al. 2006). Several changes such as increase in size and weight, reduction in sugar contents, high acidity, and high moisture content are usually observed during developmental stages of DP fruits (Al-Shahib and Marshall 2003; Amira et al. 2011). Developmental stages are briefly discussed below and their description has been shown in Fig. 2.

Stage I: Hababouk

This is the first stage of DP fruit which starts with "post fertilization" and lasts for 4–5 weeks in general. At this stage, DP fruits are immature and completely covered by the calyx. During this stage, the weight of DP fruits is about a gram (El-Sharnouby et al. 2009).

Stage II: Kimri

This is the second stage of DP fruit and it takes around 9−14 weeks for the development. At this stage, the fruits are changed from a small berry to the characteristic oblong shape. In this stage, the fruits are hard, green in color, and contain about 80% moisture and 50% sugar. The fruits at this stage are not suitable for eating due to bitter taste (Fadel et al. 2006).

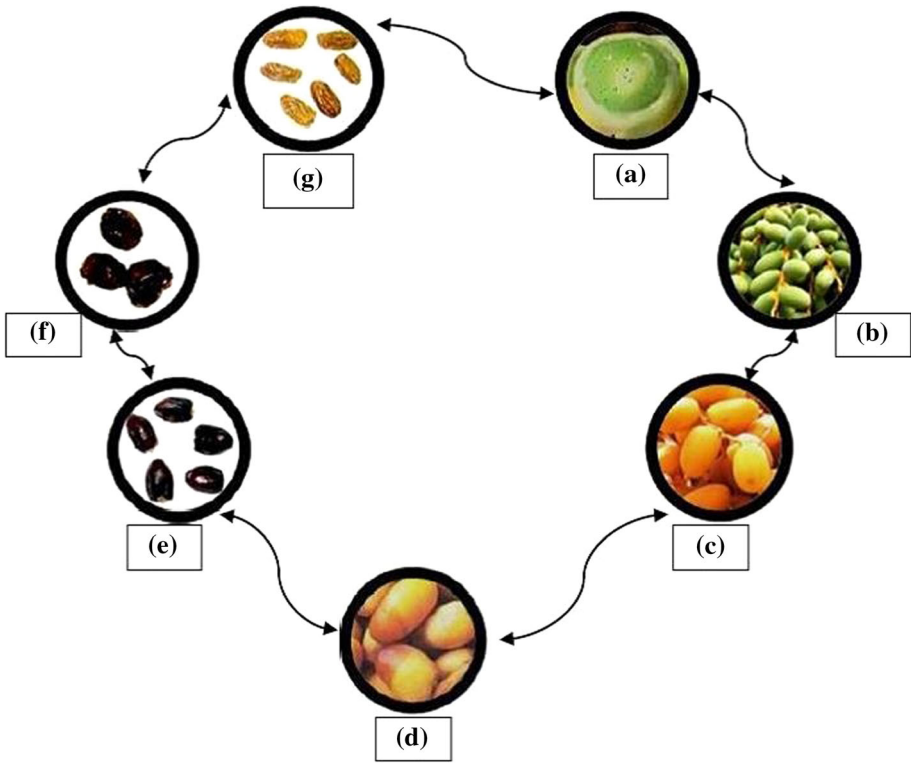


Fig. 2 Different stages of date growing **a** Hababouk, **b** Kimri, **c** Khalal, **d** Rutab, **e** Tamar (Farad), **f** Tamar (Khajur soft), **g** Tamar (Khajur hard)

Stage III: Kalal

Under this stage the color changes from green to greenish yellow, yellow, pink, scarlet or red depending on the varieties of date fruits. This stage lasts for 6 weeks and during this the fruit becomes physiologically mature, hard, and ripe. The fruits achieve higher weight and maximum size at this stage. The sugar concentration quickly increases followed by marked decrease in moisture content (El-Sharnouby et al. 2009).

Stage IV: Rutab

This stage spans for a period of 2–4 weeks. At this stage, the apex starts ripening with soft texture of the fruit. The bitter taste from the previous stage is lost gradually and the color of fruits becomes brown or black. At this stage, there is a complete loss of moisture content and decrease in the weight of the fruits. The total sugar contents and solids are increased at this stage (Nehdi et al. 2018).

Stage V: Tamar

This is the final stage of the development of DP fruits in which fruits become dehydrated. The fruits at this stage contain about 50% each of sucrose and reducing sugars. The time for ripening is around a month (Fadel et al. 2006).

Nutritional significance of *Phoenix dactylifera*

The fruits of *P. dactylifera* have provided the nutrition to many people around the globe since ancient times to till now. DP fruits have great importance in human nutrition due to their rich content of essential compounds which include carbohydrates, salts and minerals, dietary fiber, vitamins, fatty acids, amino acids, and protein (Al Juhaimi et al. 2018; Hasan et al. 2010). DP seeds also have great nutritional value and they are utilized for food applications especially in frying or cooking oil (Al-Shahib and Marshall 2003). The nutritional compositions of DP flesh and DP pit have been reported by different scientists in literature (Hasan et al. 2010; Elguerrouj et al. 2011). Moreover, DP oil has been used in cosmetic and pharmaceutical industries. In literature, the main fatty acid reported to be present in date seed oil was "oleic acid (48.67%) followed by lauric acid (17.26%), stearic acid (10.74%), palmitic acid (9.88%), and linolenic acid (8.13%)" (Ahmed et al. 2016; Elguerrouj et al. 2011; Hamad et al. 2015). The other components reported in DP seed oil are α-tocotrienol, γ-tocopherol, γ-tocotrienol, and α-tocopherol (Hamad et al. 2015; Saleh et al. 2011; Qadir et al. 2017). In a most recent study on Moroccan Medjool DP fruits carried out by Khallouki et al. (2018) chelidonic acid and di-caffeoyl shikimic acid isomers were reported as the major constituents. The HPLC-DAD-ESI-MS method identified the presence of monophenols, echinoids, and flavonoids in DP

fruits (Khallouki et al. 2018; Maier et al. 1964). Therefore, the consumption of Moroccan Medjool DP fruits can contribute to a healthy diet. Many studies suggested that DP seed oil can be used as an abundant alternative to palm olein (Elguerrouj et al. 2011; Hamad et al. 2015; Qadir et al. 2017). The nutritional contents and novel bioactives of DP and their phytoconstituents are briefly summarized in Tables 1 and 2 (Ahmed et al. 2016; Al Juhaimi et al. 2018; Saleh et al. 2011).

Pharmacology and bioactivities of *P. dactylifera*

Since long, both fruits and kernels of DP have been utilized in different traditional system of medicine. It has been found that dates were used traditionally in the treatment of diabetes and hypertension (Chaira et al. 2009; Ragab et al. 2013; Saddi et al. 2018). Dates, in ancient Egypt were used as ingredient in different aphrodisiac supplements (Hamad et al. 2015). DP fruits have served as chief food for many people around the globe. Different phytochemical investigations have shown that DP fruits have various phytochemicals such as "anthocyanins, phenolics, sterols, carotenoids, procyanidins, and flavonoids" which are known to have several beneficial effects (Benmeddour et al. 2013; Gantait et al. 2018; Mirza et al. 2018; Salem et al. 2018). Pre-clinical investigations have suggested that DP fruits have different pharmacological activities like anti-oxidant (Allaith 2008; Chaira et al. 2009; Mansouri et al. 2005; Ragab et al. 2013), anti-mutagenic (Vayalil 2002; Allaith 2008), anti-microbial (Al Juhaimi et al. 2018; Hasan et al. 2010), anti-inflammatory (Mohamed and Al-Okbi 2004; Jassim and Naji 2008; Shraideh et al. 1998), gastro protective (Al-Qarawi et al. 2003, 2005),

Table 1 Nutritional contents of *Phoenix dactylifera*

S. no.	Nutritional content	Contents	References
Date fruits			
1.	Carbohydrate	44–88%	Al-Shahib and Marshall (2003)
2.	Fats	0.2–0.5%	
3.	Protein	2.3–5.6%	
4.	Dietary fiber	11.5%	
5.	Pectin	0.5–3.9%	
6.	Ascorbic acid	30–50 mg/kg	Al-Oqla and Sapuan (2014), Ismail et al. (2006)
7.	Ash	3.5–4.2%	
8.	Vitamin A	10.50 ug/100 g	Hasan et al. (2010)
9.	Vitamin B	824.98 mg/kg	
10.	Vitamin E	12.98 mg/kg	
11.	Calcium	614.74 mg/kg	
12.	Sodium	485.86 mg/kg	
13.	Magnesium	660.74 mg/kg	
14.	Potassium	50–60%	Al Juhaimi et al. (2018)
15.	Glucose and fructose	65 and 80%	
16.	Water	7% (dried), 79% (fresh)	
17.	Essential amino acid		
	(a) Lysin	184 mg/100 g	Elguerrouj et al. (2011), Hasan et al. (2010)
	(b) Isoleucin	122 mg/100 g	
	(c) Threonin	98 mg/100 g	
Date seed oil			
	Oleic acid	48.67%	Amira et al. (2011), Nehdi et al. (2018)
	Lauric acid	17.26%	
	Stearic acid	10.74%	
	Palmitic acid	9.88%	
	Linolenic acid	8.13%	
	α-Tocotrienol	19.07%	
	α-tocopherol	17.52%	

Table 2 Phytoconstituents of *Phoenix dactylifera*

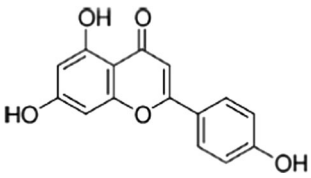
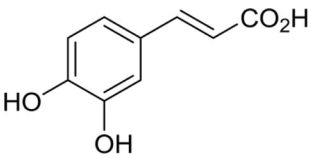
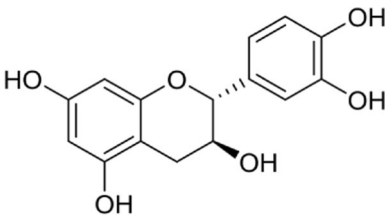
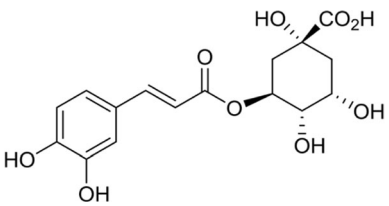
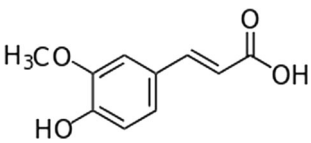
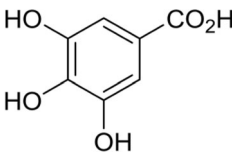
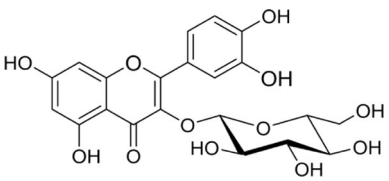
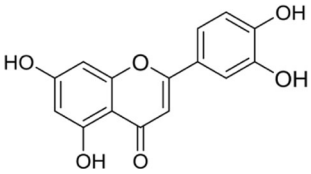
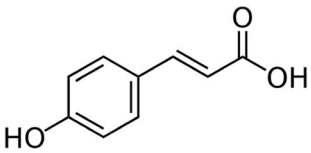
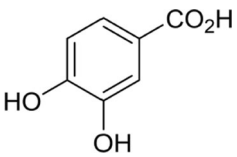
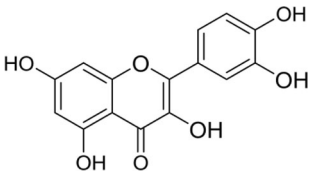
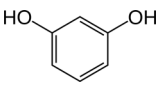
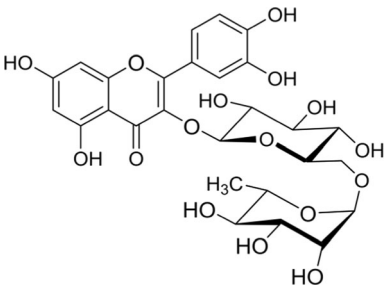
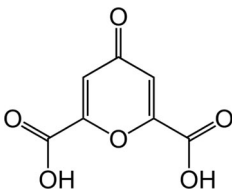
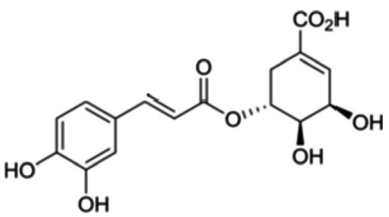
Phytoconstituent	Structure	Quantity (mg/100 g)	References
(i) *Apigenin* (IUPAC Name: 5,7-Dihydroxy-2-(4-hydroxyphenyl)-4H-chromen-4-one) (Mol. Formula: $C_{15}H_{10}O_5$)		0.26	Al Juhaimi et al. (2018), Hamad et al. (2015), Ahmed et al. (2016)
(ii) *Caffeic acid* (IUPAC Name: 3,4-Dihydroxycinnamic acid; 331-39-5; 3-(3,4-dihydroxy-phenyl)acrylic acid) (M.F.: $C_9H_8O_4$)		0.026–0.050	Ahmed et al. (2016), Hamad et al. (2015), Ragab et al. (2013)
(iii) *Catechin* (IUPAC Name: (2*R*,3*S*)-2-(3,4-dihydroxyphenyl)-3,4-dihydro-2*H*-chromene-3,5,7-triol) (M.F.: $C_{15}H_{14}O_6$)		0.50–0.80	Hamad et al. (2015), Ragab et al. (2013), Saleh et al. (2011)
(iv) *Chlorogenic acid* (IUPAC Name: (1S,3R,4R,5R)-3-[(E)-3-(3,4-dihydroxyphenyl)prop-2-enoyl]oxy-1,4,5-trihydroxycyclohexane-1-carboxylic acid) (M.F.: $C_{16}H_{18}O_9$)		0.18–0.20	Ahmed et al. (2016), Hamad et al. (2015), Qadir et al. (2017)
(v) *Ferulic acid* (IUPAC Name: (E)-3-(4-hydroxy-3-methoxyphenyl)prop-2-enoic acid) (M.F.: $C_{10}H_{10}O_4$)		2.52–3.20	Ahmed et al. (2016), Hamad et al. (2015), Ragab et al. (2013)
(vi) *Gallic acid* (IUPAC Name: 3,4,5-trihydroxybenzoic acid) (M.F.: $C_7H_6O_5$)		13.90–14.10	Ahmed et al. (2016), Hamad et al. (2015), Mansouri et al. (2005)
(vii) *Isoquercetin* (IUPAC Name: 2-(3,4-dihydroxyphenyl)-5,7-dihydroxy-3-[(2S,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]oxychromen-4-one) (M.F.: $C_{21}H_{20}O_{12}$)		0.41	Ahmed et al. (2016), Elguerrouj et al. (2011), Hamad et al. (2015)

Table 2 continued

Phytoconstituent	Structure	Quantity (mg/100 g)	References
(viii) *Luteolin* (IUPAC Name: 2-(3,4-dihydroxyphenyl)-5,7-dihydroxychromen-4-one) (M.F.: $C_{15}H_{10}O_6$)		1.21	Ahmed et al. (2016), Hamad et al. (2015), Ragab et al. (2013)
(ix) *p-Coumaric acid* (IUPAC Name: (E)-3-(4-hydroxyphenyl)prop-2-enoic acid) (M.F.: $C_9H_8O_3$)		3.08–3.50	Ahmed et al. (2016), Hamad et al. (2015), Qadir et al. (2017)
(x) *Protocatechuic acid* (IUPAC Name: 3,4-dihydroxybenzoic acid) (M.F.: $C_7H_6O_4$)		1.27–2.20	Al Juhaimi et al. (2018), Hamad et al. (2015), Saleh et al. (2011)
(xi) *Quercetin* (IUPAC Name: 2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxychromen-4-one) (M.F.: $C_{15}H_{10}O_7$)		22.10–455.80	Ahmed et al. (2016), Hamad et al. (2015), Qadir et al. (2017)
(xii) *Resorcinol* (IUPAC Name: benzene-1,3-diol) (M.F.: $C_6H_6O_2$)		0.03–0.05	Hamad et al. (2015), Mansouri et al. (2005)
(xiii) *Rutin* (IUPAC Name: 2-(3,4-dihydroxyphenyl)-5,7-dihydroxy-3-[(2S,3R,4S,5S,6R)-3,4,5-trihydroxy-6-[[(2R,3R,4R,5R,6S)-3,4,5-trihydroxy-6-methyloxan-2-yl]oxymethyl]oxan-2-yl]oxychromen-4-one) (M.F.: $C_{27}H_{30}O_{16}$)		0.86	Ahmed et al. (2016), Hamad et al. (2015), Mansouri et al. (2005), Saleh et al. (2011)
(xiv) *Chelidonic acid* (IUPAC Name: 4-Oxo-4*H*-pyran-2,6-dicarboxylic acid) (M.F.: $C_7H_4O_6$)		0.29	Khallouki et al. (2018)
(xv) *5-Caffeoylshikimic acid* (IUPAC Name: (3R,4R,5R)-5-[(E)-3-(3,4-dihydroxyphenyl)prop-2-enoyl]oxy-3,4-dihydroxycyclohexene-1-carboxylic acid) (M.F.: $C_{16}H_{16}O_8$)		0.94	Khallouki et al. (2018), Maier et al. (1964)

hepatoprotective (Al-Qarawi et al. 2004; El Arem et al. 2014; Salah and Al-Maiman 2005; El-Mougy et al. 1991), nephroprotective (Al-Qarawi et al. 2008), anticancer (Ishurd and Kennedy 2005), and immunostimulant activities etc. Some reviews indicated that the DP fruits have medicinal values and are extensively used to treat different types of diseases in various traditional systems of medicine in addition to their dietary use (Al-Alawi et al. 2017; El-Far et al. 2016; Ishurd and Kennedy 2005; El Modafar 2010; Rahimi et al. 2017; Wahab et al. 2017). The flow diagram for different pharmacological activities of DP is presented in Fig. 3. Various studies have been conducted to elaborate the pharmacology of date fruits and kernels as well. Based on the chemical constituent and the different part of *P. dactylifera*, some of the potential activity has been discussed below.

Antioxidant activity

Phoenix dactylifera demonstrates strong antioxidant activity which is possible due to the presence of "phenolics, melatonin, carotenoids, and vitamins contents" (Benmeddour et al. 2013; Chandrasekaran and Bahkali 2013; Elguerrouj et al. 2011; Hamad et al. 2015; Mansouri et al. 2005). In vitro study of aqueous extract of date fruit have shown a concentration dependent scavenger of free radicals. The effective concentration of extract was 100 µg/ml to produce these effects. The study provides sufficient evidence of having antioxidant activity (Hamad et al. 2015). Animal studies also assist the antioxidant activity as the oral administration of *p*-coumaric acid which is the chief constituent of date fruit increases the expression of antioxidant enzyme producing genes in cardiac tissue of the rat (Abdel-Magied et al. 2018; Abdul-Hamid et al. 2018; Chaira et al. 2009; Khan et al. 2018c; Salem et al. 2018; Vayalil 2002). Different researchers found in vivo antioxidant activity of date fruit extracts at different concentrations. In two different studies, the antioxidant activity was observed at the concentration of 1000 mg/kg body weight (Abdel-Magied et al. 2018; Khan et al. 2018c). However, in another study, this activity was obtained at the concentrations of 100, 200 and 400 mg/kg body weight (Salem et al. 2018). Abdul-Hamid et al. (2018) and Chaira et al. (2009) recorded antioxidant activity of date fruit extract at the concentration of 100 µg/ml and 330 µg/ml, respectively. Vayalil observed that the concentrations of 1.4 mg/ml and 4.0 mg/ml completely inhibited superoxide and hydroxyl radicals, respectively (Vayalil 2002). Phenolic compounds, anthocyanins, and flavonoids are responsible for the antioxidant activity (Allaith 2008; Al Farsi et al. 2005; Mansouri et al. 2005).

Anticancer activity

DP shows much anticancer activity against the variety of cells due to the presence of phenolic compounds such as rutin and caffeic acid. In vitro study of acetate fraction of ajwa date at the concentrations of 0.2–0.6 mg/ml showed a strong anticancer activity against prostate cancer cells (Mirza et al. 2018). Some other studies also showed strong anticancer activity of DP in literature (Abutaha et al. 2018; Khan et al. 2018b; Makhlouf-Gafsi et al. 2018; Tao et al. 2018).

Anti-mutagenic activity

The success of the use of synthetic medicines has been declined due to the emergence of resistance and tolerance in these medicines. Consequently, an enhanced drift to replace the synthetic medicines by plant-based materials has been pragmatic in pharmaceutical manufacturing. Date fruit extracts have shown to possess antimutagenic activity

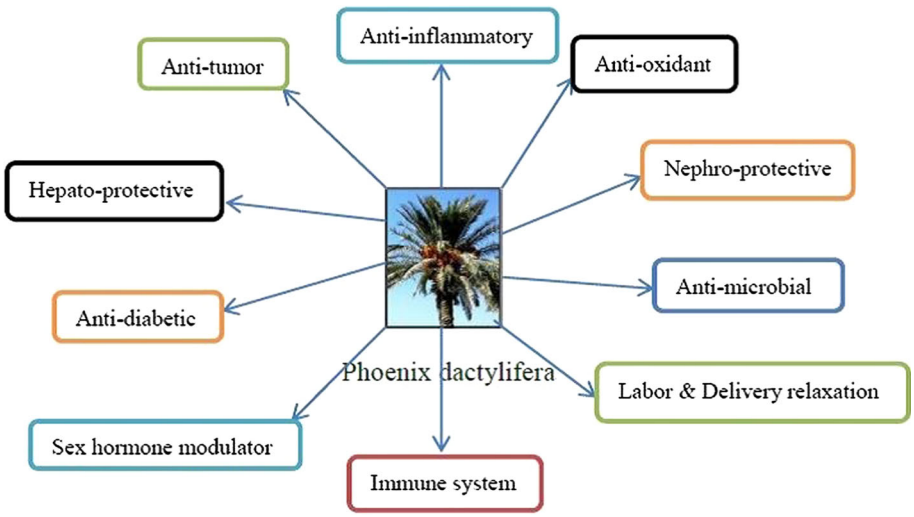


Fig. 3 Pharmacological properties of *Phoenix dactylifera*

in Ames mutagenicity assay in a dose-dependent manner. Date fruit extract at the concentrations of 3.6 and 4.6 mg/plate had shown the dose-dependent inhibition of benzo(a)pyrene-induced mutagenicity with metabolic activation on TA-98 and TA-100 strains of *Salmonella* (Vayalil 2002).

Antifungal activity

Microbial resistance has been reported as one of the major confront against antimicrobial chemotherapy. However, to overcome this crisis, the use of plant-based materials and their phytoconstituents is an excellent alternative for antimicrobial chemotherapy as they are economical and safe (Allaith 2008; Abuharfeil et al. 1999; Jassim and Naji 2008; Shraideh et al. 1998). Study reported that the treatment with the extract of date fruit at the concentrations of 5–20% w/v caused distortion, weakening, and eventual cell death by cell wall lysis in the *Candida albicans* (Shraideh et al. 1998). Flavonoids are reported to possess the antifungal activity which is a major chemical constituent of date fruit (Jassim and Naji 2008; Shraideh et al. 1998).

Anti-inflammatory activity

Inflammation is one of the imperative defense system against several factors including "burn, infection, toxicants, allergens, and other stimuli" (Jassim and Naji 2008; Mohamed and Al-Okbi 2004). The physiological changes in inflammatory defense system could results in the development of different diseases including diabetes and arthritis (Al-Qarawi et al. 2005; Jassim and Naji 2008; Mohamed and Al-Okbi 2004). A plethora of reports have been published elsewhere in literatures about anti-inflammatory potential of *P. dactylifera* (Abutaha et al. 2018; Al-Qarawi et al. 2005). In a study, the ethanolic and aqueous extracts of DP fruit pulp at the concentration of 4.0 ml/kg were found to be competent enough to suppress the inflammation in animal arthritis model (Al-Qarawi et al. 2005).

Sperm quality improvement activity

Several investigations have suggested the improvements in sperm quality with antioxidant treatment. Several medicinal plants are known to control human fertility such as the fruits of DP (*P. dactylifera* L.) are well known for this purpose. It has been reported that DP seed oil (DSO) had better oxidative stability than most vegetables (Ali et al. 1999; El-Mougy et al. 1991; Elgasim et al. 1995). Male infertility is usually caused the excessive generation of reactive oxygen species (ROS) by defective spermatozoa. Several investigations have suggested that the supplementation by antioxidants attenuated the negative effects of ROS and improved "sperm function, capacity for fertilization, and sperm membrane fluidity" (El-Mougy et al. 1991; Elgasim et al. 1995).

Hypoglycemic activity

Plant-based phytochemicals play a lead role in the control and management of diabetes and diabetic retinopathy through the modulation of metabolic and molecular pathways (El-Shaarawy et al. 1989). Various plant-based phytochemicals are known to control the functions of pancreatic cells by enhancing insulin production and reducing the glucose absorption (EI-Shaarawy et al. 1989). DP seeds were utilized in folk medicine in order to treat diabetes mellitus (DM) for several years. The efficacy of an aqueous extract of DP seeds at the concentration of 10.0 ml was evaluated successfully in the glycemic control of type 1 DM in animal models (El Fouhil et al. 2011). The antidiabetic activity of *P. dactylifera* extracts has been reported due to the presence of "saponins, phenol, steroids, and flavonoids" (Rahmani et al. 2014). Compared to insulin, date seed extract is easily administered (by oral route), easily available, and almost costless. In one of the studies carried out by El Fouhil et al., the date seed extract administration was safe on the liver and kidney (El Fouhil et al. 2011). In addition, insulin-date seed extract combination minimizes the toxic effects of diabetes on these organs. The pharmacological impact of DP till date is enlightened in Table 3.

Commercial and novel products of *Phoenix dactylifera*

Phoenix dactylifera are frequently used to prepare a wide range of products such as folklore medicines, date fruit juice concentrates (spread, syrup, and liquid sugar), fermented date products (wine, alcohol, vinegar, and organic acids), and date pastes for different uses (e.g. bakery and confectionary) besides their direct consumption (El Foouhil et al. 2011; Rahmani et al. 2014). DP industries produce a variety of DP products including "date-paste, date-syrup, date dip, date-honey, date-jam, and date-vinegar". Some of the DP products including "date pectin, dietary fiber, and date syrup" are used as gelling agents in food industries (Di Cagno et al. 2017; El Foouhil et al. 2011; Riedel 1986). The incorporation of the extract of DP seed waste has been employed effectively and confirmed as capping material which stabilized zinc-oxide nanoparticles (NPs) (El-Naggar et al. 2018). The vesicular structure of the optimized DSO loaded nano-vesicles with nano-size range and good stability features were confirmed in most recent study

Table 3 Pharmacological properties of *Phoenix dactylifera* (in vitro *and* in vivo)

S. no.	Activity	Pharmacology/bioactivity	References
In-vitro studies			
1.	Antioxidant activity	Scavenges free radical, inhibit iron-induced lipid peroxidation and protein oxidation	Allaith (2008), Al Farsi et al. (2005), Chaira et al. (2009), (2002), Chandrasekaran and Bahkali (2013), Elguerrouj et al. (2011), Hamad et al. (2015), Mansouri et al. (2005), Nehdi et al. (2018), Vayalil (2002)
2.	Antimutagenic activity	Inhibits benzo (a) pyrene-induced mutagenecity in the Ames test	Mansouri et al. (2005), Vayalil (2002)
3.	Antihaemolytic activity	Inhibits haemolytic activity of streptolysin	Abuharfeil et al. (1999), Mansouri et al. (2005).
4.	Antiviral activity	Prevent lytic activity of Pseudomonas phage ATCC 14209-B1 on *Pseudomonas aeroginosa*	Jassim and Naji (2008)
5.	Antifungal activity	Antifungal activity against *Candida albicans and C. krusei*	Shraideh et al. (1998)
Animal studies			
1.	Anti-inflammatory activity	Increases plasma antioxidant (Vitamin C, E, A, β-carotene) levels and decreases lipid peroxides. Reduce swelling, ESR and plasma fibrinogen	Abutaha et al. (2018), Mohamed and Al-Okbi (2004), Hamad et al. (2015)
2.	Action on gastrointestinal tract	Increase gastrointestinal transit time, reduces ethanol-induced gastric ulceration	Allaith (2008), Al Farsi and Lee (2008), Al-Qarawi et al. (2003), (2005)
3.	Antihyperlipidemic activity	Reduces plasma triglycerides, total and LDL cholesterol	El-Mougy et al. (1991)
4.	Hepatoprotective activity	Prevents dimethoate- induced hepatotoxicity, causes decrease in hepatic markers (ALT, AST, alkaline phosphatase, GGT and LDH), decrease vacuolization, necrosis, congestion, inflammation and enlargement of sinusoids. Has protective effect against CCl4 induced hepatotoxicity	Al-Qarawi et al. (2003), Saafi et al. (2011)
5.	Nephroprotective activity	Prevents gentamicin-induced renal damage and reduce levels of creatinine and urea	Al-Qarawi et al. (2003)
6.	Anticancer activity	Regression of Sarcoma-180 tumour in mice	Ishurd and Kennedy (2005)
7.	Immunostimulant activity	Enhances both cell mediated and humoral immunity	Puri et al. (2000)
8.	Gonadotropic activity	Increases FSH, LH, testosterone, oestrogen, increases spermatogenesis, sperm count and growth	Ali et al. (1999), Elgasim et al. (1995), El-Mougy et al. (1991)
9.	Hypoglycemic effect	Liver functions were evaluated by ALT, AST, and γ-GT activities; however the levels of BUN and serum creatinine were estimated to assess the functional capacity of the kidney. Mean values of all tested serum levels were significantly higher in Group 3 compared to Groups 1, 2 and 4 (with the exception of ALT in the case of Seed extract treated group)	El Fouhil et al. (2011), Riedel et al. (1986)

(Soliman et al. 2018). DSO loading in niosomes revealed a significant enhancement toward inflammation alleviation, which offers a promising implement in osteoarthritis remediation and prohibition. However, DP syrup has been investigated in the preparation of foodstuffs including "jams, marmalades, concentrated beverages, chocolates, ice cream, confectioneries, sweets, snacks, bakery products, and health foods" (Riedel 1986; Di Cagno et al. 2017). Macroporous natural sporopollenin exine capsules were obtained from *P. dactylifera* and coated with carboxymethyl cellulose and epichlorohydrin. The polymer coated capsules were applied in controlled delivery of model drug paracetamol. The results suggested enhanced release of paracetamol in phosphate buffer solution in comparison with simulated gastric fluid (Alshehri et al. 2016).

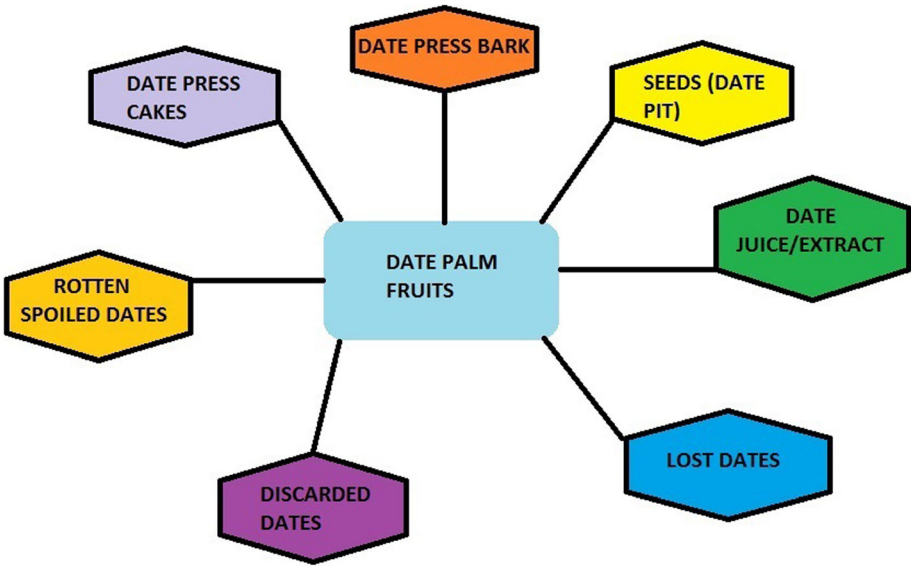


Fig. 4 Date palm fruits by-products

Utilization of *Phoenix dactylifera* in bio-processing technology

The DP (*P. dactylifera*) had an imperative role in the day-to-day life of the populace for several years (Mansouri et al. 2005). Due to the great importance of DP in human nutrition, their worldwide production, utilization, and industrialization are increasing significantly. The bioprocessing technology is the application of microorganisms in "submerged fermentation (SmF), solid state fermentation (SSF) or slurry state fermentation (SLF)" under immobilized condition and use of enzymes for biotransformations of organic materials into desired biomass production (Chandrasekaran and Bahkali 2013; Di Cagno et al. 2017; Khan et al. 2018a). The tTons of DP fruit wastes are discarded daily by DP industries which creates environmental problems (Di Cagno et al. 2017). Thus, it is essential to utilize wasted date seeds for appropriate applications. Date is a good source of sugar and hence it can be utilized as a raw material in fermentation process. This utilization is relatively cheaper and does not require any special treatment such as "acid hydrolysis, steam explosion, or enzymatic treatment". The waste products of DP have greater application in bioprocess technologies to produce several value added products (Chandrasekaran and Bahkali 2013). The health prospects of these *P. dactylifera* processing "by-products and wastes" are helpful in the production of biosurfactants, biopolymers, antibiotics, biofuels, industrial enzymes, organic acids, and other promising industrial molecules need to be thoroughly examined (Di Cagno et al. 2017). Different bye-products and waste products of DP are presented in Fig. 4. Further, novel biocatalysts and development of suitable bioprocesses, downstream processes, and modeling lessons need to be structured and developed for such a noble assignment.

Conclusion

This article gives a broad view of the major characteristics, utility, pharmacology, phytochemical, and pharmaceutical relevance of *P. dactylifera.* Some of the major established pharmacognostics reports along with the details of pharmacological and phytochemical investigations have been presented here with special attention to pharmaceutical values. The fruit is relatively cheap, nutritious, and lacks any toxic effects. Date fruits along with its seeds have remarkable medicinal value as it is reported to have useful constituents like phenolics, sterols, carotenoids, flavonoids, carbohydrates, different minerals, and vitamins. These phytochemicals have been responsible for the different pharmacological effects like antibacterial, anti-inflammatory, anti-diabetics, hepatoprotective, anti-ulcerative, and libido etc. This review will be imperative for those involved in investigation of date fruit and seed and will help the researchers to utilize the whole plant in more effective way. Further, this compilation could produce an opportunity for the neutraceutical/food industries to develop more radically bioactive functional health products.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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