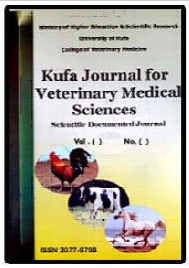
Kufa journal for Veterinary Medical Sciences Vol.(14) No.(2)

Kufa journal for Veterinary Medical Sciences

Kj.vs@uokufa .edu.iq

www.uokufa .edu.iq\journals\index.php\kjvs



Date palm [*Phoenix dactylifera*]: Description, Components, Importance, and Medical Uses: A review

Sarah Mahir Al-talaqany[1] Adel Thamer Marza[1] Falah Baiee[2]

[1]*Department of Physiology, Biochemistry and Pharmacology, Faculty of Veterinary Medicine, University of Kufa, Najaf, Iraq.*

[2]*Department of Clinical Science, Faculty of Veterinary Medicine, University of Kufa, Najaf, Iraq.*

Corresponding author: FB, email: falahhali@uokufa.edu.iq ORCID: 0000-0002-1930-9492

Co-authors: SMA, email: saraamjed87@gmail.com ; ATM, email: adelthamer993@gmail.com

Received date: 28 Apr. 2023 Accepted: 14 Dec. 2023 page: (42-53) Published:30 Dec. 2023

DOI: https://doi.org/10.36326/kjvs/2023/v14i211950

Abstract

Phoenix dactylifera is an ancient tree that belongs to the *Arecaceae* family; its leaves, barks, fruits and pollens have highly anti-oxidant, anti-cancer, hepato-protective, neuro-protective, sexual improvement, anti-hyper lipidemic, and anti-microbial potentials. The broad pharmacological effects of *Phoenix dactylifera* may be attributed to the powerful and beneficial ingredients including phenolic, flavonoids, carotenoids, vitamins, minerals, amino acids, fatty acids and organic acids. The present review was conducted to describe the beneficial and pharmacological preventive effects of *Phoenix dactylifera* through recoded the published data on web of science, Scopus and Google scholar databases to review the pharmacological effects of *Phoenix dactylifera*.

Keywords: Anti-microbial, anti-oxidant, date [*Phoenix dactylifera*], sexual booster.

INTRODUCTION

Dates [*Phoenix dactylifera*; DPD] are the members of the palm family Arecaceae. The species name *dactylifera* "date-bearing" came from two words Greek *dactyls* means "date" and the Greek word ferō meaning bearing [1]. Dates are a strategic source of food due to their nutritional value and medicinal benefits. Furthermore, many religious narratives and folklore have confirmed the economic importance of DPD. In fact, many researchers have conducted their studies and research on DPD to know and assess their unique properties, benefits and active compounds. However, what are the directions taken by this research and what are their results? Therefore, the current study highlights a review of recent scientific sources regarding the developments that science has reached in the medicinal properties of DPD.

DESCRIPTION

Dates [*Phoenix dactylifera*; DPD] are the members of the palm family Arecaceae. The species name *dactylifera* "date-bearing" came from two words Greek *dactyls* means "date" and the Greek word ferō meaning bearing [1]. The date palm is one of the oldest cultivated plants of earth and being used as food for 6000 years [2]. More than two hundred varieties of dates are available worldwide. Mainly it is found in Iraq, Middle Eastern countries, around the Arabian Gulf, Egypt and north of Africa. The Taxonomical classification of DPD is as follow:

Division: Magnoliophyta; **Class**: Liliopsida; **Subclass**: Arecidae; **Order**: Arecales; **Family**: Arecaceae; **Genus**: Phoenix; **Species**: *P. dactylifera* [3].

It was said that when it comes to food security, the date tree is considered the sacred tree in parts of Western Asia and North Africa and the DPD is one of the most abundant fruits. The date tree is also considered an endemic functional food [4]. In fact, *Phoenix dactylifera* is the scientific name for date palm. Moreover, DPD are famous for their delectable fruit which is why the Holy Quran references dates numerous times. Medium-sized 15-25 m tall single or clustered stems of the same root grow this plant [5]. While both the female and male sections of the date palm are produced from the same seed, only 50% of the date palm is fruit-bearing [feminine]. Authors were classified the stages of fruit development into four main stages which are Kimri [green color], Khalal [yellow stage], Rutab [soft and sweet], and Tamar [full ripe stage] stages [6]. The diameters of ripe fruit are varying from kind to kind such as it is large in Deglet Noor and Hallawi 45 × 22.5 mm and 39 × 22 mm, respectively; medium like Zahidi 33 × 27 mm and small like Barhi 30 × 21 mm [7]. The DPD has natural components and they have been tested for their medical properties such as phytochemicals, sterols, carotenes, and flavonoids [8]. Iron, calcium, cobalt, fluorine, manganese, sodium, copper, and zinc are abundant in the pulp [9].

Chemical Components of Date [*Phoenix Dactylifera*]:

The DPD is rich with many components such as carbohydrate [sugar], dietary fibers, phytochemicals [carotenoids, a rich source of polyphenols, flavonoids, tannins, and sterols], fatty acids, amino acids, ash, and more that 15 kinds of minerals, vitamins and salts [7,9, 10, 11, 12] as will be described below.

There are three types of sugar in DPD in percentage of 44-88% carbohydrates which are fructose, glucose and sucrose; that make them a valuable source of energy [7]. Some kind of DPD has fructose and glucose such as Khulas; and some of them have in addition to them, also contained sucrose like Zahidi. However, another kind of DPD has sucrose in some stage of developing or ripening; like in Barhi, it was found that in khalal stage had 6.2 g sucrose of total sugar 31.1 g of sugar / 100 g of fruit, while in tamr stage the percentage of sucrose was 0.0 g of total 57.2 g sugar / 100 g of fruit [12]. Thus, the levels of energy of generality types of DPD have recently been estimated and are between 239 and 322 kcal/100 g FW [7, 10]. The high levels of energy were recorded in Zahidi and Hallawi [322 and 315 kcal/ 100 g FW, respectively]. On the contrary, the lower level of energy was reported in Barhi [239 kcal / 100 g FW; 12].

Moreover, DPD contain 10.80% moisture, 89.20% dry solids, 0.2-0.5% fatty acids, 2.3-5.6% amino acids, and 6.4-11.5% dietary fibres. According the data that reported by Ghnimi *et al*. [12] the high percentage of fibre was recorded in Khadrawy 23.8% [23.8 g / 100 g FW]. Some composition of vitamins and elements were conducted by Ramchoun *et al*. [11]; Thiamine [B_1] was 82 mg and Riboflavin [B_2] was 160 mg are found in the palm's vitamin content, as folic acid was 61 mg and Ascorbic acid [C] was 2.5 mg /100 g. The DPD fruit contained well amounts of minerals includes potassium 4% from dry matter, followed by calcium 1.55%, magnesium 1.03%, phosphorus 0.39%, and sodium 0.14% [13]. The following is the most important anti-oxidant chemical compositions of DPD:

1. Carotenoids

In the lipid fractions of DPD, carotenoids are considered as a major class of phytochemicals. Carotenoids are precursors of vitamin A. Furthermore, carotenoids can protect the cells from harmful effects of free radicals as anti-oxidants [14] and play a major role in vision. The major carotenoids in DPD are lutein and b-carotene [15]. It was noted that the yellow date had high amount of carotenoids than other color of DPD [16].

2. Phyto-sterols and Phyto-estrogens

Phyto-sterols, chemical structure which similar to the cholesterol, are another major

phyto-chemicals that found in the lipid soluble fraction of the DPD [17]. It was found that DPD contains and identified several phyto-sterols includes: stigma-sterol, b-sito-sterol, campe-sterol, and isofuco-sterol [18]. Phyto-estrogens are natural compounds which could bind estrogen receptors. It exerts diverse estrogenic or anti-estrogenic effects [19]. Thompson et al. studied the phyto-estrogens content in DPD and they identified several phyto-estrogens which include: formononetin, daidzein, glycitein, genistein, matairesinol, lariciresinol, pinoresinol, and secoisolariciresinol [20].

3. Phenolic Acids

The main aromatic secondary plant metabolites are phenolic acids which considered as effective anti-oxidant due to they act as free radical scavenger. Phenolic Acids contain hydroxyl function that located on aromatic benzene ring with one or more carboxylic acid groups. In fact, phenolic acids can be divided into two main categories. The former is cinnamic acid derivatives of which contain nine carbon atoms. The latter is benzoic acid derivatives of which contain seven carbon atoms [21]. There are many researches and studies that have proven phenolic acids compounds in many varieties and in different regions, we will mention the most important of them, in order to prevent narration and repetition, which leads to boredom of the reader. It was revealed that DPD is rich with phenolic acids [16,22]. Five derivatives of benzoic acid were found in DPD which are p-hydroxybenzoic acid, vanillic acid, protocatechuic acid, gallic acid and syringic acid; and four derivatives of cinnamic acid which are o-coumaric acid, caffeic acid, p-coumaric acid, and ferulic acid on Omani DPD [16]. Algerian DPD varieties were reported that the main phenolic acids including p-coumaric acid, ferulic acid, sinapic acid, three different isomers of 5-o-caffeoyl shikimic acid, xanthoxylin acid, hydrocaffeic acid, and coumaroylquinic acid [23]. Moreover, DPD is an immune booster due to the action of phenolic acids that were confirmed by Karasawa et al. who identified protocatechuic acid, caffeic acid, syringic acid, ferulic acid, and chlorogenic acid in the UAE DPD extract using UPLC compared with those of standard phenolic acids [24]. In Tunisian DPD, Protocatechuic acid, vanillic acid, syringic acid, gallic acid, and p-coumaric acid were detected [25]. The phenolic acids in Saudi DPD varieties were gallic acid, ferulic acid and p-coumaric acid [26].

4. Flavonoids

Flavonoids are great family of poly-phenolic plant derived secondary metabolites. Flavonoids contain two aromatic benzene rings A and C which chemically bound via a heterocyclic pyrane ring C and this skeleton is often substituted with multiple substitution patterns. Flavonoids are classified into numerous subcategories that include flavonols, flavones, flavanonol, flavanones, isoflavonone, isoflavones, flavan-3-ols, and anthocyanidins. Flavonoids are found in a variety of DPD with notable health benefits as anti-oxidant and anti-inflammatory [27]. In a study was conducted in 2006 on DPD, they revealed that DPD contain luteolin, 13 flavonoid glycosides of apigenin and quercetin, 19 in isomeric forms [28]. Furthermore, in Oman, the total flavonoid content has been investigated for DPD [29]. While Michael et al. reported a new diosmetin glycosides; diosmetin 7-O-b-L-arabinofuranosy [1→2]-b-D-apiofuranoside [Diosmetin 1] and diosmetin 7-O- b-D-apiofuranoside [Diosmetin 2] that was isolated from acetone extract of DPD [87=30]. Hamad et al. identified apigenin, quercetin, isoquercetrin, luteolin, and rutin in Saudi DPD [26].

The importance of Date [*Phoenix Dactylifera*]:

The DPD is a blessed tree mentioned in the holy heavenly books [the Holy Qur'an, the Bible and the Torah]. This tree played a major role in maintaining the stability of the ecosystem and combating desertification. It is the greatest food-producing tree in the desert. It is also the main factor in sustaining life in

dry areas. The DPD can be eaten fresh [rutab] and dried; as its fruits are a complete source of food that can be stored and transported. The palm date tree could provide a perfect source of shade and protection for everything grown under it. In Arabic and Islamic culture, the Dates are one of the four main crops [wheat, barley, dates and raisins]. DPD is an excellent material for producing refined sugar, date-sugar syrup, confectionery pastes and fermentation products [6]. The DPD is conducted in food industry and all parts of the dates fruit can be used; for example, post extracted of the honey of dates [Date molasses and locally is named Dibees], the palm cake [by-product] and the seeds can be used for animal feeding. The palm cake can be used fresh or dried. The seeds are crushed in a special machine to turn the seeds into small grains that are easy for animals to eat. The DPD have been consumed traditionally in the period of pregnancy and postpartum period as well in different regions of Asia and Africa [31].

Medical uses of Date [*Phoenix Dactylifera*]

A. Anti-oxidant Activities of Date Fruit:

The increasing of free radicals in the body are related to different illnesses. For example: cancer, cardiovascular disease, Alzheimer's, Parkinson's, damage to cells, neuro-generative illnesses, even depression in some people and aging related diseases [32]. In contrast, anti-oxidant materials could surly aid to prevent these illnesses. Since these chemical compounds can neutralize the free radicals [33]. Anti-oxidants can be defined as substances that delay to prevent or eliminate oxidative damage in target tissue. Oxidation refers to a chemical reaction in which electrons are lost and the oxidative state is increased. There is a homeostatic imbalance caused by free radicals which are also known as ROS. In fact, ROS induces oxidative stress which in turn causes cell death and tissue damage. Superoxide, hydroxyl, peroxyl, hydroperoxyl and alkoxyl are all examples of ROS [34]. As a result of their attacks on lipids, proteins and nucleic acids, free radicals are responsible for a variety of health problems [35]. Thus, study and reviewed the anti-oxidant capacity of DPD is a key to understand the possible health benefits of DPD. *Phoenix dactylifera* has been shown to have anti-oxidant and anti-mutagenic effects in vitro against free radicals [36].

It is well-known that the DPD are highly anti-oxidant effect [1, 36] as DPD rich with poly-phenolic compounds [9] and the phenolic compounds can participate directly or indirectly to anti-oxidant activity by their redox properties to act as hydrogen donors, reducing agents and singlet oxygen quenchers. According to Ou et al. [38] revealed that the total anti-oxidant of dates is ranged 8212 - 12,543 μM / g. In actual fact, it was found that dates contain soluble phenolic compounds including: hydroxybenzoates, hydroxycinnamates and flavonols and flavonols [39]. Another study confirmed that dates contain about 20 – 63 mg / g ferulic acid which is the dominant phenolic acid [40]. Moreover, caffeoyl-shikimic acid, di-hexoside, caffeoyl-sinapoyl-mono-hexoside, hexoside, and different kinds of flavonoid glycosides [41].

In 2015 a study was done on the anti-oxidant potentials of DPD fruit's phenolic or flavonoid components from two kinds of date that were Hallawi and Amari; through determination of ferric-reducing anti-oxidant power, free radical scavenging capacity, inhibition of Cu^{2+}-induced LDL oxidation, and enhancement of HDL-mediated cholesterol efflux from macrophages [36]. The flavonoid fraction was found to have greater inhibition of LDL oxidation than phenolic fractions, with IC50 of 9-31 nmol/GAE mL versus 85-116 nmol/GAE mL, respectively. The phenolic and flavonoid fractions of both Amari and Hallawi dates exhibited variable capacities to reduce ferric ions, scavenge radicals, and inhibit LDL oxidation. In addition, only the flavonoid fractions stimulated cholesterol removal from macrophages.

Another *in vitro* study to evaluate the anti-oxidant activity of different kind of DPD [42], the authors found that the phenolic content was [54.66 mg/100 g fresh weight] and flavonoids content was [54.46 quercetin

equivalents/100 g fresh weights]. The percentage of lipoperoxyl radical inhibition reached 83 – 95 % in the DPD. A similar study confirmed a high positive correlation between total phenolic in methanolic extract of Mauritanian DPD the anti-oxidant capacity [43].

Recently, Abdul-Hamid et al. [44] reported that there was a high antioxidant action several varieties of dates, and they also obtained high nitric oxide and 2, 2-diphenyl-1-picrylhydrazyl inhibitions, ranging between 15-66% and 22–40%. Likewise, in a previous study which indicated that the extracts obtained from DPD of 12 different cultivars showed excellent anti-oxidant activity [26]. The authors observed a significant diminution in the level of free radicals with increasing concentration of DPD. More concretely, this research found that the scavenging capacity of DPD was up to 38% and inhibited lipid peroxidation. These investigations are in line with those obtained by Zhang et al. [45] and Chaira et al. [36] in different DPD extracts; they observed inhibitions of lipid peroxidation among 70-91% and 83–95%, respectively.

Even more, *in vivo*, it was demonstrated that the intake of benzoic acids, like ferulic acid, gallic and p-coumaric acids, existing in the DPD fruit, increased the presence of anti-oxidant enzymes in rats that suffered from cardiac issues [46]. Furthermore, in vivo research showed that the assimilation of DPD extracts in rats enhanced the serum anti-oxidant status. This was due to the increasing the level of vitamins C, A, E, and retinol, and reducing the serum malondialdehyde [lipid peroxidation] levels as well [41]. Furthermore, Al-Yahya et al. [47] found that the oral input of DPD extracts about [250 and 500 mg/kg BW] prevented the depletion of endogenous anti-oxidants [catalase, superoxide dismutase] and inhibited lipid peroxidation [malondialdehyde] in rats.

B. Anti-microbial Properties of Date Fruits:

It's common in some cultures which utilize DPD in traditional medicine to cure them from some illnesses like digestive and fevers disorders [48]. Therefore, DPD anti-bacterial action has been demonstrated in preclinical research [49]. Furthermore, DPD had been shown to have anti-bacterial properties against a variety of microbes in fruit [50, 51] and leaves [52]. It was found that treating *Streptococcus pyogenic* bacteria with DPD extract could work as anti-bacterial activity [50]; with an identical minimum inhibitor concentration of 0.5 mg/mL for *Staphylococcus aurous* and *Staphylococcus epidermis's* DPD aqueous polyphenol extract revealed a significant anti-bacterial efficacy against gram [+] and gram [-] pathogens [53].

According to Kchaou et al. [51] studied the anti-bacterial properties of Tunisian date; The anti-microbial activities of the DPD from Tunisian date against various bacterial strains, *Staphylococcus aureus*, *Bacillus cereus*, *Bacillus subtilis*, *Escherichia coli*, *Klebsiella*, and *Salmonella*, were assessed by the presence or absence of inhibition zones, the diameters of inhibition zones as well. The obtained results showed various actions and degrees of germ sensitivity towards the DPD. The results revealed that date extracts inhibited the growth of microorganisms with inhibition zone diameters ranging from 9 to 19 mm for Gram [+] bacteria and from 6 to 25 mm for Gram [-] bacteria. However, no exhibit visible antimicrobial activities towards *B. cereus* and *M. luteus*.

A study of the Berhi date effect on the cellular ultrastructure of *C. albicans* was examined with electron microscopy [54]. Weakness and distortion of *C. albicans* cell wall was seen by scanning electron microscopy. The weakness of yeast was started when it was exposed to 5 % [w/v] DPD extract. More extensive damage due to cell breaks down. They also found that the concurrent death of *C. albicans* was noticed at high concentration of DPD extract [20 %, w/v]. Another anti-microbial study of Berhi date extract [20%, w/v] on *Bacillus subtilis*, *Staphylococcus aureus*, *Salmonella typhi*, and *Pseudomonas aeruginosa* was done by Sallal and Ashkenani [49]. The DPD extract induced about 80 to 99% growth inhibition in nutrient broth cultures of all bacteria. *B. subtilis* was

extensively affected by extract treatment through cell elongation. An application of these results may be that DPD extract could be included in anti-microbial drugs and in topical ointment manufacture. It was confirmed that ethyl acetate extract of DPD exhibited from moderate to strong activity against *Pseudomonas aeruginosa, Klebsiella pneumonia, Escherichia coli, Proteus vulgaris, Proteus mirabilis* methicillin-resistant *Staphylococcus aureus* [MRSA], and *Enterococcus faecalis*; respectively [55]. The specific compositions of DPD extract lignin and tannins have been suggested as the mechanism responsible for the anti-microbial activity of DPD [56]. It was found that aqueous and methanolic DPD extracts had strong anti-bacterial activities against *Salmonella enterica*, *Escherichia coli* and *Bacillus sabtilis* [22]. The suggested mechanism of this effect could be due to the presence of 6,7-dihydroxycoumarin and tannic acid. Moreover, the moderate concentration of gallic, itaconic acid, and the traces of ferulic acid presence in DPD extracts [22, 57].

C. Anti-Inflammatory of Date Fruits:

Toxic chemicals, infection, burns, allergies, and other causes can all trigger inflammation as a physiologic defense mechanism. The reverse inflammatory process plays a critical role in the development and spread of numerous illnesses. Expression regulators like Lipoxygenase and [NF-kB] nuclear factor kappa light-chain-enhancer of activated B cells play an important role in illnesses such as inflammation, cancer and diabetes. In the fight against disease controlling transcription factors is a crucial step. Inhibitors have been hard at work to demonstrate an antagonistic impact and their levels are also quite high. Anti-inflammatory chemicals and a viable answer for suppressing NF-kB are provided by actual items. Plant compounds including phenolic and flavonoids have been shown in studies to be effective anti-inflammatory agents. When it comes to anti-inflammation properties DPD play an essential role. A study found that the enzymes COX-1 and COX2 were inhibited by extracts of DPD in ethyl acetate, methanol and water [10]. Thus, DPD extract had a critical function in reducing swelling in the feet and plasma fibrinogen levels [58]. Previous report was supported the anti-inflammatory properties of DPD which have discovered that their leaves are a rich source of anti-oxidants and anti-inflammation medications. Dates produce an up-regulation of autocrine/paracrine receptors as well as a decrease in cytokine expression [59]. Even though there is no clear procedure for the anti-inflammatory effects caused by DPD. It has been confirmed that the DPD has active compounds, which could inhibit and decrease the production of hormones that cause inflammation like prostaglandins and thromboxanes [60]. This is evident from a study that was done by Zhang et al. [60] who analysed the anti-inflammatory activity of 29 different DPD varieties by the inhibition of two cyclooxygenase enzymes [COX-1 and -2] in aqueous and methanolic DPD extracts. Furthermore, the prior administration of DPD lyophilizate for 21 days with 250 or 500 mg / kg, BW per day, down regulated the expressions of pro-inflammatory cytokines [interleukin-6, interleukin-10 and tumour necrosis factor α] on inflammation induced rats [47]. It also reported that the ear oedema which was induced by Croton oil in rats inhibited up to 74% using methanolic extract of DPD [61].

D. Sexual booster of Date Fruits:

In male: the DPD has been used as therapy when the male fertility is decreased or impotence in traditional Arab medicine. In fact, the presence of estrogen components [estrone, estradiol, estriol], α-amirin, triterpenoidalsaponins, and flavonoids in DPD could explain the role of the DPD on sexual function [21]. It's possible that the gonadotropin-like effects of DPD are caused by the steroid components. This is by increasing the release of dopamine in the nucleus accumbens [62]. The extraction of DPD has been shown to increase the total sperm count in guinea pigs, enhanced spermatogenesis, increase the concentration of testosterone, follicle stimulating hormone, and luteinizing hormone in male rats [63]. It was

revealed that male rats treated with aqueous DPD extract had high sexual behavior when exposed to estrous female counterpart than control Abedi *et al.* [62]. Oral administration of DPD suspensions at doses of 240 mg/kg improved the sperm functional parameters, total sperm count and DNA integrity. In addition, the weight of testis and epididymis was increased [59]. It appears that the main site of its action could be the testis and the hypothalamo-hypophyseal axis. The aqueous extract of DPD was tested on bull sperm cells; in chilled, frozen, and thawed semen in three independent experiments [unpublished data]. In the first experiment, the aqueous extract of DPD was added to a sodium citrate-based extender to improve the cooled semen. For the second experiment, the aqueous extract of DPD was added to the Tris-based expander to evaluate frozen semen. The third experiment had DPD added to thawed bull semen; the thawed semen was centrifuged, washed, and then the sperm were placed in a new solution [one of three solutions] containing different doses of the aqueous extract of DPD. The final results of these experiments revealed that DPD has the ability to improve and enhance sperm motility, in vivo fertility test and increase the survival time of spermatozoa under the lab environment with highly significant values compared to control groups.

In female: based on historical Islamic medical literature, DPD has been suggested to be consumed either alone or with other foods as a suitable nutritious food by pregnant women before and after childbirth. [64]. It was revealed and confirmed that the female feeding with DPD had shorter period of the latent phase of labor, less bleeding percentage post-delivery, less parturition induction, high percentage of spontaneous labor [65]. In like manner, it was confirmed that the following variables were significantly higher in the DPD consumer group: presence of intact amniotic membrane on admission, cervical effacement on admission, cervical consistency on admission, cervical position on admission, fetal station on admission, and normal labor progression rate in the 2nd stage of labor [65].

E. Anti-cancer activity

In fact, cancers impose the largest worldwide burden [66]. It is well known that the environmental factors, dietary factors, smoking, some viral infection, chemicals, poisoning and radiation are the major predisposing reasons of cancer. The primary conventional treatments of cancer are chemotherapy, radiotherapy and surgery. Phenolic and flavonoids of herbal plants have been used as powerful anti-cancer activity through up the regulation of anti-apoptotic molecules such as p_{53}, caspases and Bcl-$_2$-associated X protein [Bax] or by down regulation of apoptotic molecules as Akt, B cell lymphoma-2 [Bcl-2] and nuclear factor κB [NFκB] [67]. Functional foods, such as DPD, are known to be rich in anti-oxidants, as previously mentioned, that can prevent oxidative stress. The extracts of DPD were evaluated on pancreatic cancer to determine their activity as free radical scavengers, anti-fibrosis and anti-proliferation agents [4]. Thus, DPD extracts demonstrated a significant effect in reducing pancreatic stellate cells activation and fibrotic protein formation by means of the lowered cellular proliferation and Fibronectin 1 production. The proposed mechanism of DPD as anti-cancer was this effect may reduce the oxidative stress potential within the cells. Along with that DPD extract is well known as a rich source of anti-oxidants. Activation and fibrogenesis process of pancreatic stellate cell is always associated with increased the production of free radicals and ROS [68]. Thus, using a natural source of anti-oxidants can definitely reduce the cell activation and fibrotic potential of pancreatic stellate cells [4].

One study of DPD extract was tested the inhibition of human epithelial colorectal adeno-carcinoma [Caco-2] cells before and after pH-controlled batch culture fermentation in comparison to untreated cells [69]; they found that DPD extract to exhibit potent anti-tumor activity. In a study were used alcoholic and oil extracts of fruit and leaves of DPD that was concluded to inhibit cancer cell lines AMN3. The author revealed that the oil extract

of DPD was superior to alcoholic extract. Moreover, the presence of phytochemical in oil extract but not in the alcoholic extract could explain these findings [70].

CONCLUSION

The DPD is one of the oldest cultivated fruit of earth and has been used as food over 6000 years. DPD is commonly found in Iraq and countries in the Middle East and North Africa. In general, there are four stages of fruit development: the kamari stage [green color], the khalal stage [yellow or red, depending on the variety], the rutab stage [soft and sweet], and the date stage [full maturity stage]. However, not all varieties necessarily pass through all these stages. The date fruits are varying in diameters, color and amount of sugar depending on the varieties. The DPD is rich with many components such as carbohydrate [sugar], dietary fibres, phytochemicals, fatty acids, amino acids, ash, and the most important kinds of minerals, vitamins and salts. The collected data confirmed that certain varieties of dates contain sucrose, fructose and glucose like Zahidi; while there are varieties that contain only fructose and glucose, like Khulas. Some varieties have a fairly low percentage of sugars [57%] such as Barhi, and other varieties have a very high percentage of sugars, which may reach the level of [88%] such as Zahidi. The yellow date had high amount of carotenoids than other color of DPD. Phytoestrogens are natural compounds found in DPD that can bind to estrogen receptors. Therefore, it is recommended to take it during, the last period of pregnancy and postpartum. It is well-known that the DPD are highly anti-oxidant effect due to their active components. Studies also confirmed that the DPD has anti-bacterial efficacy against gram [+] and gram [-] pathogens. The anti-inflammatory effect of DPD has been confirmed. The sexual booster and improvement of male sexual activity of DPD were studied and confirmed. The aqueous extract of DPD can improve the chilled and frozen semen due to their active components. Furthermore, the aqueous extract of DPD could increase the life span of spermatozoa as well in environmental lab. The using DPD for feeding female in last period of pregnancy lead to shorting period of the latent phase of labour, less bleeding percentage post-delivery, high percentage of spontaneous labour, presence of intact amniotic membrane on admission, normal cervical consistency and position on admission, and normal labour progression rate in the 2nd stage of labour. It is also confirmed that the DPD are anti-cancer effect

CONFLICT OF INTERESTS

The authors declare that they have no conflict of interests.

REFERENCES

1. Vayalil, Praveen K. "Date fruits [Phoenix dactylifera Linn]: an emerging medicinal food." Crit Rev Food Sci Nutr 2012; 52.3: 249-271. https://doi.org/10.1080/10408398.2010.499824
2. Bettaieb, I., Kilani, A., Ben Othman, K., Benabderrahim, M. A., & Elfalleh, W. Phenolic Profile, Sugar Composition, and Antioxidant Capacities of Some Common Date Palm [Phoenix dactylifera L.] Cultivars as a Potential Nutraceutical and Functional Food Ingredients. J Food Qual, 2023. https://doi.org/10.1155/2023/2474900
3. Deshpande, Neeta Mahesh, Manasi M. Deshpande, and D. Dravyaguna. "Date fruit [Phoenix dactylifera Linn]–a review on nutritional values, phytochemicals and pharmacological actions. World J Pharm Res 2017; 6.8: 419-26. https://doi:10.20959/wjpr20178-8943
4. Al Alawi, R., Alhamdani, M. S. S., Hoheisel, J. D., & Baqi, Y.. Antifibrotic and tumor microenvironment modulating effect of date palm fruit [Phoenix dactylifera L.] extracts in pancreatic cancer. Biomed Pharmacother 2020; 121, 531 - 535. https://doi.org/10.1016/j.biopha.2019.109522.
5. Bahmanpour, S., Kavoosi, F., Talaei, T., & Panjehshahin, M. R. Effects of date palm [Phoenix dactylifera] gemmule extract on morphometric parameters of reproductive tissues, hormones and sperm quality in rat. Anatom Sci J 2019; 10[3]: 144-150

6. Samarawira, I. "Date palm, potential source for refined sugar." Econom Botan 1983; 37.2, 181-186. https://doi.org/10.1007/BF02858783
7. Ghnimi, S., Umer, S., Karim, A., & Kamal-Eldin, A. Date fruit [Phoenix dactylifera L.]: An underutilized food seeking industrial valorization. Nutr. Food Sci J 2017; 6, 1-10. https://doi.org/10.1016/j.nfs.2016.12.001
8. Hamdi, M., Mostafa, H., Aldhaheri, M., Mudgil, P., Kamal, H., Alamri, A. S., & Maqsood, S. Valorization of different low-grade date [Phoenix dactylifera L.] fruit varieties: A study on the bioactive properties of polyphenolic extracts and their stability upon in vitro simulated gastrointestinal digestion. Plant Physiol Biochem 2023; 200: 107764. https://doi.org/10.1016/j.plaphy.2023.107764
9. Kuras, M. J., Zielińska-Pisklak, M., Duszyńska, J., & Jabłońska, J. Determination of the elemental composition and antioxidant properties of dates [Phoenix dactyliferia] originated from different regions. J Food Sci Technol 2020; 57, 2828-2839. https://doi.org/10.1007/s13197-020-04314-8
10. Ahmed, A., Bano, N., & Tayyab, M. Phytochemical and therapeutic evaluation of date [Phoenix dactylifera]. A review. J Altern Med 2016; 9, 11-17.
11. Ramchoun, M., Alem, C., Ghafoor, K., Ennassir, J., & Zegzouti, Y. F. Functional composition and antioxidant activities of eight Moroccan date fruit varieties [Phoenix dactylifera L.]. J. Saudi Soc. Agric. Sci 2017; 16[3], 257-264. https://doi.org/10.1016/j.jssas.2015.08.005
12. Ahmed, Imad A., Abdul Wahab K. Ahmed, and Richard K. Robinson. "Chemical composition of date varieties as influenced by the stage of ripening. Food chemis 1995; 54.3, 305-309. https://doi.org/10.1016/0308-8146[95]00051-J
13. Assirey, Eman Abdul Rahman. "Nutritional composition of fruit of 10 date palm [Phoenix dactylifera L.] cultivars grown in Saudi Arabia. J Taibah Univer sci 2015; 9.1, 75-79. https://doi.org/10.1016/j.jtusci.2014.07.002
14. Julia, V.,Macia, L., and Dombrowicz, D. The impact of diet on asthma and allergic diseases. Nat Rev Immunol 2015; 15, 308–322. https://doi:10.1038/nri3830
15. Boudries, H., Kefalas, P., and Hornero-Méndez, D. Carotenoid composition of Algerian date varieties [Phoenix dactylifera] at different edible maturation stages. Food Chem 2007; 101, 1372–1377. https://doi:10.1016/j.foodchem.2006.03.043
16. Al-Farsi, M., Alasalvar, C., Morris, A., Baron, M., and Shahidi, F. Comparison of antioxidant activity, anthocyanins, carotenoids, and phenolics of three native fresh and sun-dried date [Phoenix dactylifera L.] varieties grown in Oman J Agric Food Chem 2005; 53, 7592–7599. https://doi:10.1021/jf050579q
17. Al-Laith, A. A. Degradation kinetics of the antioxidant activity in date palm [Phoenix dactylifera L.] fruit as affected by maturity stages. Arab Gulf J Sci Res 2009; 27, 16–25
18. Kikuchi, N., and Miki, T. The separation of date [Phoenix dactylifera] sterols by liquid chromatography. Microchim Acta 1978; 69, 89–96. https://doi:10.1007/BF01196983
19. Al-Turki, S., Shahba, M. A., and Stushnoff, C. J. Diversity of antioxidant properties and phenolic content of date palm [Phoenix dactylifera L.] fruits as affected by cultivar and location. J Food Agri Environ 2010; 8, 253–260
20. Thompson, L. U., Boucher, B. A., Liu, Z., Cotterchio, M., & Kreiger, N. Phytoestrogen content of foods consumed in Canada, including isoflavones, lignans, and coumestan. Nutri cancer 2006; 54[2], 184-201. https://doi.org/10.1207/s15327914nc5402_5
21. Sani, I. H., Bakar, N. H. A., Rohin, M. A. K., Suleiman, I., Umar, M. I., & Mohamad, N. Phoenix dactylifera Linn as a potential novel anti-oxidant in treating major opioid toxicity. J Appl Pharmaceut Sci 2015; 5[8], 167-172. https://DOI:10.7324/JAPS.2015.50826
22. El Sohaimy, S. A., Abdelwahab, A. E., Brennan, C. S., & Aboul-Enein, A. M. Phenolic content, antioxidant and antimicrobial activities of Egyptian date palm [Phoenix dactylifera L.] fruits. Australian J Basic Appl Sci 2015; 9[1]: 141-147. https://hdl.handle.net/10182/6571
23. Mansouri, A., Embarek, G., Kokkalou, E., and Kefalas, P. Phenolic profile and antioxidant

activity of the Algerian ripe date palm fruit [Phoenix dactylifera]. Food Chem 2005; 89, 411–420. https://doi:10.1016/j.foodchem.2004.02.051
24. Karasawa, K., Uzuhashi, Y., Hirota, M., and Otani, H. A matured fruit extract of date palm tree [Phoenix dactylifera L.] stimulates the cellular immune system in mice. J Agric Food Chem 2011; 59, 11287–11293. https://doi:10.1021/jf2029225
25. Mrabet, A., Jiménez-Araujo, A., Fernández-Bola-os, J., Rubio-Senent, F., Lama-Mu-oz, A., Sindic, M. Antioxidant phenolic extracts obtained from secondary Tunisian date varieties [Phoenix dactylifera L.] by hydrothermal treatments. Food Chem 2016; 196, 917–924. https://doi:10.1016/j.foodchem.2015.10.026
26. Hamad, I., AbdElgawad, H., Al Jaouni, S., Zinta, G., Asard, H., Hassan, S., & Selim, S. Metabolic analysis of various date palm fruit [Phoenix dactylifera L.] cultivars from Saudi Arabia to assess their nutritional quality. Molecules 2015; 20[8], 13620-13641. https://doi.org/10.3390/molecules200813620
27. Moss, J.W. E., and Ramji, D. P. Nutraceutical therapies for atherosclerosis. Nat Rev Cardiol 2016; 13, 513–532. https://doi:10.1038/nrcardio.2016.103
28. Hong, Y. J., Tomas-Barberan, F. A., Kader, A. A., and Mitchell, A. E. The flavonoid glycosides and procyanidin composition of deglet noor dates [Phoenix dactylifera]. J. Agric. Food Chem 2006; 54, 2405–2411. https://doi:10.1021/jf0581776
29. Singh, V., Guizani, N., Essa,M., Hakkim, F., and Rahman,M. Comparative analysis of total phenolics, flavonoid content and antioxidant profile of different date varieties [Phoenix dactylifera L.] from Sultanate of Oman. Int Food Res J 2012; 19, 1063–1070
30. Michael, H. N., Salib, J. Y., and Eskander, E. F. Bioactivity of diosmetin glycosides isolated from the epicarp of date fruits, Phoenix dactylifera, on the biochemical profile of alloxan diabetic male rats. Phytother Res 2013; 27, 699–704. https://doi.org/10.1002/ptr.4777
31. Ahmed, M., Hwang, J. H., Choi, S., & Han, D. Safety classification of herbal medicines used among pregnant women in Asian countries: a systematic review. BMC complement altern med 2017; 17[1], 1-11. https://doi10.1186/s12906-017-1995-6
32. Kumar, S., & Pandey, A. K. Free radicals: health implications and their mitigation by herbals. British J Med Medical Res 2015; 7[6], 438-457. https://DOI:10.9734/BJMMR/2015/16284
33. Munekata, P. E. S., Rocchetti, G., Pateiro, M., Lucini, L., Domínguez, R., & Lorenzo, J. M. Addition of plant extracts to meat and meat products to extend shelf-life and health-promoting attributes: An overview. Curr Opinion Food Sci 2020; 31, 81-87. https://doi.org/10.1016/j.cofs.2020.03.003
34. Srivastava, K. K., & Kumar, R. Stress, oxidative injury and disease. Indian J Clin Biochem 2015; 30[1], 3-10.
35. Liguori, I., Russo, G., Curcio, F., Bulli, G., Aran, L., Della-Morte, D., & Abete, P. Oxidative stress, aging, and diseases. Clin Interv Aging 2018; 757-772. https://doi.org/10.2147/CIA.S158513
36. Chaira N, Smaali MI, Martinez-Tome M, Mrabet A, Murcia MA. Simple phenolic composition, flavonoid contents and antioxidant capacities in water-methanol extracts of Tunisian common date cultivars [Phoenix dactylifera L.]. Int J Food Sci Nutr 2009; 60 Suppl 7: 316-329. https://doi.org/10.1080/09637480903124333
37. Ou, B., Hampsch-Woodill, M., & Prior, R. L. Development and validation of an improved oxygen radical absorbance capacity assay using fluorescein as the fluorescent probe. J agricul and food chemis 2001; 49[10], 4619-4626. https://doi.org/10.1021/jf010586o
38. Guo, C., Yang, J., Wei, J., Li, Y., Xu, J., & Jiang, Y. Antioxidant activities of peel, pulp and seed fractions of common fruits as determined by FRAP assay. Nutrition res 2003; 23[12], 1719-1726. https://doi.org/10.1016/j.nutres.2003.08.005
39. Regnault-Roger, C., Hadidane, R., Biard, J. F., & Boukef, K. High performance liquid and thin-layer chromatographic determination of phenolic acids in palm [Phoenix dactilifera] products. Food Chem 1987; 25[1], 61-71. https://doi.org/10.1016/0308-8146[87]90054-9

40. Hammouda, H., Chérif, J. K., Trabelsi-Ayadi, M., Baron, A., & Guyot, S. Detailed polyphenol and tannin composition and its variability in Tunisian dates [Phoenix dactylifera L.] at different maturity stages. J agricul food chem 2013; 61[13], 3252-3263. https://doi.org/10.1021/jf304614j
41. Mohamed, D. A., & Al-Okbi, S. Y. In vivo evaluation of antioxidant and anti-inflammatory activity of different extracts of date fruits in adjuvant arthritis. Pol J Food Nutr Sci 2004; 13[54], 397-402.
42. Mohamed LFM, Mohamed AMV, Ben MML, Bouna ZA, Samb A, Antioxidant activity of various Mauritanian date palm [Phoenix dactylifera L.] fruits at two edible ripening stages. Food Sci Nutr 2014; 2: 700-705. https://doi.org/10.1002/fsn3.167
43. Bolling, B. W., Chen, C. Y. O., McKay, D. L., & Blumberg, J. B. Tree nut phytochemicals: composition, antioxidant capacity, bioactivity, impact factors. A systematic review of almonds, Brazils, cashews, hazelnuts, macadamias, pecans, pine nuts, pistachios and walnuts. Nutr res reviews 2011; 24[2], 244-275. https://doi.org/10.1017/S095442241100014X
44. Abdul-Hamid, N. A., Mustaffer, N. H., Maulidiani, M., Mediani, A., Ismail, I. S., Tham, C. L., & Abas, F. Quality evaluation of the physical properties, phytochemicals, biological activities and proximate analysis of nine Saudi date palm fruit varieties. J Saudi Society Agricul Sci 2020; 19[2], 151-160. https://doi.org/10.1016/j.jssas.2018.08.004
45. Zhang, Chuan-Rui, Aldosari, S. A., Vidyasagar, P. S., Nair, K. M., & Nair, M. G. Antioxidant and anti-inflammatory assays confirm bioactive compounds in Ajwa date fruit J Agricul food chem 2013; 61.24, 5834-5840. https://doi.org/10.1021/jf401371v
46. Yeh, Chi-Tai, Li-Chien Ching, and Gow-Chin Yen. "Inducing gene expression of cardiac antioxidant enzymes by dietary phenolic acids in rats." J nutrit biochem 2009; 20.3: 163-171. https://doi.org/10.1016/j.jnutbio.2008.01.005
47. Al-Yahya, M., Raish, M., AlSaid, M. S., Ahmad, A., Mothana, R. A., Al-Sohaibani, M., & Rafatullah, S. Ajwa'dates [Phoenix dactylifera L.] Extract ameliorates isoproterenol-induced cardiomyopathy through downregulation of oxidative, inflammatory and apoptotic molecules in rodent model. Phytomedicine 2016; 23.11: 1240-1248. https://doi.org/10.1016/j.phymed.2015.10.019
48. Baliga, M. S., Baliga, B. R. V., Kandathil, S. M., Bhat, H. P., & Vayalil, P. K. A review of the chemistry and pharmacology of the date fruits [Phoenix dactylifera L.]. Food res internat 2011; 44[7], 1812-1822. https://doi.org/10.1016/j.foodres.2010.07.004
49. Sallal AK, Ashkenani A. Effect of date extract on growth and spore germination of Bacillus subtilis. Microbios 1989; 59: 203-210.
50. Maged, Nuha Qays Abdul, and Nadheema Abed Abbas. Antibacterial activity of Phoenix dactylifera L. leaf extracts against several isolates of bacteria. Kufa J Vet Med Sci 2013; 4[2]: 45-50.
51. Kchaou, W., Abbès, F., Mansour, R. B., Blecker, C., Attia, H., & Besbes, S. Phenolic profile, antibacterial and cytotoxic properties of second grade date extract from Tunisian cultivars [Phoenix dactylifera L.]. Food chemistry 2016; 194: 1048-1055. https://doi.org/10.1016/j.foodchem.2015.08.120
52. Dhaouadi, K., Raboudi, F., Estevan, C., Barrajon, E., Vilanova, E., Hamdaoui, M., & Fattouch, S. Cell viability effects and antioxidant and antimicrobial activities of Tunisian date syrup [Rub El Tamer] polyphenolic extracts. J agricul food chem 2011; 59[1], 402-406. https://doi.org/10.1021/jf103388m
53. Saleh, F. A., & Otaibi, M. M. Antibacterial activity of date palm [Phoenix dectylifera L.] fruit at different ripening stages. Journal Food Process Technol 2013; 4[12].
54. Shraideh ZA, Abu-Elteen KH, Sallal AK. Ultrastructural effects of date extract on Candida albicans. Mycopathologia 1998; 142: 119-123. https://doi.org/10.1023/A:1006901019786
55. ALrajhi, M., Al-Rasheedi, M., Eltom, S. E. M., Alhazmi, Y., Mustafa, M. M., & Ali, A. M. "Antibacterial activity of date palm cake extracts [Phoenix dactylifera]." Cogent Food Agricul 2019; 5.1: 1625479.

https://doi.org/10.1080/23311932.2019.1625479
56. Shafiei, Marzieh, Keikhosro Karimi, and Mohammad J. Taherzadeh. "Palm date fibers: analysis and enzymatic hydrolysis." International journal of molecular sciences 2010; 11.11: 4285-4296. https://doi.org/10.3390/ijms11114285
57. El-Far, A. H., Oyinloye, B. E., Sepehrimanesh, M., Allah, M. A. G., Abu-Reidah, I., Shaheen, H. M., & Mousa, S. A. Date palm [Phoenix dactylifera]: novel findings and future directions for food and drug discovery. Current drug discovery technologies 2019; 16[1], 2-10. https://doi.org/10.2174/1570163815666180320111937
58. Abutaha, N., Semlali, A., Baabbad, A., Al-Shami, M., Alanazi, M., & Wadaan, M. A. "Anti-proliferative and anti-inflammatory activities of entophytic Penicillium crustosum from Phoenix dactylifer." Pakistan J Pharmaceut Sci 2018; 31:[2].
59. Bahmanpour, S., Panjeh, S. M., Talaei, T., Vojdani, Z., Poust, P. A., Zareei, S., & Ghaemian, M. Effect of Phoenix dactylifera pollen on sperm parameters and reproductive system of adult male rats. Iran J Med Sci 2006; 208-212.
60. Zhang, C. R., Aldosari, S. A., Vidyasagar, P. S., Shukla, P., & Nair, M. G. Health-benefits of date fruits produced in Saudi Arabia based on in vitro antioxidant, anti-inflammatory and human tumor cell proliferation inhibitory assays. J Saudi Society Agricul Sci 2017; 16.3: 287-293. https://doi.org/10.1016/j.jssas.2015.09.004
61. El Hilaly, J., Ennassir, J., Benlyas, M., Alem, C., Amarouch, M. Y., & Filali-Zegzouti, Y. Anti-inflammatory properties and phenolic profile of six Moroccan date fruit [Phoenix dactylifera L.] varieties. J King Saud Univ-Sci 2018; 30.4: 519-526. https://doi.org/10.1016/j.jksus.2017.08.011
62. Abedi A, Karimian S.M, Parviz M, Mohammadi P, and Roudsari HRS.Effect of aqueous extract of Phoenix dactylifera pollen on dopamine system of nucleus accumbens in male rats.Neuroscience and medicine.2014; 5:49-59. https://DOI:10.4236/nm.2014.51008
63. Elgasim EA, Alyousif YA, Homeida AM: Possible hormonal activity of date pits and fleshfed to meat animals. Food Chem. 1995; 52: 149–150. https://doi.org/10.1016/0308-8146[94]P4195-L
64. Ali SA, Parveen N, Ali AS. Links between the Prophet Muhammad [PBUH] recommended foods and disease management: A review in the light of modern superfoods. Int J Health Sci *[*Qassim*]*. 2018; 12[2]:61-69. PMID: 29599697
65. Nasiri, M., Gheibi, Z., Miri, A., Rahmani, J., Asadi, M., Sadeghi, O., & Khodadost, M. Effects of consuming date fruits [Phoenix dactylifera Linn] on gestation, labor, and delivery: An updated systematic review and meta-analysis of clinical trials. Complem Therap Med 2019; 45, 71-84. https://doi.org/10.1016/j.ctim.2019.05.017
66. Mattiuzzi, C., & Lippi, G. Current cancer epidemiology. J Epidemiol Global Health 2019; 9[4], 217. https://doi10.2991/jegh.k.191008.001
67. Eid, N., Enani, S., Walton, G., Corona, G., Costabile, A., Gibson, G., & Spencer, J. P. The impact of date palm fruits and their component polyphenols, on gut microbial ecology, bacterial metabolites and colon cancer cell proliferation. J Nutrit Sci 2014; 3: e46. https://doi.org/10.1017/jns.2014.16
68. M.A. Jakubowska, P.E. Ferdek, O.V. Gerasimenko, J.V. Gerasimenko, O.H. Petersen, Nitric oxide signals are interlinked with calcium signals in normal pancreatic stellate cells upon oxidative stress and inflammation Open Biol. 2016; 6[8]: 160-149. https://doi.org/10.1098/rsob.160149
69. Ishurd, Omar, and John F. Kennedy. "The anti-cancer activity of polysaccharide prepared from Libyan dates [Phoenix dactylifera L.]." Carbohyd Polym 2005; 59.4: 531-535. https://doi.org/10.1016/j.carbpol.2004.11.004
70. Al-Zeiny, Saadia Saleh Mehdy, Kifah Jabbar Alyaqubi, and Duraid Abdul Hadi Abbas. "In vitro: anticancer effect of oily and methanolic extracts of Al-Zahdi [Phoenix dactylifera L.] from dry dates and leaves on AMN3, Hela and Ref cancer cell cultures." Kufa J Vet Med Sci 2022; 13.2: 1-12.