

Review Article

Therapeutic effects of date fruits (*Phoenix dactylifera*) in the prevention of diseases via modulation of anti-inflammatory, anti-oxidant and anti-tumour activity

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Abstract: The current mode of treatment of various diseases based on synthetic drugs is expensive, alters genetic and metabolic pathways and also shows adverse side effects. Thus, safe and effective approach is needed to prevent the diseases development and progression. In this vista, Natural products are good remedy in the treatment/management of diseases and they are affordable and effective without any adverse effects. Dates are main fruit in the Arabian Peninsula and are considered to be one of the most significant commercial crops and also have been documented in Holy Quran and modern scientific literatures. Earlier studies have shown that constituents of dates act as potent antioxidant, anti-tumour as well as anti-inflammatory, provide a suitable alternative therapy in various diseases cure. In this review, dates fruits has medicinal value are summarized in terms of therapeutic implications in the diseases control through anti-oxidant, anti-inflammatory, anti-tumour and ant-diabetic effect.

Keywords: Dates fruits, medicinal plants, anti-tumour activity

Introduction

Cancer and diabetes is an economical burden worldwide. The exact cause of the development of these types of diseases/disorder is not known completely but it might be due to the genetic alteration and metabolic disturbance [1-7]. The treatment approach for the cancer and diabetes based on allopath is expensive and also shows an adverse effect. Alternative approach as safe, effective and affordable is needed to control the disease development and progression. Natural products are a good remedy as they are inexpensive and easy to access without any complications. In Islam, herbs and its constituents has important value in diet and treatment of various types of diseases. The Prophet Mohammed (Peace Be Upon Him) used various herbs and recommended various medicinal plants for cure of various diseases [8, 9].

Dates fruits are used as staple food in the Middle East for thousands of years (**Figure 1**). Various types of dates are found worldwide mainly Khodry, Khalas, Ruthana, Sukkary, Sefri, Segae, Ajwa, Hilali and Munifi (**Figure 2**) and each type of dates has shown medicinal value in various type of disease prevention. Dates and their constituents show a role in diseases prevention through anti-oxidant, anti-inflammatory, anti-bacterial activity.

Antioxidant activity is recognized due to the wide range of phenolic compounds present in dates including p-coumaric, ferulic, and sinapic acids, flavonoids, and procyanidins [10, 11]. Other study showed that palm date fruits constitutes thirteen flavonoid glycosides of luteolin, quercetin, and apigenin at different stages of maturity [12, 13]. Ajwa, types of dates that is only cultivated in Saudi Arabia/Al-Madinah Al-Munawara and have significant value in several types of diseases cure and also show pro-



Figure 1. Dates plant.

protective role in hepatic toxicity [14]. In this review, dates fruits has medicinal value are summarized in terms of therapeutic implications in the various types of diseases through anti-oxidant, anti-cancerous and anti-diabetic character.

Historical overview of dates (*Phoenix dactylifera*)

Dates (*Phoenix dactylifera*) are one of the members of the palm family Arecaceae, or Palmae [15]. The species name *dactylifera* “date-bearing” originate from two words; one from greek *dáktulos* “date” [16] and the stem of the Greek verb *ferō* [17]. The date palm (*Phoenix dactylifera* L.) is one of oldest cultivated plants of human kind and used as food for 6000 years [18]. There are more than two hundred varieties [19] of dates available worldwide. It is the main crop in Egypt, Saudi Arabia, and Middle Eastern countries. It is thought that the native origin of dates is around the Persian Gulf, and has been cultivated from Mesopotamia to pre-historic Egypt as early as 4000 BCE. Due to the old historical prospective of date, the exact date of origin is very difficult to identify [20]. Most likely it originated 4000 BC from the ancient Mesopotamia area (southern Iraq) or western India [21]. Another report regarding the origin of dates is pre-Islamic archaeology;

south-eastern Arabia was predicated upon the domestication of the date palm in 2500 BC [22]. Over all the origin of dates is very old as per the information from the religious books and literature reports. Another support of the ancient times of the date palm is Egypt’s Nile Valley where it was used as the symbol for a year in Egyptian hieroglyphics and its frond as a symbol for a month [23]. Earlier report also showed that old background of dates as date cultivation in Mehrgarh around 7000 BCE and in the Indus Valley around 2600 to 1900 BCE [24]. The fruits of dates has important place in religion. In Islam dates fruits are used to break the day long fast during the holy month of Ramadan [25]. The Jews believe the date as one of the seven holy fruits and they celebrate Palm Sunday.

Prophet Muhammed (Peace Be Upon Him) said that the best assets is date palm, dates cure several disorders, and he suggested Muslims to eat the date and have a tendency the date palm [26]. The importance of dates has been documented in the Qur’an in Surah Maryam. One significant role of dates comes as when Mary gave birth to the Prophet Jesus (may peace be upon Him) under a palm tree, she heard a voice telling her: “Shake the trunk of the palm tree towards thee: it will drop fresh, ripe dates upon thee. Eat, then, and drink, and let thine eye be gladdened!” (Qur’an 19: 25-26). Ajwa is a types of dates, cultivated only in Saudi Arabia/Al-Madinah Al-Munawara and have significant value in diseases cure. The health benefit of Ajwa dates has been documented in hadith as Saud (R.A) narrated that I heard Allah’s Apostle saying, “If Somebody takes seven Ajwa dates in the morning, neither magic nor poison will hurt him that day [27]”.

Role of dates in disease prevention via anti-oxidant, anti-microbial and anti-inflammatory activity (Figure 3)

Anti-oxidant activity

Antioxidants are chemicals/materials that interact and deactivate the free radicals, therefore preventing them from causing harm. The prevention of actions of free radical is important step in the management of disease. Medicinal plants and their constituents play a vital and significant action to neutralize or inhibit the free radical by the use of antioxidant

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Figure 2. Types of dates: A: Ajwa; B: Sukhary; C: Sabaka; D: Munifi.

activity. Experimental studies support the role of reactive oxygen species in cancer and dietary antioxidants as well as endogenous antioxidants shows a vital role as cancer preventive agents via neutralization of reactive oxygen species [28, 29]. Another study also showed that plant phenolic compounds including flavonoids are effective antioxidants with reported anti-mutagenic and anti-carcinogenic effects [30, 31]. Dates fruits have high composition of carbohydrates, salts and minerals, dietary fibre, vitamins, fatty acids and amino acid gives a unique value in human nutrition [25]. On the Other side, date pit powders are a source of choice to people preferring a non-caffeinated coffee with coffee-related flavor [32]. Date palms play a significant role in neutralization of free radical and finally suppress the various types of diseases development and progression. Earlier investigation found that palm date has a potent ability to suppress free radicals [33, 34].

A recent report showed that aqueous extracts of dates have antioxidant, antimicrobial and anti-mutagenic activity [10, 35-37]. An important finding showed that dates constitutes good source of antioxidant [38] and another study has shown that dates have the highest concen-

tration of polyphenols among the dried fruits [39]. The antioxidant activity of phenolic compounds is a result of their redox properties, which can play an important role in absorbing and neutralizing free radicals [40]. Phytochemical show significant antioxidant capacities and antioxidant capability in lowering the prevalence and lower mortality rates of cancer [41].

Another finding in the support of dates as antioxidant reported that dates are a good source of antioxidants due to the carotenoids and phenolics with quantity 3942 mg/100 g and antioxidants constituents 80400 $\mu\text{mol}/100\text{ g}$ [13]. A recent study examined the antioxidant activities in different type of dates such as Fard, Khasab and Khalas and showed that Khalas is measured to be best quality, had higher antioxidant activity, total carotenoids, and bound phenolic acids than other types of dates [33].

An important study based on special type of dates; has shown significant antioxidant activity and caused a significant reversal of the lead-induced changes in the oxidative biomarkers in serum and also Ajwa dated extract has a tissue protective effect via a free radical scavenging and antioxidant properties [42].

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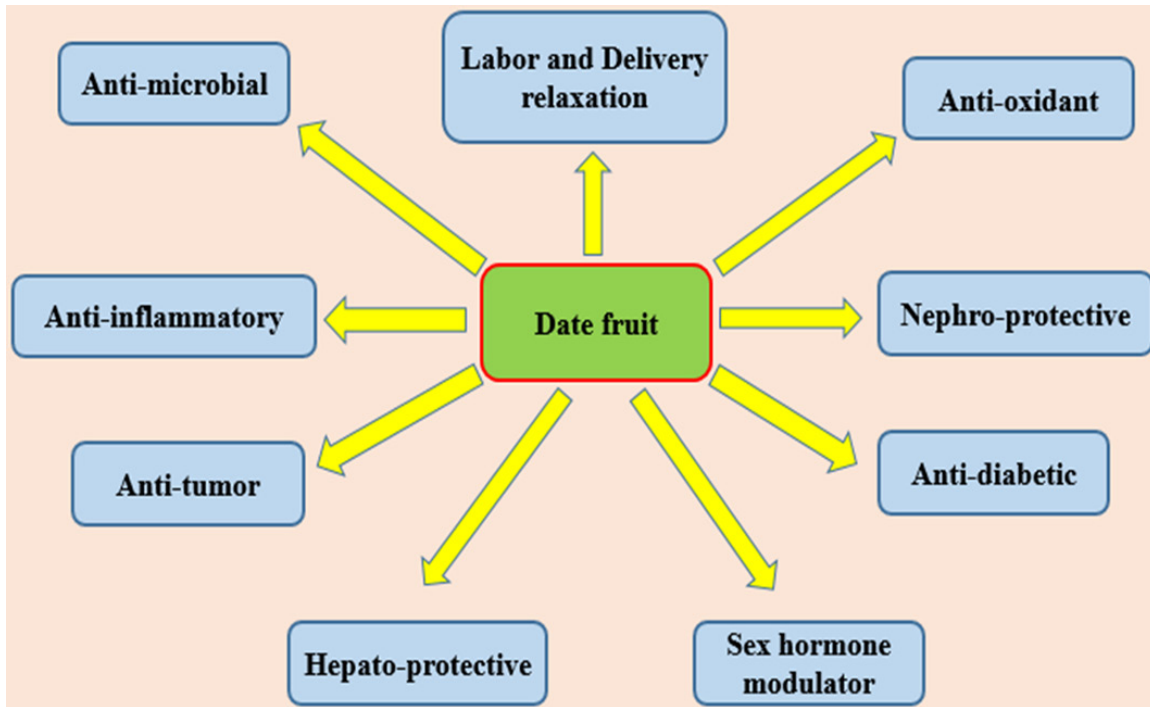


Figure 3. Pharmacological activities of dates fruits in diseases control.

Another study has shown that polyphenol concentration in different types of dates and total polyphenols in Ajwa dates water extract (455.88 mg/100 g) was the highest as compared to other varieties such as sukkari (377.66 mg/100 g) and khalas (238.54 mg/100 g) and same pattern were noticed in alcohol extract as high polyphenol in Ajwa dates [43].

Anti-tumour effect

Cancer is a multi-factorial diseases and economical burden worldwide. The alteration in normal mechanism of action of genes is a major culprit in the development and progression of cancer [44-47]. There are numerous chemopreventive agents used to cure various types of diseases including cancer. But these drugs show an adverse side effect through alteration in gene normal action. The current treatment based on radiotherapy and chemotherapy is effective but also shows adverse consequences. Constituents of medicinal plants such as flavanoid and phenol play a significant role in cancer control through the regulation of genetic pathways without any side effect [48-50]. The dates fruits constituents has shown the antitumour activity but its exact mechanism of action of dates and their con-

stituents in the prevention of tumour is not known exactly.

Earlier studies reported that beta D-glucan from dates has shown antitumour activity [51]. Study on animal model showed that glucans, constituents of date fruits exhibited a dose dependant anticancer activity with an optimum activity at a dose of 1 mg/kg in tumour [52]. Another important study has also shown that anti-tumor activity for date glucan [53].

Study on Ajwa showed a protective effect and ameliorated the lesions of Ochratoxin nephro toxicity which might lead to kidney failure [54]. An experimental study reported that severity of the histological lesions as well as the serum levels of total bilirubin and ALT enzyme activity were greatly reduced in rats pre-treated with Ajwa dates extract before ochratoxin A(OTA), compared with OTA-treated rats [14].

The date's constituents show a vital effect in the inhibition of phase I enzymes such as CYP450 and enhance the activity of phase II enzyme. An experimental study showed that the antigenotoxicity of date pits is due to its ability to scavenge the alkyl radical or inhibit the aromatase activity of cytochrome P-450 or

blocking the reaction between methane diazonium ion and DNA [55].

Anti-microbial effect

The incidence of drug resistance against microbial pathogens is increasing significantly worldwide. Bacterial resistance against antimicrobial agents is one of the major difficulties in treatment.

The present mode of treatment of bacterial infection/disease is based on antibiotics, which is expensive and also causes adverse side effects. Natural products and their constituents is good approach in the control of infection as they are inexpensive, effective without side effects. *Phoenix dactylifera* and its constituents play a significant effect in the prevention or treatment of bacterial diseases.

An important study showed that the effect of methanol and acetone extracts of leaves and pits *Phoenix dactylifera* inhibited the growth of *F. oxysporum*, *Fusarium sp.*, *F. solani*, *A. alternata*, *Alternaria sp* [56].

Some other important finding showed that methanol and acetone extracts of the *P. dactylifera* pits reasonably inhibited the growth of Gram positive and Gram negative bacteria [57, 58]. Another recent study in the support of *P. dactylifera* effect as antimicrobial on *Klebsiella pneumonia* and *Escherichia coli* and also showed a role in reducing the side effects due to the use of drugs as methylprednisolone [59].

Another study also showed that *Phoenix dactylifera* extract has antibacterial effect against *E. fecalis*, indicating that this extract can be used for treating enteric diseases [59].

Anti-diabetic effect

Diabetes mellitus is one of the common metabolic disorders, and 2.8% of the population suffers from this disease throughout the world [60]. The current mode of treatment of diabetes and its complication Diabetic Retinopathy based on synthetic medicines/oral hypoglycemic agents is effective but also shows adverse effect and alter the metabolic and genetic pathways. Natural products and their constituents is a good approach in the control of diabetes as they are less toxic and free from side effects than synthetic ones. Plants and their constitu-

ents play a significant role in the management of diabetes and its complication including Diabetic Retinopathy via modulation of metabolic and molecular pathways [61, 62]. Plants also show significant effects to manage the function of pancreatic tissues via an increase in insulin production and inhibit the intestinal absorption of glucose [63]. The exact mode of action of dates in the control of diabetes is not fully understood but it might be due to increases the output of insulin and inhibit absorption of glucose. Various active compounds present in *Phoenix Dactylifera* Extract (PDE) such as flavonoids, steroids, phenol and saponines, which play a role as anti-diabetic and these compounds from other plants, also scavenge the free radical liberated by alloxan in diabetic rat. A recent study on flavonoid compounds from date fruits epicarp showed that this compound play a significant role in the improvement of the different biochemical results in diabetic rats [64].

An experimental study showed that oral administration of PDE and its fractions improved body weight via decreased water intake and caused hypoglycaemia in alloxan-induced diabetic rats [65]. Another important study showed that consumption of dates may be of benefit in glycaemic and lipid control of diabetic patients [66].

Anti-inflammatory effect

Inflammation is one of the important physiologic defence mechanisms against various factors such as infection, burn, toxic chemicals, allergens and other stimuli [67]. The unbalance inflammatory process shows a vital role in development and progression of various diseases. Transcription factors LOX and NF- κ B play a significant role in the inflammation, cancer, diabetes and other diseases. Regulation of transcription factors is important and critical step in the prevention of disease. Inhibitors of transcription factors showed a vital role in the prevention of action of transcription factors. Unfortunately, presently used inhibitors shows an adverse effect and are also expensive. Natural products are a good remedy in the suppression of NF- κ B and acts as anti-inflammatory agents. Earlier studies have shown that constituents of plants such as phenolics and flavonoids act as excellent anti-inflammatory agents [68]. Date fruits play a significant role as anti-inflammatory and recent report on the Ajwa dates showed that ethyl acetate, metha-

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nolic, and water extracts of Ajwa dates inhibit the lipid peroxidation cyclooxygenase enzymes COX-1 and COX2 [69]. A study in animal model showed that *Phoenix dactylifera* pollen has potential protective effect via modulation of cytokines expressions [70]. Another important finding in the support of dates fruits reported that the methanolic extract of edible portion of the fruit showed a vital role in reducing foot swelling and plasma fibrinogen [71]. A study in the support of dates as anti-inflammatory showed that the leaves of dates can be considered as a good source of natural antioxidant and anti-inflammation drugs [72].

Nephro-protective effect

An important report of extracts of the flesh and pits of *Phoenix dactylifera* in gentamicin treated nephrotoxicity rat model showed significantly reduced the increase in plasma creatinine and urea concentrations induced and ameliorated the proximal tubular damage [73].

Delivery and labor relaxation

Plants and their constituents play a significant role as pain-relievers and also cause relaxation in childbirth. Several medicinal plants show an effect in the stimulation of all phase of labor. A study in the support of medicinal plants role in labor showed that several plants have contractile properties on uterine myometrial cells [74]. Another study also showed that raspberry leaf play role in labor relaxation [75]. An important and first study on the dates role in labor has shown that dates showed a significant effect as higher mean cervical dilatation, reduced the induction and labor rise in women who ate dates fruits as compared to non-date fruit consumers [76].

Effect of dates on infertility

Dates fruits have unique constituents and each constituent play a role in the management of diseases and fertility. Dates; a fruits with good taste and gives a hope for the person who has infertility or problem in reproductive system. Numerous studies or reports are in the support of dates in solving the problem of infertility. Earlier investigators have shown that micro elements from date palm pollen extract (DPP) such as estrone, sterols, and other agents that influence male fertility [77, 78]. A study based on animal model showed that DPP contains cho-

lesterol, rutin, carotenoids, as estrone which is recognized to explain gonadotrophin action in the rat [79]. An important finding showed that DPP concentrations up to 120 mg/kg showed the best effects on sperm parameters [80] and DPP suspension increases the plasma levels of estradiol and testosterone [80].

Conclusion

The current treatment approach for the diseases prevention such as cancer and diabetes based on synthetic drugs is expensive, shows unwanted adverse effects; alter the genetic and metabolic pathways. Thus, a safe, effective, affordable approach is needed to control the disease development and progression. Dates and their constituents are a good remedy as they are inexpensive, effective and easy to access. Earlier finding showed that therapeutic effect of dates in the diseases management via anti-oxidant, anti-inflammatory and anti-tumour properties. Dates fruits in the control of disease create optimism towards the novel therapeutic strategy. Keeping all information in hand as anti-oxidant, anti-inflammatory and anti-tumour, further research based on clinical trial and animal model is required to authenticate the exact mechanism the of action of dates and their constituents in diseases prevention.

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References

- [1] Rahmani A, Alzohairy M, Mandal AK, Rizvi MA. Expressional Evaluation of Androgen Receptor in Transitional Cell Carcinoma of Urinary Bladder Patients. *Brt J Med Medical Res* 2011; 1: 233-238.
- [2] Rahmani A, Alzohairy M, Babiker AY, Rizvi MA and Elkarimahmad GH. Clinicopathological significance of PTEN and bcl2 expressions in oral squamous cell carcinoma. *Int J Clin Exp Pathol* 2012; 5: 965-971.
- [3] Rizvi MMA, Alam MS, Mehdi SJ, Ali A, Batra S. Allelic loss of 10q23. 3, the PTEN gene locus in cervical carcinoma from Northern Indian population. *Pathol Oncol Res* 2012; 18: 309-313.
- [4] Alyasiri NS, Mehdi SJ, Alam MS, Ali A, Mandal AK, Gupta S, Singh I and Rizvi MMA. PTEN mediated AKT activation contributes to the reduced apoptosis among Indian oral squamous

Dates fruits in the management of diseases

- cell carcinoma patients. *J Cancer Res Clin Oncol* 2011; 138: 103-109.
- [5] Teng J, Wang ZY, Jarrad DF and Bjorling DE. Roles of estrogen receptor a and b in modulating urothelial cell proliferation. *Endorenal Cancer* 2008; 15: 351-364.
- [6] Shen SS, Smith CL, Hsieh JT, Yu J, Kim IY, Jian W, Sonpavde G, Ayala GE, Younes M and Lerner SP. Expression of estrogen receptors-a and -b in bladder cancer cell lines and human bladder tumor tissue. *Cancer* 2006; 106: 2610-2616.
- [7] Zhuang YH, Blauer M, Tammela T and Tuohimaa P. Immunodetection of androgen receptor in human urinary bladder cancer. *Histopath* 1997; 30: 556-562.
- [8] Dar-ul-Iman Healing, 2000. Food of the Prophet (Sallallahu Alayhi Wasallam). Available at: http://chishti.org/foods_of_the_prophet.
- [9] Marwat SK, Khan MA, Rehman F and Bhatti IU. Aromatic plant species mentioned in the Holy Qura'n and Ahadith and their ethnomedicinal importance. *Pak J Nut* 2009; 8: 1472-1479.
- [10] 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.
- [11] Gu L, Kelm MA, Hammerstone JF, Beecher G, Holden J, Haytowitz D and Prior RL. Screening of foods containing proanthocyanidins and their structural characterization using LCMS/MS and thiolytic degradation. *J Agric Food Chem* 2003; 51: 7513-7521.
- [12] Hong YJ, Tomas-Barberan FA, Kader AA, Mitchell AE. The flavonoid glycosides and procyanidin composition of Deglet Noor dates (*Phoenix dactylifera*). *J Agric Food Chem* 2006; 54: 2405-2411.
- [13] Bilgari F, Alkarkhi AFM, Easa AM. Antioxidant activity and phenolic content of various date palm (*Phoenix dactylifera*) fruits from Iran. *Food Chem* 2008; 107: 1636-1641.
- [14] Abdu SB. The protective role of Ajwa date against the hepatotoxicity induced by Ochratoxin A. *Egypt J Nat Tox* 2011; 8: 1-15.
- [15] Zohary D and Hopf M. Date palm *Phoenix dactylifera*. Domestication of Plants in the Old World. 2nd edition. Oxford: Clarendon; 1993.
- [16] δάκτυλος. Liddell, Henry George; Scott, Robert; *A Greek-English Lexicon* at the Perseus Project.
- [17] fëro. Charlton T. Lewis and Charles Short. *A Latin Dictionary* on Perseus Project.
- [18] Sulieman A, Elhafise I and Abdelrahim A. Comparative study on five Sudanese date (*Phoenix dactylifera* L.) fruit cultivars. *Food Nut Sci* 2012; 3: 1245-1251.
- [19] Amer WM. Taxonomic and Documentary Study of Food Plants in Ancient Egypt. Ph.D. Thesis, Cairo University, Giza, 1994.
- [20] Chao CT and Krueger RR. The date palm (*Phoenix dactylifera* L.): Overview of biology, uses, and cultivation. *Hortsci* 2007; 42: 1077-1082.
- [21] Wrigley G. Date palm. In: Smartt J and Simmonds NW, editors. Evolution of crop plants. 2nd edition. Essex, UK: Longman Group 1995; pp: 399-403.
- [22] <http://www.uaeinteract.com/ancient/ar04.html>.
- [23] Dowson VHW. Date production and protection. Plant Production and Protection Paper 35. Rome, Italy: United Nations Food and Agric. Org., 1982.
- [24] Kenoyer JM, Heuston KB. The Ancient South Asian World. The World in Ancient Times. Oxford University Press 2005. ISBN 978-0-19-522243-2. Retrieved 30 July 2013.
- [25] Al-Shahib W and Marshall RJ. The fruit of the date palm: Its possible use as the best food for the future. *Int J Food Sci Nutr* 2003; 54: 247-259.
- [26] Zaid A and De Wet PF. Origin, geographical distribution and nutritional values of date palm. Date Production Support Programme, FAO.
- [27] Al-Bukhari MI. The collection of authentic sayings of Prophet Mohammad (peace be upon him), division 71 on medicine. In: Al-Bukhari S, editor. 2nd edition. Hilal Yayinlari, Ankara, Turkey, 1976.
- [28] Borek C. Antioxidants and cancer. *Sci Med (Phila)* 1997; 4: 51-62.
- [29] Borek C, Ong A, Mason H, Donahue L and Biaglow JE. Selenium and vitamin E inhibit radiogenic and chemically induced transformation in vitro via different mechanisms. *Proc Nat Acad Sci U S A* 1986; 83: 1490-1494.
- [30] Middleton E Jr, Kandaswami C. The impact of plant flavonoids on mammalian biology: implications for immunity, inflammation and cancer. In: Harborne JB, editor. The Flavonoids. London: Chapman & Hall 1994; pp: 619-652.
- [31] Rice-Evans CA, Miller NJ and Paganga G. Antioxidant properties of phenolic compounds. *Trends Plant Sci* 1997; 2: 152-159.
- [32] Baliga MS, Baligab BRV, Kandathilc SM, Bhatd HP, Vayalile PK. A review of the chemistry and pharmacology of the date fruits (*Phoenix dactylifera* L.). *Food Res Inter* 2011; 44: 1812-22.
- [33] 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.
- [34] Guo C, Yang J, Wei J, Li Y, Xu J and Jiang Y. Antioxidant activities of peel, pulp and seed fractions of common fruits as determined by FRAP assay. *Nut Res* 2003; 23: 1719-1726.

Dates fruits in the management of diseases

- [35] Saddiq AA and Bawazir AE. Antimicrobial activity of date palm (*Phoenix dactylifera*) pits extracts and its role in reducing the side effect of methyl prednisolone on some neurotransmitter content in the brain, hormone testosterone in adulthood. *Acta Hort (ISHS)* 2010; 882: 665-690.
- [36] Vayalil PK. Antioxidant and antimutagenic properties of aqueous extract of date fruit (*Phoenix dactylifera* L. Arecaceae). *J Agric Food Chem* 2002; 50: 610-617.
- [37] Mohamed DA and Al-Okbi S. In vitro evaluation of antioxidant activity of different extracts of *Phoenix dactylifera* L. fruits as functional foods. *Dtsch Lebensm Rundsch* 2005; 101: 305-308.
- [38] Zineb G, Boukouada M, Djeridane A, Saidi M, Yousfi M. Screening of antioxidant activity and phenolic compounds of various date palm (*Phoenix dactylifera*) fruits from Algeria Mediterranean. *Journal of Nutrition and Metabolism* 2012; 5: 119-126.
- [39] Vinson JA, Zubic L, Bose P, Samman N and Proch J. Dried Fruits: Excellent in Vitro and in Vivo Antioxidants. *J Am Coll Nutr* 2005; 24: 44-50.
- [40] In: Garcia VV and Mendoza EM, editors. *Post-harvest Biochemistry of Plant Food-Materials in the Tropics*. Tokyo, Japan: Japan Sci Soc Press 1994.
- [41] Velioglu YS, Mazza G, Gao L and Oomah BD. Antioxidant activity and total phenolics in selected fruits, vegetables, and grain products. *J Agric Food Chem* 1998; 46: 4113-4117.
- [42] Ragab AR, Elkablawy MA, Sheik BY and Baraka HN. Antioxidant and tissue-protective studies on Ajwa extract: dates from Al Madinah Al-Monwarah, Saudia Arabia. *J Environ Anal Toxicol* 2013; 3: 2161-0525.
- [43] Saleh EA, Tawfik MS and Abu-Tarboush HM. Phenolic contents and antioxidant activity of various date palm (*Phoenix dactylifera* L.) Fruits from Saudi Arabia. *Food Nutr Sci* 2011; 2: 1134-1141.
- [44] Rahmani A, Alzohairy M, Khadri H, Mandal AK and Rizvi MA. Expressional evaluation of vascular endothelial growth factor (VEGF) protein in urinary bladder carcinoma patients exposed to cigarette smoke. *Int J Clin Exp Pathol* 2012; 5: 195-202.
- [45] Aldebasi YH, Rahmani AH, Khan AA and Aly SM. The effect of vascular endothelial growth factor in the progression of bladder cancer and diabetic retinopathy. *Int J Clin Exp Med* 2013; 6: 239-251.
- [46] Mehdi SJ, Alam MS, Batra S and Rizvi MA. Allelic loss at 6q25-27, the Parkin tumor suppressor gene locus in cervical carcinoma. *Medical Oncol* 2010; 28: 1520-1526.
- [47] Rahmani AH, Alzohairy M, Babiker AAY, Khan AA, Aly SM and Rizvi MA. Implication of androgen receptor in urinary bladder cancer: a critical mini review. *Int J Mol Epidemiol Genet* 2013; 4: 150-155.
- [48] Gali-Muhtasib H, Roessner A and Schneider-Stock R. Thymoquinone: a promising anti-cancer drug from natural sources. *Int J Biochem Cell Biol* 2006; 38: 1249-1253.
- [49] El-Mahdy MA, Zhu Q, Wang QE, Wani G and Wani AA. Thymoquinone induces apoptosis through activation of caspase-8 and mitochondrial events in p53-null myeloblastic leukemia HL-60 cells. *Int J Cancer* 2005; 10: 409-417.
- [50] Khan MA, Chen H, Tania M and Zhang D. Anti-cancer activities of *Nigella Sativa* (Black Cummin). *Afr J Tradit Complement Altern Med* 2011; 8: 226-232.
- [51] Ishurd O, Sun C, Xiao P, Ashour A and Pan Y. A neutral beta-D-glucan from dates of the date palm, *Phoenix dactylifera* L. *Carbohydr Res* 2002; 337: 1325-1328.
- [52] Ishurda O and John FK. The anti-cancer activity of polysaccharide prepared from Libyan dates (*Phoenix dactylifera* L.). *Carbohydr Polymers* 2005; 59: 531-535.
- [53] Ishurd O, Zgheel F, Kermagi A, Flefla M and Elmabruk M. Antitumor activity of beta-D-glucan from Libyan dates. *J Med Food* 2004; 7: 252-255.
- [54] Ali A and Abdu S. Antioxidant protection against pathological mycotoxins alterations on proximal tubules in rat kidney. *Func Foods Heals Dis* 2011; 4: 118-134.
- [55] Diab KAS and Aboul-Ela EI. In vivo comparative studies on antigenotoxicity of date palm (*Phoenix Dactylifera* L.) pits extract against DNA damage induced by N-Nitroso-N-methylurea in mice. *Toxicol Int* 2012; 19: 279-286.
- [56] Bokhari NA and Perveen K. In vitro inhibition potential of *Phoenix dactylifera* L. extracts on the growth of pathogenic fungi. *J Medicin Plants Res* 2012; 6: 1083-1088.
- [57] Jassim SAA and Naji MA. In vitro evaluation of the antiviral activity of an extract of date palm (*Phoenix dactylifera* L.) pits on a *Pseudomonas* phage 2007. *Evid Based Complement Alternat Med* 2010; 7: 57-62.
- [58] Ammar NM, Lamia T, Abou E, Nabil HS, Lalita MC and Tom JM. Flavonoid constituents and antimicrobial activity of date (*Phoenix dactylifera* L.) seeds growing in Egypt. In: *Proceedings of 4th conference on research and development of pharmaceutical industries (Current Challenges)*. *Med Arom PI Sci Biotech* 2009; 3: 1-5.
- [59] Aamir J, Kumari A, Khan MN and Medam SK. Evaluation of the combinational antimicrobial effect of *annona squamosa* and *phoenix dac-*

Dates fruits in the management of diseases

- tylifera* seeds methanolic extract on standard microbial strains. *Int Res J Biol Sci* 2013; 2: 68-73.
- [60] Fatima A, Agrawal P and Singh PP. Herbal option for diabetes: an overview. *Asian Pac J Trop Dis* 2012; 536-544.
- [61] Aldebasi YH, Aly SM, Rahmani AH. Therapeutic implications of curcumin in the prevention of diabetic retinopathy via modulation of anti-oxidant activity and genetic pathways. *Int J Physiol Pathophysiol Pharmacol* 2013; 5: 194-202.
- [62] Gupta SK, Kumar B, Nag TC, Agrawal SS, Agrawal R, Agrawal P, Saxena R and Srivastava S. Curcumin prevents experimental diabetic retinopathy in rats through its hypoglycemic, antioxidant, and anti-inflammatory mechanisms. *J Ocul Pharmacol Ther* 2011; 27: 123-130.
- [63] Malviya N, Jain S and Malviya S. Antidiabetic potential of medicinal plants. *Acta Poloniae Pharmaceut Drug Res* 2010; 67: 113-118.
- [64] Michael HN, Salib JY and Eskander EF. 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.
- [65] Mard SA, Jalalvand K, Jafarnejad M, Balochi H and Naseri MKG. Evaluation of the antidiabetic and antilipaemic activities of the hydroalcoholic extract of *Phoenix dactylifera* palm leaves and its fractions in alloxan-Induced diabetic rats. *Malays J Med Sci* 2010; 17: 4-13.
- [66] Miller CJ, Dunn EV and Hashim IB. The glycaemic index of dates and date/yoghurt mixed meals. Are dates 'the candy that grows on trees'? *Eur J Clin Nut* 2003; 57: 427-430.
- [67] Sharma GN, Dubey SK, Sati N and Sanadya J. Anti-inflammatory activity and total flavonoid content of aegle marmelos seeds. *Int J Pharm Sci Drug Res* 2011; 3: 214-218.
- [68] Talhouk R, Karam C, Fostok S, El-Jouni W and Barbour E. Anti-inflammatory bioactivities in plant extracts. *J Med Food* 2007; 10: 1-10.
- [69] Zhang CR, Aldosari SA, Vidyasagar PS, Nair KM and Nair MG. Antioxidant and anti-inflammatory assays confirm bioactive compounds in Ajwa Date fruit. *J Agric Food Chem* 2013; 61: 5834-5840.
- [70] Elberry AA, Mufti ST, Al-Maghrabi JA, Abdel-Sattar EA, Ashour OM, Ghareib SA and Mosli HA. Anti-inflammatory and antiproliferative activities of date palm pollen (*Phoenix dactylifera*) on experimentally-induced atypical prostatic hyperplasia in rats. *J Inflamm (Lond)* 2011; 23: 40.
- [71] Mohamed DA and Al-Okbi SY. 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.
- [72] Eddine LS. Antioxidant, anti-inflammatory and diabetes related enzyme inhibition properties of leaves extract from selected varieties of *Phoenix dactylifera* L. *Innovare J Life Sci* 2013; 1: 14-18.
- [73] Al-Qarawi AA, Abdel-Rahman H, Mousa HM, Ali BH and El-Mougy SA. Nephroprotective action of *Phoenix dactylifera*. in gentamicin-induced nephrotoxicity. *Pharm Biol* 2008; 4: 227-230.
- [74] Attah AF, O'Brien M, Koehbach J, Sonibare MA, Moody JO, Smith TJ and Gruber CW. Uterine contractility of plants used to facilitate childbirth in Nigerian ethnomedicine. *J Ethnopharmacol* 2012; 30: 377-382.
- [75] Simpson M, Parsons M, Greenwood J and Wade K. Raspberry leaf in pregnancy: its safety and efficacy in labor. *J Midwifery Womens Health* 2001; 46: 51-59.
- [76] Al-Kuran O, Al-Mehaisen L, Bawadi H, Beitawi S and Amarin Z. The effect of late pregnancy consumption of date fruit on labour and delivery. *J Obstet Gynaecol* 2011; 31: 29-31.
- [77] Bennet RD, Ko ST and Heftmann E. Isolation of estrone and cholesterol from the date palm *Phoenix dactylifera*. *Phytochem* 1966; 5: 231-235.
- [78] Mahran GH, Abdel-Wahab SM and Attia AM. A phytochemical study of date palm pollen. *Planta Med* 1976; 29: 171-175.
- [79] Dostal LA, Faber CK and Zandee J. Sperm motion parameters in vas deferens and cauda epididymal rat sperm. *Reprod Toxicol* 1996; 10: 231-235.
- [80] Bahmanpour S, Talaei T, Vojdani Z, Panjehshahin MR, Poostpasand A, Zareei S, Ghaemina M. Therapeutic effect of *Phoenix dactylifera* pollen on sperm parameters and reproductive system of adult male rats. *Iran J Med Sci* 2006; 31: 8-12.