



## Review Article

**Selected Pharmaceutical Values of Date Fruit**

M ABD ELGADIR

Department of Food Science &amp; Human Nutrition, College of Agriculture and Veterinary Medicine, Qassim University, 51452 Buraydah, Saudi Arabia.

| ARTICLE DETAILS  | ABSTRACT   |
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| <p><i>Article history:</i><br/>Received on 15 February 2021<br/>Modified on 8 March 2021<br/>Accepted on 13 March 2021</p> <hr/> <p><i>Keywords:</i><br/>Date Fruit,<br/>Pharmaceutical Values,<br/>Antioxidant Activity,<br/>Anticancer Function.</p> | <p>The date fruits are rich sources of protein, vitamins, alkaloids, carbohydrates, carotenoids, fatty acid (stearic acid, lauric, linoleic, and palmitic), dietary fibers, tannins, polyphenolic compounds, and flavonoids. The fruits also contain different types of nutrients such as calcium, phosphorus, potassium, and magnesium. The date fruits are also utilized in different pharmaceutical and medicinal aspects. From the pharmaceutical overview, the date fruits contain many pharmaceutical compounds such as anthocyanins, sterols, procyanidins and flavonoids, and phenolic carotenoids. These compounds possess multiple beneficial pharmaceutical effects. Preclinical investigations have shown that the date fruits have antioxidant, free radical scavenging, antimicrobial, anti-mutagenic, and anti-inflammatory, hepatoprotective, gastroprotective, nephroprotective, anticancer, and immunostimulant activities. There is a lack of literature about the pharmaceutical benefits of date fruit particularly in the Qassim Region, Saudi Arabia where the mass of different varieties of date fruits are produced and available in the markets. Therefore, this article highlights selected pharmaceutical properties of the fruits.</p> |

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**INTRODUCTION**

Dates fruits (*Phoenix dactylifera* L.) are considered as an important food with high nutritional values due to their phytochemical components [1]. They have great importance in human nutrition due to their high and rich content of nutrients including dietary fibre, salts and minerals, carbohydrates, vitamins, protein and amino acids [2]. The nutritional value of dates fruits is due to their high sugar content (50–60%), calcium, potassium (2.5 times more as compared to bananas), iron, B1 & B2 vitamins, niacin and magnesium, pectin (0.5–3.9%), moisture (10% to 22%) and unsaturated fatty acids (linoleic and linolenic, palmitoleic, and 41.1% to 58.8% oleic acid in the seed [3]. Date fruits are also rich in phytochemicals contents which include carotenoids, tannins, polyphenols, flavonoids, sterols, phenolic acids and lignans [4]. Many researches considered the date fruits as food of interest due to their nutritional values [5–9] as well as their pharmaceutical activities such as anti-inflammatory, antioxidant and anti-tumor activities [10] and antibacterial activity [11–17].

**Nutritional and General Pharmaceutical Values of Date Fruit**

The date fruits contain high percentages of carbohydrates as total sugars which is considered as the main component of the fruits (Table 1). They are mainly glucose, fructose, maltose, mannose, and small amounts of polysaccharides such as cellulose, starch and non-reducing sugars [18]. The date fruit contains some minerals such as cobalt, boron, copper, fluorine, calcium, magnesium, iron, manganese, sodium, zinc, potassium and phosphorus. On the other hand, lead, cadmium, aluminum, chloride and sulphur are present in the date seed in various proportions. There are about 23 types of amino acids in several date varieties. Dates contain six vitamins including B1 thiamine, vitamins B2 riboflavin, vitamin C, vitamin A and nicotinic acid (niacin). The seeds contain 7.7/9.7%, whereas the flesh contains between 0.2 to 0.5% saponifiable oil [19]. The carbohydrates in date fruits are the predominant components followed by moisture lipids, proteins, and ash [20]. Date fruits are well known as rich sources of dietary fiber, which is defined as the lignin and polysaccharides components. The total dietary fiber in dates ranges from 6.5 to 11.5%

**\*Author for Correspondence:**

Email: m.saeed@qu.edu.sa

depending on the variety and climate [21]. Soluble and insoluble dietary fiber types amount 6–16% and 84–94%, respectively based on total dietary fiber in date fruits [21]. Soluble and insoluble dietary fibers could help in the formation of a viscous gel in the intestine which slows the intestinal absorption of anti-nutritional factors like cholesterol, fermentation and generation of short chain fatty acids in the intestine [22]. However, dates fruits dietary fiber contains uronic acids (10.7–16.7%), neutral sugars (15.6–25.7%), klason lignin (33.3–50.4%) and cellulose (17.0–24.8%) [23].

In the folk medicine, date fruits have many pharmaceutical properties when consumed alone or in combination with other herbs for treatment of different types of diseases [24–28].

Date fruits could help in protecting teeth against decay because they contain elemental fluorine. Selenium elements in dates are also believed to help in improving immune function and cancer prevention [29]. Phytochemical studies have approved that the fruits contain flavonoids, anthocyanins, phenolics, procyanidins, carotenoids and sterols which are recognized to possess multiple beneficial effects such as anti-inflammatory, gastro protective, anti-mutagenic, antimicrobial, antioxidant, hepatoprotective, anticancer and free radical scavenging [30–34]. The date fruits have been used in many traditional medicine systems such as treatment of diabetes and hypertension [35–37]. It was also utilized as an ingredient in many aphrodisiac supplements [38].

**Table 1:** Nutritional values and recommended dietary allowance of date fruit (*Phoenix dactylifera* Linn – medjool variety) as per 100 gm (USDA, 2020) [39]

| Principle        | Nutrient value | Recommended dietary allowance (RDA) |
|------------------|----------------|-------------------------------------|
| Carbohydrate     | 74.97 g        | 58 %                                |
| Proteins         | 1.81 g         | 3 %                                 |
| Dietary fiber    | 6.7 gm         | 18 %                                |
| Total fat        | 0.15 g         | < 1 %                               |
| Energy           | 277 Kcal       | 14%                                 |
| Cholesterol      | 0 mg           | 0%                                  |
| Folate           | 15 µg          | 4 %                                 |
| Pantothenic acid | 0.805 mg       | 16 %                                |
| Niacin           | 1.610 mg       | 10 %                                |
| Riboflavin       | 0.060 mg       | 4.5 %                               |
| Pyridoxine       | 0.249 mg       | 19 %                                |
| Thiamin          | 0.050 mg       | 4 %                                 |
| Vitamin A        | 149 IU         | 5 %                                 |
| Vitamin C        | 0 mg           | 0 %                                 |
| Vitamin K        | 2.7µg          | 2 %                                 |
| Potassium        | 696 mg         | 16 %                                |
| Calcium          | 64 mg          | 6.5 %                               |
| Iron             | 0.90 mg        | 11 %                                |
| Magnesium        | 54 mg          | 13 %                                |
| Zinc             | 0.44 mg        | 4 %                                 |
| Phosphorus       | 62 mg          | 9 %                                 |
| Manganese        | 0.296 mg       | 13 %                                |

Several phytochemical studies have shown that date fruits have many phytochemical compounds such as anthocyanins, flavonoids, sterols, phenolics, procyanidins and carotenoids which, very well recognized to have several beneficial effects.

Earlier, several investigations on pre-clinical studies have suggested that date fruits have different pharmacological effects such as anti-mutagenic [40–44], nephroprotective [45], anticancer [25], anti-oxidant [37], anti-inflammatory [46, 47], anti-microbial [48, 49] and gastro protective [6].

### Antioxidant Activities

The date fruits have excellent antioxidant activity due to the presence of carotenoids, vitamins contents, melatonin and phenolics [2, 32, 39]. The main antioxidants present in date fruits are carotenoids and polyphenols [50]. About 52 phenolic compounds have been identified in the date fruit mainly including glycosides of quercetin, apigenin, flavonoid, chrysoeriol, isorhamnetin, luteolin, 3-methyl-isorhamnetin, kaempferol, malonyl derivatives and sulfates [51]. Six commercially used date fruit varieties namely Deglet Nour cultivated in California, Deglet Nour imported from Algeria, Deglet Nour imported from Tunisia, Khudri imported from Saudi Arabia, Shahia imported from Tunisia and, Barni imported from Saudi [52] were investigated for their antioxidants activity and reported considerable antioxidant. The lowest content obtained was found in variety Shahia whereas the highest value of total phenolic content was observed in Barni one. Hamad et al. [38] investigated aqueous extract of date fruit *in vitro* and revealed that a concentration of 100 µg/ml was effective in scavenging free radicals which was considered as a good evidence of having antioxidant activity. The administration of p-coumaric acid orally presents in the constituent of date fruit revealed increases the expression of antioxidant in cardiac tissue of rats [53-55]. An *in vivo* antioxidant activity of date fruit extracts observed at the concentration of 1000 mg/kg body weight [53]. The Phenolic compounds, flavonoids and anthocyanins are responsible for the antioxidant activity in the date fruits [56, 57]. An aqueous extract of date fruit at a concentration of 0.8 mg/mL was proven to scavenge 100% of superoxide radicals at 1.5 mg/mL and 50% of superoxide radicals formed by photoreduction of riboflavin [53]. A concentration of 2.2 mg/mL inhibited 50% of hydroxyl radical formation while a concentration of 4.0 mg/mL inhibited 100% of hydroxyl radical formation. A reduction in protein oxidation by 50% was observed when a concentration of 2.3 mg/mL was utilized. It was also reported that lipid peroxidation was inhibited by 100% at 2 mg/mL and by 50% at 1 mg/mL [40].

### Anticancer Function

Date fruits shows great anticancer activity [58-61]. The fruits showed anticancer activity against the variety of cells due to the presence of phenolic compounds like caffeic acid and rutin. An acetate fraction of date fruit (ajwa) in concentrations of 0.2-0.6 mg/ml revealed a strong anticancer

activity against prostate cancer cells [33]. When prostate cancer cells (PC3 cell line) was treated with ethyl acetate fractions of date fruit (Ajwa date), strong inhibitory increased oxidative stress and loss of mitochondrial membrane potential were observed in the extract treated cells which, suggested mitochondrial involvement in apoptosis [33]. Date fruit extracts (Khalas date fruit) had significant effect in reducing cell pancreatic stellate cells activation and fibrotic protein formation as judged by the lowered cellular proliferation [4]. There are several effective mechanisms by which this effect may have been proven. One of them is via potential reducing of oxidative stress within the cells due to high content of antioxidants such as flavonoids and polyphenols [4, 8] because fibrogenesis and activation process of pancreatic stellate cells is always associated with reactive oxygen species (ROS) and production of free radicals [62]. Moreover, Date fruit extract reported to inhibit intestinal microbiota growth and act as colon cancer cell antiproliferative agents which suggested that consumption of date palm fruit regularly may reduce colon cancer risk [63].

### Anti-bacterial and Anti-fungal Activity

Several studies have been reported in bacterial growth of date fruits (Sukari variety) [64]. Perveen and Bokahri [65] studied the antibacterial activity of extracts from three varieties of dates namely Bharh, Rothana and Sukri (crude extracts) and revealed that the extracts were more effective against gram-positive bacteria as compared to gram-negative bacteria. It is well documented that dates fruits are recognized for a good amount of alkaloids, phenolic compounds and flavonoids [66, 67]. These compounds inhibit the bacterial growth and cause damage to bacterial cell membranes either functional or structural [68]. Farhana et al. [16] have observed that methanolic extract of date's fruits was more effective in inhibiting the bacterial growth compared with other solvents extracts. In other studies methanolic and aqueous extracts of Ajwa date fruit were investigated in concentrations of 100 and 200 mg/mL for their antibacterial activities against the gram-negative bacterial using well-diffusion assay method [17]. The extract in the concentrations of 100 mg/mL of the fruit did not exhibit any antibacterial activities. It is revealed that the concentration of 200 mg/mL of methanolic extract of Ajwa date could inhibit bacterial growth. The inhibition average zones ranged between 15 mm to 34 mm for methanolic extract compared to the aqueous

extract which resulted in average zones of inhibition between 13 mm to 17 mm. These results approved that Ajwa date fruits extractions (methanolic and aqueous) could potentially suppress the bacterial growth. Moreover, the extract of date fruit showed antifungal activity at concentrations of 5–20% w/v caused weakening, distortion as well as eventual cell death of *Candida albicans* [47, 69].

### Antidiabetic Activity

Date fruits possess anti-diabetic effect, low glycemic index, and antioxidant properties. Date fruits and their paste, jelly and syrup products could add pharmaceutical value to many types of foods as antidiabetic [70]. The extract of date seed showed excellent positive effect on diabetic induced animals in concentration of 10.0 ml [71]. These effects are due to the presence of phenol, flavonoids, saponins and steroids. Date extract however was almost costless and easily administered by oral route as compared to insulin in addition it was reported as safe on the kidney and liver of animals [71]. An investigation studies on the effect of Aseel date fruit variety as an antidiabetic in diabetic induced animals revealed that it possessed anti hyperglycemic activity because of its low glycemic index, high fiber, and phytochemicals, which makes it an effective medicinal food that significantly lowering glucose concentration effects. However

data collected during study needs to be substantiated through preclinical studies on large numbers of animals as well as clinical studies.

### Prevention of Alzheimer and Stroke Diseases

Alzheimer's disease is considered as one of the most leading neurodegenerative diseases which affect elderly persons. According to the World Alzheimer Report in 2015, there are an estimated 46 million persons worldwide living with dementia with expected global dementia costs of US\$ 818 billion [72]. Different doses of date fruit extract at concentrations of 100, 200 and 400 mg/kg revealed significant in preventing the chemically induced memory deficits in mice [73]. This could help in exploring the potential of the date fruits in controlling Alzheimer's disease patients. Stroke which is known as a cerebrovascular disease leading to damage or death of brain cells due to the cerebral blood flow reduction. The interruption of the blood supply to a part of the brain occurs embolus occlusion or by hemorrhage or by thrombus. It is revealed that feeding rats with the aqueous extract of Sukari dates (200 – 800 mg/kg) could offer potential benefits in the management of stroke because of its effects against ischemia-reperfusion induced injury in rats [74].

**Table 2:** Selected pharmaceutical activities of date fruit

| Functional property              | Observation   | References |
|----------------------------------|---|------------|
| Anticancer                       | Significant effect in reducing pancreatic stellate cells activation was observed  | [1]        |
| Antiviral activity               | Prevent lytic activity of Pseudomonas phage ATCC 14209-B1 on Pseudomonas aeruginosa   | [47]       |
| Anticancer activity              | Regression of Sarcoma-180 tumour in mice  | [25]       |
| Antioxidant activity             | Scavenges free radical, inhibit iron-induced lipid peroxidation and protein oxidation   | [75]       |
| Anti-inflammatory activity       | Increase plasma antioxidant (Vitamin C, E, A, $\beta$ carotene) levels and decrease lipid peroxides. Reduce swelling, ESR and plasma fibrinogen | [76]       |
| Action on gastrointestinal tract | Increase gastrointestinal transit time, reduces ethanolinduced gastric ulceration   | [77]       |
| Antihyperlipidemic activity      | Reduce plasma triglycerides, total and LDL cholesterol  | [43]       |
| Antifungal activity              | Antifungal activity against <i>Candida albicans</i> and <i>C. krusei</i>  | [69]       |
| Gonadotropic activity            | Increases testosterone, oestrogen sperm count and spermatogenesis   | [78]       |

### CONCLUSION

This article summarizes the potential nutritional and pharmaceutical values of date fruits which could enhance the knowledge for utilizing these fruits in daily diets because of their great contribution in improving our health.

### REFERENCES

- [1] Al Alawi R., Alhamdani M. S., Hoheisel J. D., Baqi Y. Antifibrotic and tumor microenvironment modulating effect of date palm fruit (*Phoenix dactylifera* L.) extracts in pancreatic cancer. *Biomedicine & Pharmacotherapy*. 2020; 121: 109522.

- [2] Chandrasekaran M., Ali H. B. Valorization of Date palm (*Phoenix dactylifera*) fruit processing by-products and wastes using bioprocess technology- Review. *Saudi Journal of Biological Sciences*. 2013; 20: 105–120.
- [3] Aljaloud S., Colleran H. L., Ibrahim S. A. undefined. *Food and Nutrition Sciences*. 2020; 11(06): 463-480.
- [4] Ali, H.E.F., Oyinloye, B.E. Sepehrimanesh, M., Gab Allah, M.A., Abu Reidah, I. *et al.* Date Palm (*Phoenix dactylifera*): novel findings and future directions for food and drug discovery *Curr. Drug Discov. Technol.* 2018; 15: 1–11.
- [5] AbdulQadir, I., Garba, I., Esegbe, E., Omofonmwan, E.I., Development R. Nutritional components of Date palm and its production status in Nigeria. *Int. J. Agric. Econ. Rural Develop.* 2011; 4 (2): 83–89.
- [6] Tang Z.X., Shi L.E., Aleid S.M. Date fruit: chemical composition, nutritional and medicinal values, products. *J. Sci. Food Agric.* 2013; 93 (10): 2351–2361.
- [7] Mohamed R. M.A., Fageer, A. S.M., Eltayeb M. M., Mohamed A., Isam A. Chemical composition, antioxidant capacity, and mineral extractability of Sudanese date palm (*Phoenix dactylifera* L.) fruits. *Food Sci. Nutrition* 2014; 2 (5): 478–489.
- [8] Al-Alawi R.A., Al-Mashiqri, J.H., Al-Nadabi J.S.M., Al-Shihi B.I., Baqi Y. Date palm tree (*Phoenix dactylifera* L.): natural products and therapeutic options *Front. Plant Sci.* 2017; 8: 845.
- [9] Ortiz-Urbe N., Salomón-Torres R., Krueger R.J.A. Date palm status and perspective in Mexico. *Agriculture*. 2019; 9 (3): 46.
- [10] Zhang C.R., Aldosari S.A., Vidyasagar P.S.P.V., Shukla P., Nair M.G. Healthbenefits of date fruits produced in Saudi Arabia based on *in vitro* antioxidant, antiinflammatory and human tumor cell proliferation inhibitory assays. *J. Saudi Soc. Agric. Sci.* 2017; 16: 287–293.
- [11] Shakiba, M., Kariminik, A., Parsia, P. Antimicrobial activity of different parts of *Phoenix dactylifera*. *Int. J. Mol. Clin. Microbiol.* 2011; 1: 107–111.
- [12] Saleh F. A., Otaibi M.M. Antibacterial Activity of Date Palm (*PhoenixDectyliferaL.*) Fruit at Different Ripening Stages. *J. Food Process. Technol.* 2013; 4: 285.
- [13] 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. *Aust. J. Basic Appl. Sci.* 2015; 9 (1): 141–147.
- [14] Samad M., Hashim S., Simarani K., Yaacob J. Antibacterial properties and effects of fruit chilling and extract storage on antioxidant activity, total phenolic and anthocyanin content of four date palm (*Phoenix dactylifera*) cultivars. *Molecules*. 2016; 21(4): 419.
- [15] Mainasara M.M., Sanusi S.B., Maishanu H.M., *et al.*, 2017. Antibacterial activity and nutritional content of fresh and dried date fruits (*Phoenix dactylifera*) L. *Int. J. Sci. Healthcare Res.* 2017; 2 (1): 15–20.
- [16] Farhana M.I.N., Nadia, M. Z. Z., Natasha, A., Shahida, W.S.W. Effect of date fruits (*Phoenix dactylifera*) on human pathogenic bacteria: a systematic review. *Bottom of Form. Adv. Sci. Lett.* 2017; 23 (5): 4676–4680.
- [17] Abdullah N., Mohd N. F. I., Wan S. W. S. *In-vitro* antibacterial activities of ajwa date fruit (*phoenix dactylifera* l.) extract against selected gram-negative bacteria causing gastroenteritis. *International journal of Pharmaceutical Sciences and Research.* 2019; 10 (6): 2951– 2955.
- [18] Ahmed J., Al-Jasass F. M., Siddiq M. Date fruit composition and nutrition. In: Siddiq, M., S. M. Aleid and A. A. Kader, (Eds.), *Dates: Postharvest Science, Processing Technology and Health Benefits*, 1st ed. *John Wiley & Sons, Ltd., West Sussex, UK.* 2014; Pp. 261– 280.
- [19] Al-Hooti S.N., Sidhu J.S., Al-Saqer J.M., Al-Othman, A. Chemical composition and quality of date syrup as affected by pectinase/cellulase enzyme treatment. *Food Chem.* 2002; 79: 215–220.
- [20] Sami G., Syed U., Azharul K., Afaf K. Date fruit (*Phoenix dactylifera* L.): An underutilized food seeking industrial valorization. *NFS Journal.* 2017; 6: 1–10.
- [21] Al-shahib W., Marshall R. J. The fruit of the date palm: its possible use as the best food for the future?. *International Journal of Food Sciences and Nutrition.* 2003; 54: (4) 247–259.
- [22] Otles S., Ozgoz S. Health effects of dietary fiber. *Acta Sci. Pol. Technol. Aliment.* 2014; 13 (2): 191–202.

- [23] Mrabet A., Rodríguez-Arcos R., Guillén-Bejarano R., Chaira N., Ferchichi A. Jiménez-Araujo A. Dietary fiber from Tunisian common date cultivars (*Phoenix dactylifera* L.): chemical composition, functional properties, and antioxidant capacity, *J. Agric. Food Chem.* 2012; 60 (14): 3658–3664.
- [24] Ishurd O., Kennedy J. F. The anti-cancer activity of polysaccharide prepared from Libyan dates (*Phoenix dactylifera* L.). *Carbohydr. Polym.* 2005; 59:531–535.
- [25] El Modafar C. Mechanism of date palm resistance to Bayoud disease: current state of knowledge and research prospects. *PhysiolMol Plant Pathol.* 2010; 74:287–294.
- [26] El-Far A.H., Shaheen H.M., Abdel-Daim M.M., Al Jaouni S.K., Mousa S.A. Date palm (*Phoenix dactylifera*): protection and remedy food. *Curr Trends Nutraceuticals.* 2016; 1:2.
- [27] Rahimi S., Alaei H., Reisi P., Zolfaghari B., Siahmard Z., Pourshanazari A. Evaluation of the effect of hydro-alcoholic extract of *Phoenix dactylifera* on sleep and EEG. *Avi. J. Phytomed.* 2017; 7:511–518.
- [28] Wahab N. A. A., Zulkifli N. Z., Shamaan N. A., Hamid N. A., Zahir N. N. M. A systematic review on the beneficial effect of date palm (*Phoenix dactylifera*) consumption on energy metabolism. *Adv Sci. Lett.* 2017; 43:4712–4716.
- [29] Vayalil P.K. Date Fruits (*Phoenix dactylifera* Linn): an emerging medicinal food. *Crit. Rev. Food Sci. Nutr.* 2012; 52: 249 –271.
- [30] 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. Int.* 2011; 44: 1812–1822.
- [31] Benmeddour Z., Mehinagic E., Meurlay D.L., Louaileche H. Phenolic composition and antioxidant capacities of ten Algerian date (*Phoenix dactylifera* L.) cultivars: a comparative study. *J.Funct Foods.* 2013; 5:346 –354.
- [32] Mirza M.B., Elkady A.I., Al-Attar A.M., Syed F.Q., Mohammed F.A., et al. Induction of apoptosis and cell cycle arrest by ethyl acetate fraction of *Phoenix dactylifera* L. (Ajwa dates) in prostate cancer cells. *J. Ethnopharmacol.* 2018; 218:35–44.
- [33] Salem G. A., Shaban A., Diab H. A., Elsaghayer W. A., Mjedib M. D., Hnesh A. M., et al. *Phoenix dactylifera* protects against oxidative stress and hepatic injury induced by paracetamol intoxication in rats. *Biomed Pharmacother.* 2018; 104:366–374.
- [34] Gantait S., El-Dawayati M.M., Panigrahi J., Labrooy C., Verma S.K. The retrospect and prospect of the applications of biotechnology in *Phoenix dactylifera* L. *ApplMicrobiolBiotechnol* 2018; 102:8229–8259.
- [35] Chaira N., Smaali M. I., Martinez-Tomé M., Mrabet A., Murcia M. A., Ferchichi A. Simple phenolic composition, flavonoid contents and antioxidant capacities in water-methanol extracts of Tunisian common date cultivars (*Phoenix dactylifera* L.). *Internaltional Journal of Food Sciences and Nutrition.* 2009; 60: 316–329.
- [36] Ragab A. R., Elkablawy M. A., Sheik B. Y., Baraka H. N. Antioxidant and tissue-protective studies on Ajwa extract: dates from Al Madinah Al-Monwarah, *Saudi Arabia. J. Environ. Anal. Toxicol.* 2013; 3:1–8.
- [37] Saddi A. A., Mohamed A. M., Shaikh A. M. Prophylactic mechanisms of *Cucumis melo* var. *flexuosus* and *Phoenix dactylifera* fruit extracts against diabetic cardiomyopathy in streptozotocin induced diabetic rats. *Pak J Pharm Sci* 2018; 31:S699–S707.
- [38] Hamad I., AbdElgawad H., Al Jaouni S., Zinta G., Asard H., Hassan S., Hegab M., Hagagy N., Selim S. Metabolic analysis of various date palm fruit (*Phoenix dactylifera* L.) cultivars from Saudi Arabia to assess their nutritional quality. *Molecules.* 2015; 20:13620–13641.
- [39] USDA. *United States National Nutrient Database for Standard Reference.* 2020; Accessed on 8/12/2020.
- [40] Vayalil P. K. Antioxidant and antimutagenic properties of aqueous extract of date fruit (*Phoenix dactylifera* L. *Arecaceae*). *J Agric Food Chem.* 2002; 50: 610–617.
- [41] Allaith A.A.A. Antioxidant activity of Bahraini date palm (*Phoenix dactylifera* L.) fruit of various cultivars. *Int J Food SciTechnol* 2008; 43:1033–1040.
- [42] Al-Qarawi A.A., Mousa H.M., Ali B.H., Abdel-Rahman H., El-Mougy S.A. Protective effect of extracts from dates (*Phoenix dactylifera* L.) on carbon tetrachloride-induced hepatotoxicity in rats. *Int J Appl Rese Vet Med.* 2004; 3:176 –180.
- [43] Salah A., Al-Maiman. Effect of date palm (*Phoenix dactylifera*) seed fibers on plasma lipids in rats. *Journal of King Saud University.* 2005; 17: 117–123.

- [44] El Arem A., Ghrairi F., Lahouar L., Thouri A., Saafi E. B., Ayed A., et al. Hepatoprotective activity of date fruit extracts against dichloroacetic acid-induced liver damage in rats. *Journal of Functional Foods*. 2014; 9: 119–130.
- [45] Al-Qarawi A. A., Abdel-Rahman H., Mousa H. M., Ali B. H., El-Mougy S. A. Nephroprotective action of Phoenix dactylifera in gentamicin-induced Nephrotoxicity. *Pharmaceutical Biology*. 2008; 46(4), 227–230.
- [46] 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. *Polish J. Food Nutr.Sci*. 2004; 13:397–402.
- [47] Jassim, S. A. A., Naji, M. A. *In vitro* evaluation of the antiviral activity of an extract of date palm (Phoenix dactylifera L.) pits on a pseudomonas phage. *Evidencebased complementary and alternative medicine*. 2008; 15: 1– 6.
- [48] Hasan N.S., Amom Z.H., Nor A.I., Mokhtarrudin N., Esa N.M., Azlan A. Nutritional composition and *in vitro* evaluation of the antioxidant properties of various dates extracts (Phoenix dactylifera L) from Libya. *Asian J Clin Nutr* 2010; 2:208–214.
- [49] Al Juhaimi F., O., Zcan M.M., Adiamo O.Q., Alsawmahi O.N., Ghafoor K., Babiker E.E. Effect of date varieties on physicochemical properties, fatty acid composition, tocopherol contents, and phenolic compounds of some date seed and oils. *J Food ProcPreserv*. 2018; 42: E13584.
- [50] Al-Habsi, Al-Khusaibi N. M. The Potential Antioxidant Properties of Date Products: A Concise Update. *Canadian Journal of Clinical Nutrition*. 2018; 6: 84–104.
- [51] Abu-Reidah I.M., Gil-Izquierdo Á., Medina S., Ferreres F. Phenolic composition profiling of different edible parts and by-products of date palm (Phoenix dactylifera L.) by using HPLC- AD-ESI/MS n. *Food Research International*. 2017; 100: 494 – 500.
- [52] Aljasass F. S., Muhammad S. D. Antioxidants Activity and Color Evaluation of Date Fruit of Selected Cultivars Commercially Available in the United States. *Advances in Chemistry*. 2015; 2015: 1 – 5.
- [53] Abdul-Hamid N.A., Mediani A., Maulidiani M., Shadid K., Ismail I.S., Abas F., Lajis N.H. Metabolite characterization of different palm date varieties and the correlation with their NO inhibitory activity, texture and sweetness. *J Food Sci Technol*. 2018; 55:1541–1551.
- [54] Abdel-Magied N., Ahmed A.G., Abo Zid N. Possible ameliorative effect of aqueous extract of date (Phoenix dactylifera) pits in rats exposed to gamma radiation. *Int J Rad Biol*. 2018; 94:815–824.
- [55] Khan F., Aldahri M., Hussain M.A., Gauthaman K., Memic A., Abuzenadah A., et al. Encapsulation of 5-fluorouracil into PLGA nanofibers and enhanced anticancer effect in combination with Ajwa-dates-extract (Phoenix dactylifera L.). *J. Biomed.Nanotechnol*. 2018; 14:553–563.
- [56] Mansouri A., Embarek G., Kokkalouc E., Kefalas P. Phenolic profile and antioxidant activity of the Algerian ripe date palm fruit (Phoenix dactylifera). *Food Chem* 2005; 89:411–420.
- [57] Al-Farsi M., Alasalvar C., Morris A., Baron M., Shahidi F. Compositional and sensory characteristics of three native sundried date (Phoenix dactylifera L.) varieties grown in Oman. *J Agric Food Chem*. 2005; 53:7586–7591.
- [58] Tao J., Li Y., Li S., Li H. B. Plant foods for the prevention and management of colon cancer. *J Funct Foods*. 2018; 42:95–110.
- [59] Khan T.J., Kuernan A., Razvi S.S., Mehanna M.G., Khan K.A., Almulaiky Y.Q., et al. In vivo evaluation of hypolipidemic and antioxidative effect of 'Ajwa' (Phoenix dactylifera L.) date seed-extract in high-fat diet-induced hyperlipidemic rat model. *Biomed. Pharmacother*. 2018; 107: 675–680.
- [60] 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 dactylifera. *Pak J Pharm Sci*. 2018; 31:421–427.
- [61] Makhlof-Gafsi I., Krichen F., Mansour R.B., Mokni A., Sila A., Bougatef A., Blecker C., et al. Ultrafiltration and thermal processing effects on Maillard reaction products and biological properties of date palm sap syrups (Phoenix dactylifera L.). *Food Chem* 2018; 256:397–404.
- [62] Jakubowska. M. A., Ferdek. P.E., Gerasimenko.O.V., Gerasimenko. J. V., and Petersen. O.H. Nitric oxide signals are

- interlinked with calcium signals in normal pancreatic stellate cells upon oxidative stress and inflammation. *Open Biol.* 2016; 6 (8): 160149.
- [63] Eid N., Osmanova H., Natchez C., Walton G. *et al.* Impact of palm date consumption on microbiota growth and large intestinal health: a randomised, controlled, cross-over, human intervention study. *Br. J. Nutr.* 2015; 114: 1226 –1236.
- [64] Al-Daihan, S., Bhat, R.S. Antibacterial activities of extracts of leaf, fruit, seed and bark of Phoenix dactylifera. *Afr. J. Biotechnol.* 2012; 11: 10021–10025.
- [65] Perveen K., Bokahri. N.A. Comparative analysis of chemical, mineral and *in-vitro* antibacterial activity of different varieties of date fruits from Saudi Arabia. *Saudi Journal of Biological Sciences* 2020; 27: 1886–1891.
- [66] Alghamdi A. A., Awadelkarem A. M., Sharif H., Ibrahim A.B.M. Nasir A., *et al.* Nutritional assessment of different date fruits (Phoenix dactylifera L.) varieties cultivated in Hail province, Saudi Arabia. *Biosci. Biotech. Res. Comm.* 2018; 11 (2): 263–269.
- [67] Biglari F., AlKarkhi A.F., Easa A.M. Antioxidant activity and phenolic content of various date palm (Phoenix dactylifera) fruits from Iran. *Food Chem.* 2008; 107 (4): 1636 –1641.
- [68] Jharia, S.K.A. Evaluation of anthelmintic and antimicrobial activity of the leaves of Lantana camara. *Int. Res. Pharm. Sci.* 2011; 2 (1): 12–15.
- [69] Shraideh Z. A., Khaled S. A. Ultrastructural effects of date extract on *Candida albicans*. *Mycopathologia.* 1998; 142: 119 – 23.
- [70] Ghnimi S., Kamal-Eldin A. Fruit nutraceuticals seeking clinical evidence and technological exploitations, J. Bioequival. Bioavail. 2015; 7 (6): 525–5526.
- [71] El-Fouhil A.F., Ahmed A.M., Darwish H.H., Atteya M., Al-Roalle A.H. An extract from date seeds having a hypoglycemic effect. Is it safe to use? *Saudi Med J.* 2011; 32:791–796.
- [72] www.alz.co.uk/research. London: Alzheimer Disease International. Available from:[http://www.alz.co.uk/research/World Alzheimer Report](http://www.alz.co.uk/research/World%20Alzheimer%20Report). 2015.
- [73] Shalam M. H., Ibrahim A., Mostafa T., Omar K. A laboratory quest on use of date fruit (Phoenix Dactylifera, L) extract in prevention of chemically induced memory deficit in mice. *Asian Journal of Biomedical and Pharmaceutical Sciences.* 2015; 5(49): 5 –11.
- [74] Ibrahim A. A., Shalam M. H. A laboratory quest on use of date fruit (Phoenix Dactylifera, L) extract in prevention of chemically induced memory deficit in mice. *Asian Journal of Biomedical and Pharmaceutical Sciences.* 2015; 5 (51): 31–35.
- [75] Abdul A., Allaith, A. Antioxidant activity of Bahraini date palm (Phoenix dactylifera L.) fruit of various cultivars. *International Journal of Food Science and Technology.* 2008; 43: 1033–1040.
- [76] Doha M. A., Al-Okbi S. Y. *In vivo* evaluation of antioxidant and antiinflammatory activity of different extracts of date fruits in adjuvant arthritis. *Polish Journal of Food and Nutrition Sciences.* 2004; 13: 397–402.
- [77] Al-Qarawi A.A. A., Hassan A., Badreldin M., El-Mougy H. S. A. The ameliorative effect of dates (Phoenix dactylifera L.) on ethanol-induced gastric ulcer in rats. *Journal of ethnopharmacology.* 2005; 98: 313 – 7.
- [78] Simon A. U., Oluwa A. A., Philemon K. C., Kenneth O. A., Ijeoma C. C., Samson E., A., *et al.* Effects of date fruit (Phoenix dactylifera) on sperm cell morphology and reproductive hormonal profiles in cypermethrin-induced male infertility in Wister rats. *Scientific African.* 2021; 11: E 00713.