ABSTRACT

Objective: Phoenix dactylifera Linn (Fam. arecaceae) or date fruits are commercial crops that are utilized in human literature. 70% aqueous MeOH extract of the fruits led to isolation of six compounds; its chemical structures were determined as, β-sitosterol (1), caffeic acid (2), ferulic acid (3), protocatechuic acid (4), p-hydroxybenzoic acid (5) and luteolin (6).

Methods: The accurately weighed date fruits were washed, sliced and soaked freshly in 70% methanol then exhaustively extracted under reflux for about 2 w and filtered, then fractionated by different solvent; finally the butanol extract evaporated and fractionated on a polyamide glass column. Using Sephadex LH-20 column to purify the compounds obtained. In our preliminary study, the extracts and compounds were subjected to in vitro cytotoxicity against HepG2 cell line through the MTT assay and the antioxidant potential of the extracts and pure compounds were assayed through in vitro model using (DPPH) and phosphomolybdenum assays.

Results: Compounds 2 and 3 exhibited promising antitumor activity with IC₅₀ values of 6 and 10 μg/ml, respectively. Moreover compounds 1, 4, 5 and 6 showed cytotoxic activity with IC₅₀ values of 13, 15, 21 and 35 μg/ml, respectively. The antioxidant potential of the compounds showed the inhibition percentage values (SC₅₀) ranged from 4.36 to 10.25 μg/ml, while the total antioxidant capacity ranged from 583.66 to 702.00 mg AAE/g compound.

Conclusion: Our study demonstrated that; dates constituents are powerful as antioxidant and antitumor; hence it is the best potential for pharmaceutical applications.

Keywords: Phenolics, Phoenix dactylifera, MTT assay, Extraction, Antioxidant

INTRODUCTION

Cancer is the second most regular reason for death around the world, according to the World Health Organization evaluations. Since the past time, medicinal plants are utilizing as a part of numerous natural reservation [1-4]. In addition, a considerable lot of the drugs sold for the treatment of tumor, are very costly, carcinogenic and mutagenic. Thus, there is a need to discover elective medications, which are profoundly powerful at non-harmful doses, economical and available to ordinary person. A need is in this way felt to look more up to date remedies, which are less expensive financially and don’t have adverse effects [5]. Mainly, the existence of phenolic cancer prohibition factors is acknowledged to have the covering mechanisms thus these phenolic compounds have antioxidative properties that useful as cancer chemopreventive agents and at most inhibit carcinogenesis during the initiation phase, since they act as radical scavengers, for example, reactive oxygen species (ROS) [6-8]. Phoenix dactylifera, ordinarily known as date palm is belonging to palm family, arecaceae, edible plant used for sweet fruits and it is an important and one of the oldest trees cultivated by man [9]. Dates are the major fruit in Egypt, Saudi Arabia, and Middle Eastern countries. The species is generally developed and is naturalized in numerous tropical and subtropical areas around the world [10-12]. Some types of date fruits have promising effect in a few kinds of diseases and hepatotoxicity [13].

Cancer prevention phenolic compounds present in dates including flavonoids, kaurenic, p-coumaric, sinapic acids, and procyanidins [14, 15].

Our study was planned to evaluate the phenolic profile, antitumor activity against HEPG2 cell line and antioxidant potential in different in vitro antioxidant assays including 1,1-diphenyl-2-picryl-hydrazyl (DPPH) free radical scavenging, Total antioxidant capacity and total phenolic contents of Phoenix dactylifera Linn fruits.

MATERIALS AND METHODS

Sample sources and collection

The date fruits were collected in Cairo, Egypt, during the winter season. This plant was taxonomically identified by Prof. Dr. Wafaa M. Amer, Professor of Plant Taxonomy, Faculty of Science, Cairo; University, Giza, Egypt; a voucher specimen (No. Ph. 1) was deposited at the herbarium of Medicinal Chemistry Department, Theodor Bilharz Research Institute, Giza, Egypt. The plant was washed and protected from light at 25 °C until analysis.

General experimental procedure

1H (300 MHz) and 13C (75 MHz) NMR spectra were recorded on a JEDL GLM spectrometers, the chemical shifts were expressed in δ (ppm) with reference tetramethylsilane (TMS) as an internal standard in DMSO-d₆ and coupling constant (J) in Hertz. Mass spectra were recorded with an ESI-MS mass spectrometer in its negative mode, Finnigan TSQ 700 GC/MS coupled with a Finnigan electro spray source. IR spectra were recorded on PERKIN ELMER 1650 and on BRUKER vector 22 Germany apparatus. The melting points (m. p.) were determined using (SMDP3 Stuart Scientific UK) Melt Apparatus. For antioxidant activity, the absorbance measurements were recorded using the UV-Vis spectrophotometer Spectronic 601 (Milton Roy, USA). The microplate reader (SunnyLab, TECAN, Inc, USA) was used to determine the percentage of viability and the number of viable cells. For column chromatography; cellulose C (Merck), sephadex LH 20 (Pharmacia, Uppsala, Sweden) and polyamide 6S (Riedel de Darmstadt, Germany) were used. For TLC pre-coated TLC plates and an aluminum sheet ready made were used within silica gel 60 F₂₅₄ (Merck, Darmstadt, Germany). Whatman No. 1 sheets (Whatman International Ltd., Maidstone UK)
were performed for paper chromatography (PC). The authentic samples were obtained from Medicinal Chemistry Laboratory [Biochemistry and Molecular Biology and Medicinal Chemistry Department, Theodor Bilharz Research Institute (TBDRI), Cairo, Egypt]. The spots were observed by using UV radiation (254 and 366 nm), and spraying with methanolic FeCl₃ (1%), AlCl₃ (2%) and 10% H₂SO₄, followed by heating. The chemistry works were done at the Medicinal Chemistry Department, Theodor Bilharz Research Institute.

**Extraction procedure**

The accurately weighed date fruits (3 kg) were washed, sliced and soaked freshly in 70% methanol (3 × 5) then exhaustively extracted under reflux for about 2 w and filtered. The filtrate was evaporated using rotary evaporator and the dark brown crude extract was kept in desiccators for using. The obtained dry residue, was defatted firstly with petroleum ether (60-80 °C) (3 × 2 l) to give petroleum ether extract (44 g) and a residue, which was extracted with chloroform (3 × 2.5 l) to afforded, (70 g) chloroform extract and finally ethyl acetate (3 × 2 l) to obtain ethyl acetate extract (61 g) and a residue. The residue was partitioned between butanol and water; then the butanol extract evaporated to give (20 g) extract which was fractionated on a polyamide glass column (110 × 6 cm, 350 g) using a stepwise gradient elution from 100% H₂O / H₂O:MeOH mixtures up to MeOH pure. The obtained individual 110 fraction (150 ml) each were collected into 5 fractions (A-E) according to 1% FeCl₃, Natursstoff spray reagents for detection and their chromatographic properties (Co-PC) with the use of UV light. Fraction A (H₂O, 20 g) totally has free sugar characters with disappearance of phenolic characters, and then was left behind. Fraction B (10% methanol, 18 g) was purified on a sephadex LH-20 column using 10% aqueous MeOH elution to afford a pure compound 1. Fraction C (20-40% MeOH, 23 g), was chromatographed on sephadex LH-20 column for purification two times using 30% aqueous MeOH for elution, the first run afforded a pure compound 2 and the second rechromatographing using (n-BuOH:2-propanol:H₂O, 4:1:5, organic layer) (BIW) elution system, yielded a pure compound 3. Fraction D (50-70% MeOH, 23 g), was fractionated on a cellulose column using H₂O/MeOH (7:3), resulted in 41 subfractions, finally purified by successive fractionation on sephadex LH-20 CC using H₂O/MeOH (50%), resulted in chromatographically pure compounds 4, 5. Fraction E (80-100% MeOH, 21 g) was rechromatographed three times on a sephadex LH-20 column using H₂O/MeOH (95%) eluent to afford pure compound 6. The isolation processes were carried out by using comparative PC using Whatman No. 1 paper and TLC plates with solvent systems (S1 n-BuOH:AcOH: H₂O (4:1.5, upper layer) (PC), (S2) 15% aqueous AcOH (PC), (S3) CHCl₃:MeOH: H₂O (9:5:0.5) (TLC), (S4) CH₂Cl₂:MeOH (8:1.5) (TLC), (S5) CHCl₃:MeOH (7:2.5) (TLC) and (S6) CH₂Cl₂:MeOH:H₂O: H₂SO₄ (7:3:0.1) (TLC).

**Statistical analysis**

All data information was exhibited as mean±SD (standard deviation) for at least three separate results in triplicate for each trial point utilizing SPSS 13.0 program. Relation investigation of the antioxidant properties and free radical scavenging activities against the total phenolic contents of the plant extracts were done utilizing the relation by Microsoft Excel program.

**Free-radical scavenging assay (DPPH assay)**

The free-radical scavenging activity of the plant was measured as described before previously within some adaptations in which an electron-transfer that produces a violet solution in ethanol and it reduced in the presence of an antioxidant molecule, awarding led to a colorless ethanol solution [16]. Briefly, the reaction mixture composed of 2 ml of (100 µM) 1,1-diphenyl-2-picrylhydrazyl (DPPH) in ethanol added to 2 ml of selected concentrations (12-100 µg/ml) of the extracts and compounds followed by incubation for 20 min in the dark, at room temperature. Absorbance of the mixture correspondingly decreases in the changes in concentration deep violet to yellow (at the bottom). The percentage inhibition is given by the following equation:

\[
\% \text{Inhibition} = \left( \frac{A_{blank} - A_{sample}}{A_{blank}} \right) \times 100
\]

Where, \(A_{sample}\) is the absorbance of the control reaction mixture (DPPH solution appropriately diluted with ethanol) and \(A_{sample}\) is the absorbance of the test extract or compound. IC₅₀ (the sample concentration mediating 50% inhibition) was calculated from a graph plot of inhibition percentage against sample concentration. The lower the IC₅₀ value, the higher the antioxidant activity of the examined sample.

**Total antioxidant capacity assessment**

Total antioxidant capacity (TAC) of P. dactylifera Linn extracts and pure compounds was spectrophotometrically determined according to the phosphomolybdenum assay by using the method represented by Prieto et al. [17, 18]. According to this method, 0.5 ml of a 200 µg/ml sample solution in methanol was mixed with 5 ml phosphomolybdenum reagent solution (28 mmol sodium phosphate, 0.6 M sulfuric acid and 4 mmol ammonium molybdate) in dried test tubes. Incubation was then carried out to the reaction mixture for 90 min at 95 °C in water bath. After cooling the solutions at room temperature, their absorbances were measured using a spectrophotometer at 695 nm against a blank (0.5 ml methanol without the sample). Every test was accomplished in triplicate and the antioxidant activity of the samples was expressed as the number of equivalents of ascorbic acid (AAE) [18].

**Total phenolic assay**

The total phenolic content was determined by using the Folin-Ciocalteu assay for the plant extracts and pure compounds [19]. An aliquot (100 µl) of sample (100 µg/ml) was added to 500 µl of Folin-Ciocalteu phenol reagent and 1.5 ml of 20% Na₂CO₃ and shaken, the volume was then made up to 10 ml of volumetric flask using distilled water. A blank was prepared using distilled water. Incubation to the reaction mixture for 120 min at room temperature, then the absorbance against the reagent blank was measured at 765 nm using an UV-Visible spectrophotometer. Total phenolic content was expressed as mg Gallic Acid Equivalents (GAE) per g extract/compound.

**Cytotoxicity analysis by MTT assay**

The cytotoxic effect of methanol and butanol extracts of Phoenix dactylifera Linn was evaluated by MTT assay using human liver cancer (HepG2) cell line. This MTT assay was outright by a slight modification of the strategy reported by Mosmann, 1983. The cells were grown as monolayers in growth RPMI-1640 medium supplemented with 10% inactivated fetal calf serum and 50 µg/ml gentamycin. The monolayers of 10.000 cells involved at the bottom of the wells in a 96-well microtiter plate incubated for 24 h at 37 °C in a moisten incubator with 5% CO₂. The monolayers were then washed with sterile phosphate buffered saline and together the cells were handled with 100 µl from different dilutions of the tested sample in fresh conservation medium and incubated at 37 °C. A control of untreated cells was made in the lake of tested sample. A positive control containing doxorubicin drug was also tested as reference drug for differentiation. Six wells were used for each concentration of the tested sample. The observation under the inverted microscope was made each 24 h. The number of the surviving cells was determined by smearing the cell lysing using 33% glacial acetic acid and read the absorbance at 590 nm by using ELISA reader (SunRise, TECAN, Inc, USA) after wall binding. 100% proliferation correspondence to the absorbance values from untreated cells. The number of viable cells was determined using ELISA reader as formerly (ODt/ODc) x100% where ODt is the mean optical density of wells treated with the tested sample and ODc is the mean optical density of untreated cells. The 50% inhibitory concentration (IC₅₀), which is the concentration required to cause toxic effects in 50% of intact cells, was evaluated from graphic plots [20].

**RESULTS AND DISCUSSION**

**Compound 1 (β-sitosterol)**

It is a white amorphous powder, m. p. 139 °C, R value 0.65 (S3), gave positive Liebermann and Salkowski tests indicating its steroidal nature [21]. Its negative ESI-MS has a molecular ion peak at
m/z 143. 1H NMR of 1 showed two singlet signals at δ 0.63 and 0.95 assignable for methyl groups attached at C-18 and C-19, respectively. In addition three doublets were assigned at δ 0.85 (d, J = 6.95 Hz), 0.81 (d, J = 4.9 Hz) and 0.83 (d, J = 4.9 Hz) for methyls attached at C-21, C-26 and C-27. Moreover, the methyl triplet at δ 0.77 assignable for C-29. Also, a singlet signal at δ 5.30 assigned for olefinic proton at C-6. The 13C-NMR exhibited 29 carbon signals for the β-sitosterol molecule, table (1). According to the above data compound 1 identified as β-sitosterol [22].

Compounds 2 (caffeic acid) and 3 (ferulic acid)

Compound 2 is yellowish white powder, m. p. 224 °C, Rf values 0.75 (S1) and 0.50 (S2), gives blue color under long UV light and compound 3 is creamly white powder, m. p. 170 °C. Rf values 0.72 (S3) and 0.48 (S4) and 0.50 (S5) and 0.49 (S6), gives blue color under long UV light. Compounds 2 and 3 were expected to be cinnamic acid derivatives depending on their chromatographic characters and UV spectral data. Negative ESI-MS of 2 and 3 exhibited a molecular ion peak at m/z 179 and 193 [M-H]− corresponding to a molecular formula of C9H8O4 and C10H8O4, respectively. In the 1H NMR spectrum of the compounds 2 and 3 an AX-spin coupling system related to two ß-olefinic protons were observed at δ 7.43, 7.41 (H-7) and 6.25, 6.24 (H-8), respectively (each, d, J = 15.7 Hz). Also, the ABM-system, at δ 6.94, 6.85 (dd, J = 7.04, 6.95 (d) and 6.74, 6.27 (each, d, J = 8.1 Hz) of H-6, H-2 and H-5, respectively were expecting for a caffeoyl moiety in case of compound 2 and feruloyl moiety in case of compound 3 because of the presence of methoxy group signal at δ 3.74 (3H, s). Representative 10 carbon signals of ferulic acid in case of 3 were confirming for a caffeoyl moiety. The 13C-NMR exhibited 29 carbon signals for compound 3 at δ 148.62 (~+∆ 2 ppm), table (1) with respect to those of caffeic acid 2; C-3 at δ 148.62 (~+∆ 2 ppm), table (1) with respect to those of caffeic acid 2; C-3 at δ 148.62 (~+∆ 2 ppm), table (1) with respect to those of caffeic acid 2.

Table 1: 1H and 13C-NMR spectral data of compounds 1, 2, 3 and 6 (300/75 MHz, DMSO-d6; TMS as internal standard)

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δ in ppm and J in Hz.
Free-radical scavenging antioxidant activity (DPPH assay)

Cancer prevention agents or antioxidants are firmly identified with their biofunction, which is summarized for example, lowering the chronic diseases like carcinogenesis, mutagenesis, DNA harming [27]. Subsequently, antioxidant capacity is broadly utilized as a parameter for therapeutic bioactive molecules.

The phenolic compounds antioxidant activity is generally because of their redox properties, that can plays a promising role in absorbing and neutralizing the free radicals, or decomposing peroxides [28].

The antioxidant activity of P. dactylifera fruits was assessed by DPPH free radical method and ascorbic acid was used as standard (SC_{50} = 7.97±1.34 μg/ml) table (2). Our study shows the scavenging effect of the plant extracts on DPPH radical was in the following order butanol>methanol>ethyl acetate. In the present study, n-butanol extract was the most efficient for recovery of phenols; since at which the highest content of polyphenols was observed, its SC_{50} value was 17.63±0.38. The SC_{50} values for free radical scavenging activity among the plant extracts were observed to be; 29.60±1.05, 38.19±1.51 and 31.45±1.29 μg/ml for the fresh date’s methanolic, dried dates methanolic and ethyl acetate extracts, respectively. So n-butanol extract proved to be the most effective solvent for isolation of phenolic compounds. Ideal structure for the scavenging of free radicals since structure of these molecules incorporates various hydroxyls acting as hydrogen donors which make them very powerful antioxidant factor. Caffeic acid represents the maximum scavenging activity between the samples studied with SC_{50} value of 4.36±2.10 μg/ml, followed by ferulic acid with SC_{50} value of 5.12±1.10 μg/ml while compounds 1, 4, 5 and 6 was found to be have SC_{50} Value of 10.25±1.35, 6.63±0.46, 7.65±0.39 and 8.50±2.11 μg/ml, respectively, table (2). Our study showed that, a significant positive correlation between the antioxidant activity and phenolic compounds. These findings agreed with Saleh et al., (2011) who notify that date fruits can be viewed a rich of hydrophilic antioxidants and this reducing power is generally correlated with the existence of polyphenols [28].

Recently the research serves; caffeic acid was always behaves as potent antioxidant compared with ferulic acid, in inhibiting LDL oxidation and quenching radicals [28-30]. Thus, antioxidant compounds might influence on malignancy cells by giving high intensity of oxygen by acting with its radicals shape and thus aggravates tumor hypoxia required for these cells and also causes apoptosis [31-33]. Our study presents that, the total antioxidant capacity of P. dactylifera Linn ranged from (298.66 mg AAE/g compound) to (702.00 mg AAE/g compound), table (2).

Total phenolic contents assay

The total phenolic contents of P. dactylifera Linn extracts decreased in the order n-BuOH>MeOH>EtOAc; these results also, agreed with the results concluded from the DPPH free radical assay which revealed that, n-BuOH extract indicated high total antioxidant capacity when compared with the other extracts of the plant which might be because of the presence of high percentages of phenolic compounds. As shown from results in table (2) the highest product of total phenolic content was found to be in n-BuOH extract (533.92 mg gallic acid equivalent/g extract), followed by EtOAc extract (299.05 mg gallic acid equivalent/g extract), MeOH fresh dates extract (253.06 mg gallic acid equivalent/g extract), and MeOH dried dates extract (206.21 mg gallic acid equivalent/g extract), table (2). From our point of view it has been appeared that, the higher contents of total phenolics in P. dactylifera Linn may be contributed by presence of caffeic acid, ferulic acid, protocateucic acid, p-hydroxybenzoic acid and luteolin which are represents a promising antioxidant activity.
Table 2: Free radical scavenging potential (DPPH) and total antioxidant capacity (TAC) of the extracts and isolated pure compounds from *Phoenix dactylifera* Linn

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<th>Sample</th>
<th>DPPH SC (μg/ml)</th>
<th>Total antioxidant capacity (mg AAE/g sample)</th>
<th>Total phenolic content (mg GAE/g ext.)</th>
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<td>362.00±2.00</td>
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<td>Methanol ext. dried dates</td>
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<td>206.21±1.56</td>
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<td>253.06±1.85</td>
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</tr>
<tr>
<td>Compd. 3</td>
<td>5.12±1.10</td>
<td>692.66±2.08</td>
<td>299.05±2.67</td>
</tr>
<tr>
<td>Compd. 4</td>
<td>6.63±0.48</td>
<td>600.3±1.52</td>
<td>533.92±1.18</td>
</tr>
<tr>
<td>Compd. 5</td>
<td>7.65±0.39</td>
<td>592.3±1.52</td>
<td>253.06±1.85</td>
</tr>
<tr>
<td>Compd. 6</td>
<td>8.50±2.11</td>
<td>584.66±1.15</td>
<td>206.21±1.56</td>
</tr>
</tbody>
</table>

Data are expressed as mean±standard deviation (n = 3). *DPPH results are expressed as μg compound/ml (μg/ml), Total antioxidant capacity results are expressed as mg ascorbic acid equivalent/g extract (mg AAE/g compound), Total phenolic content are expressed as mg gallic acid equivalent (mg GAE/g ext.)*

Mexican and Chinese studies concluded that, betasitosterol dose-dependently reduced the level of free radicals by the scavenging of ROS and causes conservation of mitochondrial membrane constancy and increased antioxidant enzymes [34-37]. Protocatechuic acid was showed to have several pharmacological impacts which might be firmly agreed with its antioxidant activities [38-41]. It was noticed that the radical scavenging activity assay and total antioxidant capacity assay of the extracts was strong directly positive correlated with their total phenolic contents (Correlation coefficients; R² = 0.912 and 0.909, respectively), fig. (2,3). This is in agreement with other studies in the literature which present positive correlations between the quantity of phenolic compounds in the extract and the DPPH free radical scavenging activity [42].

Cytotoxic activity

MTT assay is a fast with high precision colorimetric approach that generally used to decide cell growth and cell cytotoxicity, especially in the improvement of new medication. A sample is generally considered to have *in vitro* cytotoxic activity if the IC₅₀ value (concentration that causes a 50% cell kill) in carcinoma cells, is less than 20 g/ml [43]. Our study demonstrated a strong *in vitro* toxicity towards HepG2 cell lines obtained from methanol, ethyl acetate, and butanol extracts within the pure compounds. Butanol extract being more active than the other extracts within a high inhibitory effect with IC₅₀ value of 18 μg/ml, while methanol and ethyl acetate...
extracts showed moderate effect with IC_{50} values of 34 and 35 
μg/ml, respectively following 24 h treatment, fig. (4). Due to the 
active constituents of the butanol extract guided us to some isolation 
of valuable compounds that have the ability to damaged carcinoma 
cells. Therefore compounds 2 and 3 exhibited pronounced 
cytotoxicity against HepG2 cell lines with IC_{50} values of 6 and 10 
μg/ml, respectively, fig. (5). Furthermore, compounds 1, 4, 5 and 6 
showed cytotoxic activity with IC_{50} values of 13, 15, 21 and 35 
μg/ml, respectively against liver carcinoma cell lines.

Protocatechuic acid (PCA) is generally dispersed and introduce in 
most edible plants utilized in folk medicine [44], additionally it 
shows an anticarcinogenic effectiveness in liver and encourage 
apoptosis in human leukemia cells [45, 46].

luteolin, 4-hydroxybenzoic acid and protocateucic acid as minor 
constituents showed greatest hepatoprotective activity [47]. β-
sitosterol furthermore, exhibited antiproliferative and apoptosis 
activities in human leukemic L937 and prostate cancer cells [48, 49]. 
Ethyl protocatechuate was established to neutralize the H_{2}O_{2} 
induce cytotoxicity in Chinese hamster v79 cells [50].

Structure activity relationship

The presence of–CH=C-COOH groups in caffeic and ferulic acids 
guarantees greater H-donating capability and consequent radical 
stability than the carboxylic group in p-hydroxybenzoic acids. The 
reduced potentials of radicals resulted from benzoic acid and 3,4-
dihydroxybenzoate decrease with the electron donating power at 
Cl. Along these lines, caffeic and ferulic acids were found to be more 
active than protocatechuic and p-hydroxybenzoic acids [51]. Since 
the phenolic profile of date fruits is predominantly depends on 
caffeic and ferulic acids; so this potential antioxidant activity was 
normally expected. At last, this phenolic profile present a right tool 
to rationalize the geographic source of date fruits activities.

CONCLUSION

The present study revealed the phenolic and cytotoxic spectrum of 
medicinally date fruits. Moreover the high contents of phenolic 
compounds specified that these compounds contribute to the 
antioxidant activity profile, so Phoenix dactylifera Linn can be 
regarded as promising natural plant sources of antioxidants. Our 
study conducted the presence of different phytochemicals such as 
phenolic compounds and sterols; they are β-sitosterol (1), caffeic 
acid (2), ferulic acid (3), protocatechuic acid (4), p-hydroxybenzoic 
acid (5) and luteolin (6). In vitro antioxidant activity revealed that, 
the most efficient extraction medium for phenolic compounds was 
butanol extract followed by methanol extract which showed 
moderate phenolic contents and ethyl acetate extract which showed 
the lowest content of phenolic compounds. Caffeic acid exhibited a 
potent cytotoxic activity among the tested compounds against liver 
carcinoma HepG2 cell line. The present review demonstrated that; 
the Egyptian date fruits include a great percentage of phenolic 
metabolites with high level of antioxidant potential which support 
its uses as a utilitarian food. Therefore this report may be serving as 
a footstep regarding the biological and pharmacological activities of 
a natural plant source Phoenix dactylifera Linn fruits and sustain 
their use in healthcare.

CONFLICT OF INTERESTS

Declared none

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