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*Research Article*

# Evaluation of the anticancer potential of Iraqi Date *Palma dactylifera* L. seed extract on breast cancer MCF7 and prostate cancer PC3 cell lines

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**Abstract**
Date seeds are rich in many dietary elements, antioxidants, and anti-inflammatory and anticancer phytochemical compounds. The present study aimed to evaluate the anticancer potential of Iraqi Date *Palma dactylifera* L. seed extracts on breast cancer MCF7 and prostate cancer PC3 cell lines. The seeds were extracted with 70% ethanol and explored for the presence of many anticancer compounds by High-performance liquid chromatography (HPLC) analysis . The cytotoxicity of date seed extracts on cell lines was studied using 3-(4, 5-dimethylthiazolyl-2)-2, 5-diphenyltetrazolium bromide (MTT) assay. The cytotoxic assay of multi-parameters was carried out to detect the extract activity on valid cell count, total nuclear intensity, cell membrane permeability, mitochondrial membrane potential and cytochrome C release by using High-Content Screening (HCS) assay. The results of HPLC confirmed the presence of caffeic acid, sinapic acid and gallic acid. The results of MTT assay showed significantly reduced cell viability of MCF7, PC3 and control HdFn cell lines with IC50 of 269,325 and 1499 µg/ml, respectively. Analysis of HCS findings indicated significant changes in all tested parameters at concentrations of 100 µg/ml. Ethanolic extract of seeds was rich in many antioxidant compounds and the extract appeared to have strong cytotoxic activity against both MCF7 and PC3 cancer cell lines. The cells of MCF7 were more sensitive to extract than PC3. The viability of normal HDFn cells was not affected by the extract. The study showed the importance of date seeds as a very effective antioxidant and can contribute to reducing the risk of breast and prostate cancer.

**Keywords:** Apoptosis, Breast cancer Date seeds, *Phoenix dactylifera*, Prostate cancer

## INTRODUCTION

The second leading cause of death worldwide is cancer. Despite the great development in methods of treating and controlling cancer, it has been observed that there is an increase in the incidence of cancer, especially prostate cancer and breast cancer, in men and women, respectively (Serhani *et al*., 2019)) .The anticancer effect of medicinal plants is widely investigated by researchers and treated by medicinal plants belong to the —biologically-based treatments, which include galenicals, herbals, industrial pharmaceutical, phytopharmaceuticals, and traditional medicines ( Hussein *et al*.,2021). Medicinal plants are an alternative source of effective and inexpensive medicines instead of manufactured chemotherapy (Inanc *et al*., 2006). There are many side effects of conventional treatment used in cancer management due to their lack of specificity for target cells. More than 5000 phytochemicals have been recorded as key elements in cancer treatment, such as alkaloids, phenols, terpenes, glucosinolates and carotenoids (Rizeq *et al*., 2020).

Surgery, chemotherapy, immunotherapy, and radiotherapy are the most prominent types of treatment used by cancer patients. The main causes of drug failure were side effects, drug resistance and drug specificity (Rockwell *et al*., 2005; Qu *et al*., 2020). Cancer phytotherapy deals with many compounds like Terpe-

noids, alkaloids and phenolics, which have potential antioxidant activities that may prevent cancer cell proliferation and differentiation (Molassiotis *et al*., 2005; Pinto *et al,*2020). Phenoles and other secondary metabolites which are present in medicinal plants, have anti-apoptotic regulating functional groups, so it is considered potent preventive drugs against cancer cells. (Reddy *et al*., 2003; Pinto *et al*,2022). *Phoenix dactylifera* L. (date palm tree) is a member of the Arecaceae family. It has numerous nutritional and pharmacological benefits (Abiola *et al*., 2015). Many secondary metabolites found in the date palm have strong antioxidant, anticancer, neuroprotective, hepatoprotective, nephroprotective, and gastrointestinal protective (Surh, 2003).

Although date seeds are a rich source of economic resources, they are considered the most significant waste product of the Date industry. If they are highly concentrated in the natural environment, they may pose an environmental risk. (Al-Farsi and Lee, 2008; Garcia-Oliveira *et al*,2021). According to recent research, dates' seeds have elevated levels of Flavonoids, phenols, and antioxidants and higher dietary fibre content than recorded in the fresh portions. There are large amounts of Glutathione, ascorbic acid and α-Tocopherol, as compounds of polyphenol like caffeic acid, sinapic acid, with an amount of protocatechnic acid **(**Al-Farsi *et al*., 2007; Baldassari *et al,*2023 **)**. Date seeds are rich in multi-aromatic compounds such as alcohols, citrates, aldehydes, ketones, and saturated and unsaturated hydrocarbonates (Ardekani *et al*.,2010; Pinto *et al.*,2019).

This research aimed to investigate the phytochemical components and evaluate antioxidant and anticancer activity of date seeds of *Palma dactylifera* ethanolic extract by studying the cytotoxicity of this extract against human breast cancer MCF7 and prostate cancer PC3 cell lines.

## MATERIALS AND METHODS

### Preparation of raw powder of date seeds

The seeds of *P. dactylifera* were separated from the dates after obtaining the Halawi date seed from the local Hilla market. Then, the seeds were washed and dried in the oven at 45 C .°They were milled to a fine powder by an Electric miller. Afterwards, they were stored in a sterile and closed cup for later use (Al Ghezi1 *et al*., 2020).

### Preparation of date seeds ethanolic extract

The raw powder of date seeds was extracted with methanol-water solvent (1:1V/V) following Akowuah *et al*., 2014 with a few modifications. The mixture was prepared by mixing one gram of raw powder of date seeds 10 ml of solvent. Firstly, the mixture was shaken at a high speed for 1 hour and then put in a water path under 40 C °for 2 hour. The filter paper was used to filter the mixture. The oven was used to concentrate the filtered liquid by dryness under 45 C°. The dried and concentrated material was ground using an electric grinder, and then the resulting powder was sterilized with UV for 20 minutes. Finally, it was saved in a sterile, dark and closed cup for use (Akowuah *et al*., 2014).

### High-performance liquid chromatography (HPLC) analysis for qualitative and quantitative analysis

### Caffeic acid

Preparative reversed-phase HPLC analysis was performed on C18-ODS (25.0cm X 4.6 mm X 5.0 µm) column. The moving phase was specified by using Akowuah *et al*.(2014) method, which consisted of Methanol (A) and Distilled water(B). The linear gradient started with A: B (90:10) V/V over 4 minutes, changing to A: B (85:15) for 3 minutes, A: B (80:20) for 3 minutes, A: B (70:30) for 10 minutes, A: B (60:40) for 8 minutes, A: B (50:50) for 4 minutes. The flow rate was 0.5 ml/minute. The Injection volume was100 µL with a rate of flow 0.5 ml/minute, the recognition wavelength was 340 nm and the line temperature was 25 °C. (Akowuah *et al*., 2014).

### Sinapic acid

HPLC analysis was carried out on C18-ODS (25cm X 4.6 mm X 5.0 µm) column. There was a liner gradient during the moving phase with *O*- phosphoric acid 25% (A): acetonitril (B) beginning at 95:5 A: B for 2 minutes, altering to 90:10 A: B for 5 minutes, 85:15 A: B for 3 minutes, 80:20 A: B for 13 minutes, 70:30 A: B for 5 minutes, 50:50 A: B 23 for 4 minutes. The inflow rate was 1 ml/minute. 100 µL was the Injection volume for all specimen standard solutions, the detection wavelength was 360 nm, and the column temperature was 25 °C (Hajimehdipoor *et al*., 2012).

### Gallic acid

HPLC technique, C18-ODS (25cm X 4.6 mm X 5 µm) column was used. The mobile phase was identified according to Zubillaga and Maerker (1990); and Ioele *et al.* (2022) method, which included two different kinds of solutions: (A) Methanol: Acetic acid: Distilled water (10:2:88) and (B) Methanol: Acetic acid: Distilled water (90: 3: 7), starting at 40% of A, 60% of B for 4 minutes, 50% of A, 50% of B for 5 to 8 minutes, and 60 % of A,40% of B for 8 to 10 minutes was the gradient. Each specimen and the standard solution had an injection volume of specimens and standard solutions 100 µL, the identification wavelength was 280 nm and the column heat was 25 °C. (Hajimehdipoor *et al*., 2012).

The concentration of each phytochemical ( Caffeic acid, Sinapic acid, Gallic acid) was set by following the equation, which depended on the area under the peak.

(Hajimehdipoor *et al*., 2012).

$$\text{Conc. of sample}(\mu g/ml) = \frac{\text{Conc.of standard} \times \text{A of sample}}{\text{A of Standard}} \times \text{DF} \quad \text{Eq. 1}$$

Conc = Concentration, DF= Delusion factor, A = Area

**Preparation of sample for High-performance liquid chromatography (HPLC)**

One hundred µl of date seed extract was added to 1 ml of methanol grade after 3 minutes of vortex. 100 µl of the sample was injected into the HPLC device (Akowuah *et al*., 2014).

**Preparation HPLC standard**

A standard solution was set up by breaking down 1 mg in 100 ml of methanol grade for HPLC for each phytochemical (Akowuah *et al*., 2014).

**Cell line culture**

Human breast cancer MCF7 , human prostate cancer PC3 cell lines and type of normal cell HDFn were stored in vapor phase of liquid nitrogen at a temperature below -130 C° in frozen vial. The frozen cell line vials were stored in the Tissue Culture Laboratory in the Center for Natural Product Research and Drug Discovery, Department of Pharmacology, Faculty of Medicine, University of Malaya Kuala Lumpur, following Al-Saffar *et al*. ( 2017).

**Estimation of cytotoxicity of the extract using 3-(4, 5-dimethylthiazol-2-yl)-2, 5-diphenyltetrazolium bromide (MTT) assay**

The cells were multiplied ( 1 x $10^4$ to $10^6$ cells/mL) in a 96 flat-well plate with a latter volume of 200 mL/well. The sterilized parafilm was wrapped on the plate and incubated at 37C°, 5% $CO_2$ for 24 hrs. Thereafter incubation, the medium was taken away and 200 mL of the one-fold sequent dilution of ethanolic extract of *P. dactylifera* seeds (25, 50, 100, 200 and 400 µg/ml were collected. Three replicates of each concentration were prepared in addition to the control. Plates were brood at 37C°, $CO_2$5% for 24 hrs. Then the phosphate buffer solution was used to wash the cells in the well two times. the plate was incubated at 37° C after adding 20 µL of the MTT smearing solution to each well . Then, 4h, 100 µL of dimethyl sulfoxide (DMSO) was introduced to each well to dissolve the formazan crystals, and absorbance was pointed out with a 575 nm . The mean absorbance for each group of replicates was enumerated. The percentage viability of cells exposed to ethanolic extract of date seeds was calculated using the following equation (Al-Saffar *et al*., 2017).

$$\text{Cell viability \%} = \frac{absorbance\ of\ treated\ cells}{absorbance\ of\ control} \times 100 \quad \text{Eq. 2}$$

**Multi-parameter assessment for cytotoxic**

After exposure to date seeds extract in vitro, the five orthogonal MCF7cell health factors were determined using a multi-parameters cytotoxic analysis. The criteria were: count of cell viability, total intensity of nuclear, cell membrane, the permeability of mitochondrial membrane and release of cytochrome C. later than 24 hrs. of the display to various doses of date seeds extract. Staining solutions (MMP dye and permeability dye) were used to stain the treated MCF7 cells over 30 minutes at 37 C .˚Cells were rectified, permeable and plugged prior to checking with primary cytochrome C antibody and secondary Daylights 649 paired goat anti-mouse IgG for 60 min and by Array Scan High-Content Screening (HCS) analyzer, each plate was tested (Abraham *et al*., 2008).

**Statistical analysis**

The significance of the differences between the groups was estimated by a one–way analysis of variance (ANOVA). Information was revealed as mean ± Standard Deviation (SD) and statistical importance was executed by utilizing version 6 of Graph Pad Prism.

## RESULTS AND DISCUSSION

**Identification of caffeic acid, sinapic acid and gallic acid in date seeds**

The results of caffeic acid, sinapic acid and gallic acid presence and concentration in date seeds extract using HPLC analysis ( Fig. 2, 3, 4) showed the appearance of retention time of the extract as 4.28 , 6.80, 3.95 minutes, respectively. The area was 90224.59, 54182.69, 65748.90 mAU, respectively and when compared with standards retention times and areas, results indicated the presence of caffeic acid, sinapic acid and gallic acid in the respectively after doses of 42.65, 66.29,80.22 ppm. Many studies have been performed to investigate the phytochemical composition of different types of date seeds' extracts, such as Bouhlali *et al.* (2015) and Adeosun *et al*. (2016) and confirmed the presence of many important phytochemical compounds in ethanolic date *Palma dactylifera* seeds' extract, including caffeic acid, sinapic acid and gallic acid.

**Cytotoxic activity of ethanolic date seeds extract on human cancer cell lines and normal cells *in vitro***

The results on cytotoxic activity of ethanolic date seeds extracts of different concentrations of 70% ethanolic extract of date seeds (400, 200, 100, 50 and 25 µg/ml) on human cancer cell lines: human breast cancer MCF7 and human prostate cancer PC3 cell lines compared to one type of normal cell HDF *in vitro* are given in Table 1 and Fig. 4,5 and 6. It showed that incubation

**Table 1.** Viability of MCF-7, PC3 and HDFn cell lines at different concentrations of date seeds extract after incubation for 24 hour

| Date seeds Extract concentration (µg/ml) | Cell viability % (mean ± SD) | | |
|---|---|---|---|
| | PC3 | MCF-7 | HdFn |
| 25 | 84.81 ± 1.38 | 86.65 ± 6.47 | 95.83 ± 2.23 |
| 50 | 71.87 ± 4.39 | 74.30 ± 3.06 | 95.06 ± 0.37 |
| 100 | 63.07 ± 2.12 | 63.07 ± 2.12 | 91.89 ± 1.00 |
| 200 | 56.75 ± 2.38 | 50.92 ± 3.24 | 82.44 ± 7.22 |
| 400 | 46.87 ± 4.11 | 39.58 ± 2.11 | 73.68 ± 4.33 |

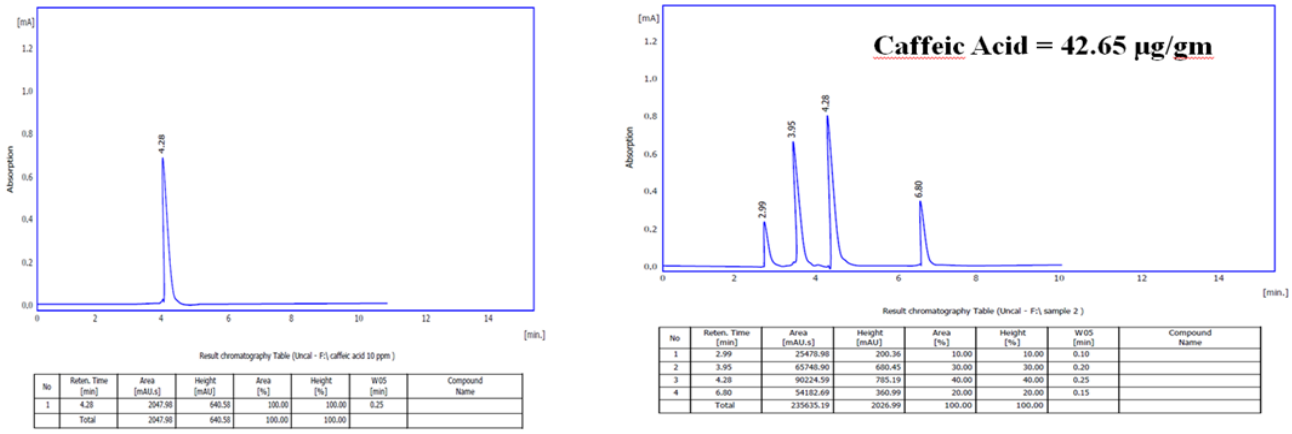


**Fig. 1 .** *High-performance liquid chromatography (HPLC)detection of Caffeic acid in date seeds ethanolic extract*

of these cells with the extract at various concentrations for 24 hours was significantly decreased ($p>0.05$) in the cell viability of MCF7 breast cancer cells and PC3 prostate cancer cells in a dose-dependent pattern compared to normal cells line HDFn.The concentration 400 µg/ ml was the most affected than other doses. The MCF7 breast cancer cells were more sensitive than PC3 prostate cancer cells. The viability of MCF7 cells was 86.65, 74.30, 63.07, 50.92, and 39.58 % in concentrations of 25,50,100,200,400 µg/ml, respectively, with IC50 (269) µg/ml. The viability of PC3 cells was 84.81,71.87,63.07,56.75, and 46.87 µg/ml in concentrations of 25,50,100,200,400 µg/ml, respectively, with IC50 (325) µg/ml. While the viability of HDFn was 95.83,95.06,91.89,82.44,73.68 µg/ml in concentrations of 25,50,100, 200 and 400%, respectively, with IC50 (1499) µg/ml.

The extract appeared selectively cytotoxic on MCF7 cancer cell line and PC3 compared to normal cell line HDFn. The cytotoxic activity of date seeds' extract may contribute to many active substances for cancer treatment like caffic acid, sinapic acid and gallic acid as shown in Fig. 1,2 and 3. All these compounds have a strong anticancer and antioxidant activity (Habib *et al*., 2014; Siddiqui *et al.*,2019). Gallic acid has been known as a stimulator of prgrammed cell death in tumor cell lines (Kim *et al*., 2006; Ung *et al*.,2021 ). Kaur *et al.* ( 2009) and Zhang *et al.* (2019) showed that gallic acid is specifically cytotoxic for cancer cells and much less poisonous for normal cells . Other research showed that the anticancer efficiency of gallic acid stimulated the programmed cell death over various processes such as the production of reactive oxygen species (ROS), activated caspase 7 and 3 to induction intrinsic apoptosis pathway, regulation of apoptotic and anti-apoptotic proteins (Kawada *et al* ., 2020). Veluri *et al* . (2006) pointed to the antioxidant strength of gallic acid for their anticancer activity, so it could be considered a powerful drug for cancer medication alone or in conjugation with other anticancer drugs to improve their activity.

**Multi-parameters cytotoxic activity using High-Content Screening (HCS( of date seeds extract on MCF7 breast cancer cell line**

HCS has been used to investigate the mechanism of date seeds' extract cytotoxic effect on cancer cells and demonstrated whether the extract stimulated apoptosis in their cytotoxic activity (Persson *et al*., 2014; Pinto *et al.*,2020).

The results based on IC50 values from MTT assay of the present study, the subsequent doses (100, 50, 25 and 12.5) µg/ml of 70% ethanolic extract of date seeds were tested on breast cancer cell line to discover the variations in five factors of the cell (count of valid cell, nuclear intensity, permeability of cell membrane, poten-

**Table 2.** Cytotoxic activity of banana peels extract on the multicellular parameters of the A549 cell line by using the Reader of Array Scan HCS

| High-content screening (HCS) parameters ( Mean ± SD ) | | | | | |
|---|---|---|---|---|---|
| Concentration µg/ml | Valid Cell Cont. | Total Nuclear Intensity | permeability of cell membrane | Mitochondrial permeability of membrane | Releasing of cyto-chrome C |
| Control un-treated Cell | 3460.5 ± 297.69 a | 419.5 ± 14.84 b | 108 ± 16.97a | 275 ± 19.79 a | 488 ± 67.88b |
| 100 | 2115 ± 81.31<br>61.1%b | 503.5 ± 19.09<br>120.0 % a | 105 ± 7.07<br>97.2%a | 203 ± 11.31<br>73.8% b | 687.5 ± 81.31<br>140.9%a |
| 50 | 3087.5 ± 108.18<br>89.2% a | 429.5 ± 12.02<br>102.4% B | 100 ± 11.31<br>92.6%a | 232 ± 12.72<br>84.4% a | 621.5 ± 14.84<br>127.4%a |
| 25 | 3140 ± 33,94<br>90.7% a | 403.5 ± 16.26<br>96.2 b | 107 ± 5.65<br>99.1%a | 272 ± 31.11<br>98.9% a | 482 ± 41.01<br>98.8%b |
| 12.5 | 3341 ± 77.78<br>96.5% a | 418.5 ± 9.19<br>99.8% b | 101.5 ± 16.26<br>94.0%a | 282 ± 15.55<br>102.5%a | 488.5 ± 51.61<br>100.1%b |
| 6.25 | 3443 ± 207.88<br>99.5% a | 409.5 ± 14.84<br>97.6% b | 105.5 ± 17.67<br>97.7%a | 268 ± 18.38<br>97.5%a | 481 ± 62.22<br>98.6%b |

High-content screening (HCS), also known as high-content analysis (HCA) or cellomics, is a method that is used in biological research and drug discovery to identify substances; The litter a,b mean significant differences and the similar letter is an alternative to the absence of significant differences

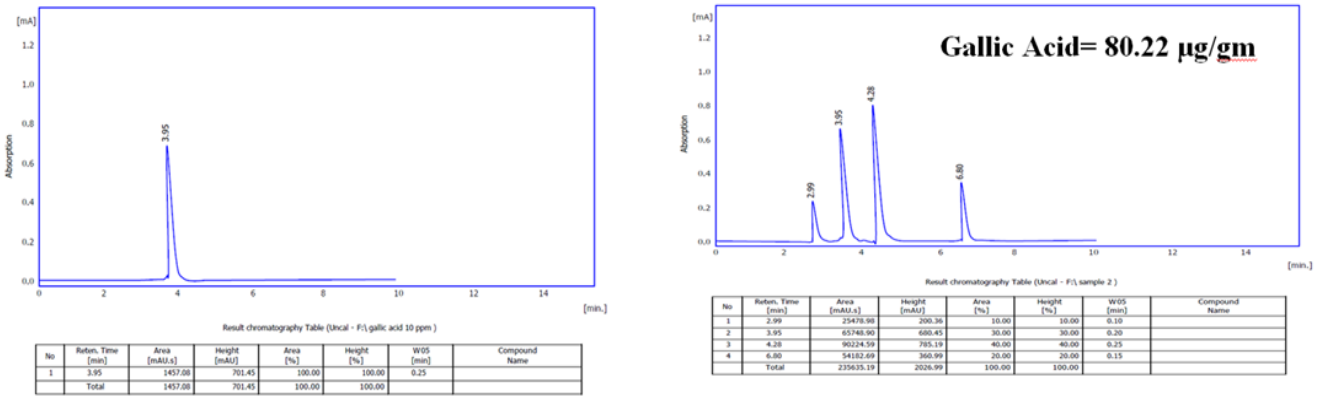


**Fig. 2.** *HPLC detection of sinapic acid in date seeds ethanolic extract*

tial of mitochondrial membrane and releasing of cyto-chrome C) after 24 hours of exposition to the concentrations of the extract are shown in Table 2.

The results in Table 2 revealed that date seed extract decreased the Valid cell count of breast cancer cells when treated with date seed concentrations in contrast to control untreated Cells. The percentages of decrease were 61.1, 89.2, 90.7, 96.5, and 99.5 % in concentrations 100 , 50 , 25 , 12.5 and 6.25µg/ml, respectively, but statistically, only decreasing per cent of concentration 100 µg/ml was significantly in contrast to control untreated cells. The cell viability is one of the key tests which can be used in toxicity assays (Wellington, 2015). The cytotoxicity of date seeds' extract against breast cancer cell lines may be attributed to the richness of the extract in many polyphenols and phenolic acids like caffeic acid, sinapic acid and gallic acid, which was confirmed by their presence in present results by HPLC analysis Fig. 2, 3 and 4. Caffeic acid can stimulate the intrinsic programmed cell death pathway in cancer cells by promoting ROS amount and declining mitochondrial activity and is beneficial in decreasing aggressive action of tumors through reducing metastasis by decreasing the epithelial-to-mesenchymal transmission mechanism (Jiang *et al*., 2005). Caffeic acid has an anti-tumor role by motivating programmed cell death, blocking proliferation, migration, invasion, and cell cycle capture, and repressing epithelial-mesenchymal transition (EMT) that has proved in modern pharmacological research (Simal-Gandara and Prieto, 2021).

Table 2 revealed that date seed extract increased the total nuclear intensity of breast cancer cell lines When compared with untreated control. The increase was

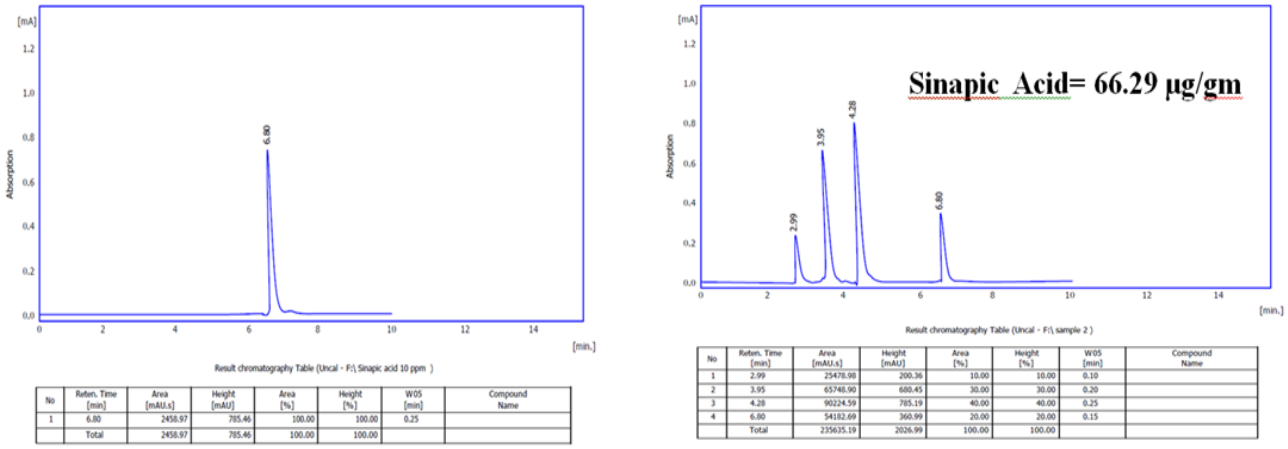


**Fig.3 .** *HPLC detection of gallic acid in date seeds ethanolic extract*

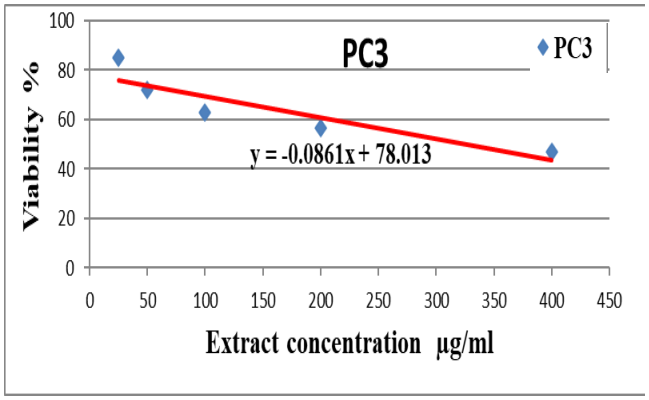


**Fig. 4.** *Cytotoxicity effect and IC50 of date seeds extract on PC3 cells*

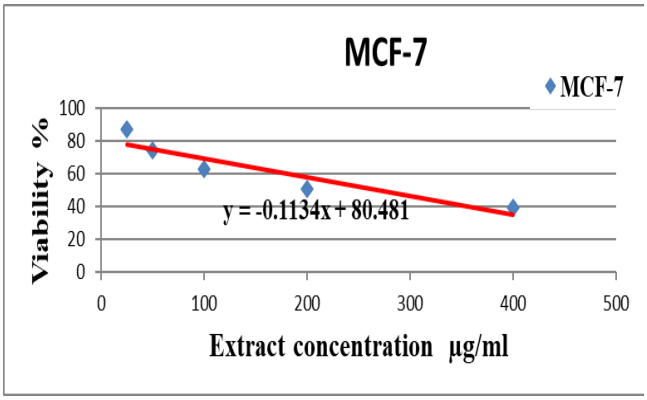


**Fig. 5 .** *Cytotoxicity effect and IC50 of date seeds extract on MCF-7 cells*

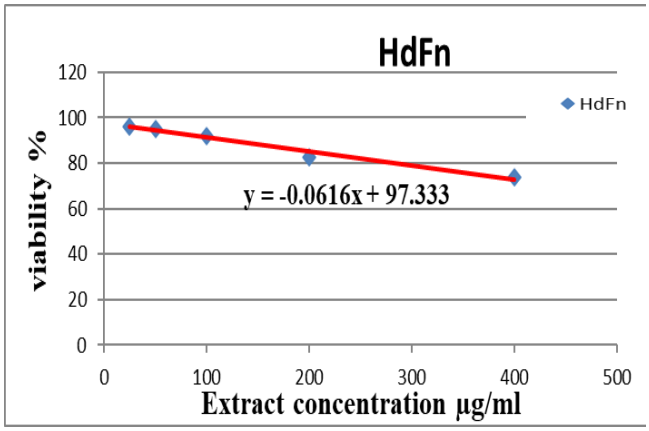


**Fig. 6.** *Cytotoxicity effect and IC50 of date seeds extract on HdFb cells*

dose-dependent. It was 120,102.4, 96.2, 99.8, and 97.6 % in 100, 50, 25, 12.5, 6.25 µg/ml concentrations, respectively. Statistically, only a concentration of 100 µg/ml has significantly increased when compared with untreated control, when the percentage of increase reached 120 %. Nuclear condensation is one of the most important characteristics of apoptosis (Bertheloot *et al*., 2021). Apoptosis involves a series of morphological and biochemical changes that lead to nuclei variations, including DNA ladder, peripheral chromatin clumping, and inter-nucleosomal DNA cleavage (Blankenberg *et al*., 2000).The elevating activity of the date seeds extract for total nuclear intensity may be regarded as sinapic acid, one of the most important constituents of the extract (Fig. 3) . Sinapic acid is associated with DNA damage by phosphorylated H2AX histone to γ-H2AX, which is followed by the formation of DNA double strands breaks due to DNA damage (Bertheloot *et al*., 2021).

The results in Table 3 showed a non-significant increase in cell membrane permeability compared with untreated control treatment. The increase percentages were 97.2, 92.6, 99.1,94, 79 .7 % in 100, 50, 25, 12.5 and 6.25 µg/ml concentrations, respectively. The extract contains many compounds like flavonols and polyphenols, which can induce oxidative stress for cancer cells membranes, leading to peroxidation of their lipids that affect cell membrane integrity and consequently increase cell membrane permeability (Powell and Brown, 2021).

Table 2 revealed decreased mitochondrial membrane permeability and reduced percentages of 73.8, 84.4, 98.9, 102.5, and 97.5 % in 100, 50, 25, 12.5 and 6.25 µg/ml concentrations, respectively. Only 100 µg/ml concentration appears to significantly decrease the

mitochondrial membrane permeability compared with negative control (73.8%). Other concentrations did not show any significant differences from the negative control. Ghazzawy *et al*. (2019,2022) referred to the anticancer ability of date seed extract by induction apoptosis. The transference pore of Mitochondrial permeability transference (mPTP) is a powerful modulator of programmed cell death (Kale *et al* .,2018). The wasting of proton driving force is caused by the loss of its barrier activity to protons, which leads to oxidative phosphorylation uncoupling, which may oppose the reaction of ATP synthase after synthesising ATP to consumption of ATP. Additional effects of mPTP opening include increased internal mitochondrial membrane permeability to small molecules, which raises the osmotic pressure of the mitochondrial matrix and may disrupt the mitochondrial membrane. (Kamini *et al* ., 2021).

The outcome of cytochrome C release in Table 2 revealed that date seed extract increased the cytochrome C release in breast cancer cells when treated with the extract concentrations in contrast to control untreated cells. The percentages of increase were 140.9, 127.4, 89.8, 100.1 and 98.6 % in concentrations of 100, 50, 25, 12.5 and 6.25 µg/ml, respectively. Statistically, only the 100 µg/ml concentration significantly increased cytochrome C release compared with control untreated Cells. The cytotoxicity of date seed extract on cancer cells *in vitro* possesses complicated ways that affect multiple pathways and parameters after toxic stress signals. In response to toxic stress signals, activated BH3- proteins, which lead to activation of BAK and BAX proteins (Huang *et al* ., 2021). Mitochondrial membrane permeability induced by BAX and BAK allows cytochrome C to escape into the cytoplasm from the mitochondrial intermembrane space (Kerkhofs *et al* ., 2021).

## Conclusion

The study concluded that the ethanolic extract of *P. dactylifera* seeds had a strong antioxidant and was rich in many antioxidant compounds. The extract appears to have strong cytotoxicity against breast cancer MCF7 and prostate cancer PC3 cancer cell lines, but MCF7 is more sensitive than PC3. The viability of normal HDFn cells was not affected by the extract. Date seeds can be helpful as a therapeutic alternative in eliminating cancer, which is considered the greatest threat to humanity and the problem of the present day time.

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## Conflict of interest

The authors declare that they have no conflict of interest.

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