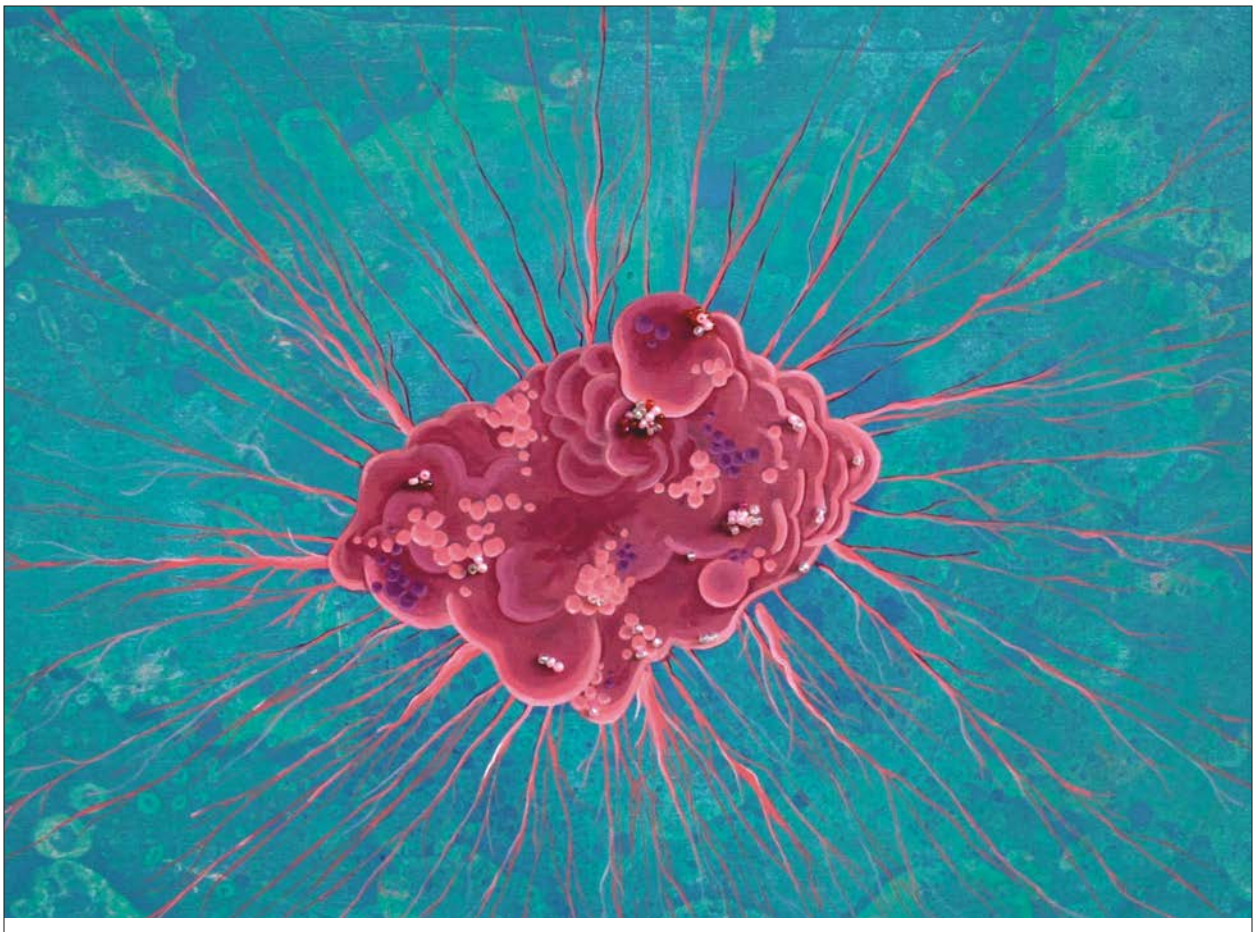

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Research Article
Cancer-fighting Phytochemicals of *Prunus armeniaca* and *Prunus domestica* Seeds Extracts

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Abstract

Background and Objectives: Several studies have been investigated the natural components as an alternative cancer therapy. This study aimed to address the antitumor efficacy of *Prunus armeniaca* seed extract (PASE) and *Prunus domestica* seed extract (PDSE). **Materials and Methods:** Phytochemical analysis and gas chromatography-mass spectroscopy (GC-MS) profile, human breast (MCF-7), hepatic (HepG-2) cancer cell lines and Ehrlich ascetic carcinoma (EAC) were used to determine the anticancer efficacy. **Results:** Total phenolic, flavonoids, saponin and anthocyanin in PASE were 1291 μg mL^{-1}, 159 μg mL^{-1}, 16 mg g^{-1} and 65 μg mL^{-1}, respectively. While, in PDSE were 729 μg mL^{-1}, 63 μg mL^{-1}, 7.6 mg g^{-1} and 89 μg mL^{-1}, respectively. The GC-MS analysis showed that the highest peak area (%) in PASE was octasiloxane-hexadecamethyl (17.04%) and in PDSE was hexadecanoic acid, trimethylsilyl ester (31.92%). *In vitro* inhibition concentration (IC_{50}) of PASE and PDSE against MCF-7 were 31.5 and 306, respectively. The IC_{50} of PASE and PDSE against HepG-2 were 22.8 and 430 μg mL^{-1}, respectively. The PASE had a potent anticancer activity higher than PDSE against EAC-bearing mice. **Conclusion:** PASE had a potent anticancer activity than PDSE due to their phytochemical's contents.

Key words: Anticancer, antioxidant, phytochemicals, *Prunus armeniaca*, *Prunus domestica*, seeds extracts

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

In traditional and alternative therapy, millions of people are using the medicinal plants for treatment of various diseases including cancer[1]. Medicinal plants are considered as potential sources of several chemical ingredients that used in drug discovery[2]. Plant-derived products led to reduce the chemical remedies in treatment and may reduce the adverse side effects of chemotherapy during the treatment of cancer patients[3].

Several treatment protocols have been applied to control cancer progression such as chemotherapy and radiotherapy. Efforts to reduce the side effects of the current treatment approaches are required. So far, the chemotherapy is still the best choice to treat the several types of cancer. Chemotherapy kills normal tissues leading to severe side effects such as leukopenia[4], renal and hepatic failure[5], as a result of increasing the free radicals and oxidative stress agents[6].

Many plant products have shown promising anti-cancer properties *in vitro* but have to be evaluated in humans[7]. Further study is required to determine the efficacy of such these plant products in treating cancers in pre-clinical and clinical settings. Several pre-clinical screenings for finding new anticancer agents were used the natural products of derived from plants resources[1]. The continuous efforts to find new therapeutic agents from natural products, several applied anticancer agents are approved such as paclitaxel, vinblastine and vincristine[8]. Plant-derived products could decrease the mortality rate in cancer patients, now-a-days the percentage of cure rates is 90% mainly due to the use of the plant in combination with synthetic chemotherapy for treatment[9].

Prunus armeniaca and *Prunus domestica* are members of the Rosaceae family, commonly cultivated under different climatic conditions. These fruits showed health-promoting properties associated with their nutritional value and potent antioxidants contents[10]. Apricot kernel is a good source of protein, fiber, oil and phenolic compounds. Pharmacologic studies have also shown that apricot kernels have antioxidant, antimicrobial and antitussive effects[11,12].

Prunus armeniaca fruit contains vitamin C, carotenoids and polyphenolics as antioxidant molecules, their extract has anti-inflammatory effect in rats and exhibited beneficial effects on growth performance, antioxidants and immune status of chickens[13,14]. In pre-clinical studies, Hwang *et al.*[15] proved that amygdalin from *P. armeniaca* has anti-inflammatory and antibacterial activities[15]. Screening chemical constituents in *P. domestica* fruit showed the presence of vitamin E, furfural, phytosterol, fatty acids, eugenol and maltol which have different therapeutic uses such as antiulcer potentials on Wistar albino rats and anti-diabetic effects in alloxan induced diabetic rats, due to its flavonoids content[16]. The PDSE induced apoptotic changes in human colon tumor cells and showed anti-proliferative activity due to their chemical composition[17]. This study was carried out to address the antioxidant and anticancer activities of PASE and PDSE. Human breast (MCF-7) and hepatic (HepG-2) cancer cell lines were used for *in vitro* anticancer assessments; in addition, Ehrlich ascetic carcinoma (EAC) mouse model was used for evaluating the antitumor efficacy *in vivo*. These findings demonstrated that PASE have potential antioxidant and antitumor properties much higher than PDSE.

MATERIALS AND METHODS

This study was carried out in Department of Zoology, Faculty of Science, Tanta University, Egypt, March, 2019.

Chemicals: Cisplatin (Cis-diamminedichloroplatinum II) was purchased from Sigma-Aldrich (St Quentin Fallavier, France). Vials were diluted by distilled water and the concentration was adjusted to 2 mg kg^{-1} b.wt. Aspartate amino transferase (AST), alanine amino transferase (ALT), urea, creatinine, superoxide dismutase (SOD), catalase (CAT) and malondialdehyde (MDA) kits were purchased from Biodiagnostic Company, Egypt.

Preparation of plant seeds extract: *Prunus armeniaca* and *P. domestica* were purchased from local market in Tanta city, Egypt. To prepare the methanolic extracts of the plant seeds, 50 g of seeds were collected, dried in shade and then crushed in a mortar and the powder mixed vigorously with 500 mL 70% (v/v) ethanol. The hydro-alcoholic extracts were filtered, the solvent was air-dried and the extracts were weighed and suspended in 0.9% sterile saline for further processing.

Phytochemicals analysis: Total phenolic of the extracts were determined using the Folin-Ciocalteu reagent, the absorbance was determined at 730 nm using a spectrophotometer. The total phenolic content was expressed as milligrams (mg) gallic acid equivalents (GAE g^{-1}) of extracts using gallic acid equivalents (GAE) calibration curve[18]. Total flavonoids were determined using the aluminum chloride colorimetric method and expressed as (mg) quercetin equivalent/gram of extract from a calibration curve of quercetin[19]. Phosphomolybdenum method was used to determine the total antioxidant capacities (TAC) that expressed as ascorbic acid equivalent[20]. Free radical scavenging capacity was evaluated spectrophotometrically. The absorbance of sample (As) and control (Ac) were measured at 517 nm, the scavenging activity on the DPPH radical was expressed as inhibition percentage[21]. Furthermore, saponin and anthocyanin contents were determined[22].

Gas chromatography and mass spectrum (GC-MS) profiling: The chemical composition and secondary metabolites constituents in the two seeds extract were performed using Trace GC 1310-ISQ mass spectrometer "GC-MS" (Thermo Scientific , Austin , TX , USA) with a direct capillary column TG-5MS (30 m×0.25 mm×0.25 µm film thickness). The column oven temperature was initially held at 50°C and then increased by 7°C min^{-1} to 230°C hold for 2 min increased to the final temperature 300°C by 30°C min^{-1} hold for 2 min. The injector and MS transfer line temperatures were kept at 270, 260°C, respectively. Helium was used as a carrier gas at a constant flow rate of 1 m min^{-1}. The diluted samples of 1 µL were injected using Auto-sampler (AS1300) coupled with GC in the split mode. The EL mass spectra were collected at 70 eV ionization voltages over the range of m/z 45-600 in full scan mode. The ion source temperature was set at 200°C. The components were identified by comparison of their retention times and mass spectra with those of WILEY 09 and NIST 11 mass spectral database.

Cell lines culture and cytotoxicity assessment by MTT assay: The human breast cancer (MCF-7) and hepatocellular carcinoma cell lines (HepG-2) were obtained from VACSERA Tissue Culture Unit (Cairo, Egypt). The cells were cultured in DMEM medium (GIBCO, New York, USA) supplemented with 10% heat-inactivated fetal bovine serum, 1% penicillin/streptomycin and 2% L-glutamine and centrifuged at 37°C for under 5% CO_2, 95% air. Passaging was done at 70-80% confluence. To assess the cytotoxic effects of the seeds extracts on the two cell lines, 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-tetrazolium bromide (MTT) assay protocol was used. The seeds extracts were diluted with saline to different concentrations (from 5-500 µg mL^{-1}) and applied to the MCF-7 and HepG-2 cells in triplicate, incubated at 37°C and 5% CO_2 for 24 h, then, 10 µL of MTT solution was added and incubated at 37°C for 4 h. The purple formazan crystal formed was dissolved by using DMSO. Cisplatin (Cis) was used as a positive standard. The absorbance was read at 570 nm using ELIZA reader. The concentration of the extracts that inhibit 50% of cells (IC_{50}) was calculated from the sigmoidal curve.

Mice and Ehrlich ascites carcinoma (EAC) tumor cells inoculation: Female swiss albino mice (20±2 g) were obtained from National Research Center (NRC, Cairo, Egypt). Animals were housed (5/cage), in 12 h/12 h dark/light cycle under laboratory condition of temperature and humidity. Mice were kept for a week before starting the experiment for adaptation and then handled according to the ethical guidelines approved by the animal care and use committee, Faculty of Science, Tanta University (ACUC-SCI-TU), Egypt. The EAC cells were collected from the tumor bearing mice purchased from the National Cancer Institute (NCI, Cairo, Egypt). The viable and dead cells were counted using trypan blue method and then adjusted at 2×10^6 cells/mouse for intraperitoneal (i.p) inoculation.

Experimental design: Fifty female albino mice were divided into 5 groups (n = 10/group). The 1st group (Group 1) was used as a negative control. From the 2nd to the 5th groups of mice were inoculated i.p with 2×10^6 EAC cells/mouse. After 1 day of tumor cells inoculation, the 2nd, 3rd, 4th and 5th groups of mice were injected daily for 6 consecutive days with 200 µL of PBS, Cis (2 mg kg^{-1}), PASE (100 mg kg^{-1}) and PDSE (100 mg kg^{-1}), respectively. At day 14, all mice were bled via the orbital plexus to collect blood for hematological and biochemical assessments. Mice were then sacrificed to harvest tumor cells for tumor volumes, counts, live and dead cells assessment. Finally, liver tissues were collected for detection of some of oxidative stress parameters.

Determination of total body weight changes: All groups of mice were weighted at the beginning (initial b.wt.) and at the end of the experiment (final b.wt). The percentage of the change in the total body weight (TBW) was calculated as follow:

$$\text{TBW (\%)} = \frac{\text{Final b.wt.-Initial b.wt.}}{\text{Initial b.wt.}} \times 100$$

Hematological and biochemical analysis: Platelets, hemoglobin content (Hb g dL^{-1}), red blood cells (RBCs), white blood cell (WBCs) and differential counts were determined from fresh blood samples obtained from the orbital plexus of all groups under the study using the electronic blood counter.

Alanine transaminases (ALT), aspartate transaminases (AST), urea, creatinine, superoxide dismutase (SOD), catalase (CAT) and malondialdehyde (MDA) were determined by the colorimetric methods using their commercial research kits (Diamond-Diagnostics, Egypt).

Statistical analysis: One-way analysis of variance (ANOVA) was used to assess the significant differences among treatment groups. Dunnett test was used to compare all groups against the control group to show the significant effect of treatment. The criterion for statistical significance was set at $p<0.05$ or $p<0.01$. All data are presented as Mean±SD.

RESULTS

Phytochemical analysis of PASE and PDSE: Both extracts were quantitatively analyzed, the data showed that the concentrations of the total phenolic, flavonoids, saponin and

anthocyanin in PASE were 1291 and 159 μg mL^{-1}, 16 mg g^{-1} and 65 μg mL^{-1}, respectively. Interestingly, the concentrations of these compounds in PDSE were 729 μg mL^{-1}, 63 μg mL^{-1}, 7.6 mg g^{-1} and 89 μg mL^{-1}, respectively. The results showed that in PASE, TAC, DPPH and (IC_{50}) were 152 μg mL^{-1}, 61% and 81 μg mL^{-1}, respectively, while in PDSE were 72 μg mL^{-1}, 40% and 125 μg mL^{-1}, respectively (Table 1).

GC-MS profiling of PASE and PDSE: The GC-MS analysis which is considers one of the most important techniques for identification chemical constituents. The GC-MS profiling showed that in PASE, the peak area (%) of octasiloxane hexadecamethyl/1-monolinoleoylglycerol trimethyl silyl ether/9,10-secocholesta-5,7,10 (19)-triene-1,3-iol 25-[(trimethyl silyl)oxy]/2,3-dihydroxypropyl palmitate/4α-phorbol 12,13-didecanoate and Pregnane-320á-diol14à18à-[4-thyl-3-oxo-(1-oxa-4-azabutane-1,4-diyl)]-diacetate were 17.04, 9.33, 8.56, 5.09, 4.29 and 4.08 μg g^{-1} extract, respectively (Table 2). In PDSE, GC-MS analysis showed that the peak area (%) of hexadecanoic acid trimethylsilyl ester/linolenic acid trimethylsilyl ester/9,12-Octadecadienoic acid-trimethylsilyl ester and phosphoric acid dioctadecyl ester were 31.92, 24.30, 12.37 and 5.31 μg g^{-1} extract, respectively (Table 3).

Table 1: Quantitative analysis of phytochemical components in PASE and PDSE

Parameters	PASE	PDSE
Total phenolic (μg mL^{-1})	1291	729
Total flavonoids (μg mL^{-1})	159	63
TAC (μg mL^{-1})	152	72
DPPH scavenging (%)	61	40
IC_{50} of DPPH (mg mL^{-1})	81	125
Saponin (mg g^{-1})	16	7.6
Anthocyanin (μg mL^{-1})	65	89

Table 2: GC–MS profiling of PASE

No.	RT (min)	Name	MF	M.Wt	Peak area (%)
1	6.10	Cevane-3,4,14,15,16,20-hexol, 4,9-epoxy, 3-acetate	$C_{29}H_{45}NO_8$	535	1.63
2	11.91	Chlortetracycline	$C_{22}H_{23}ClN_2O_8$	478	1.11
3	13.22	D-ribitol, 1,4-anhydro-1-c-(1,3-diphenyl-2-imidazolidinyl)-2,3-o-(1 methylethylidene)-5-o-(phenylmethyl)	$C_{30}H_{34}N_2O_4$	486	1.40
4	15.43	3-[18-(3-Hydroxy-propyl)-3,3,7,12,17-pentam ethyl-2,3,22,24-tetrahydro-porphin-2-yl]propan-1-ol	$C_{31}H_{38}N_4O_2$	498	1.16
5	16.03	3-[3-(1,5-Dimethylhexyl)-7-(2-hydroxy-1-methylethyl)-3a,6,9b-trimethyl-2,3,3a,4,5,6,7,8,9,9b-decahydro-1H-cyclopenta-6-naphthylpropanoate, methyl ester	$C_{31}H_{54}O_3$	474	2.48
6	20.52	4α-Phorbol 12,13-didecanoate	$C_{40}H_{64}O_8$	672	4.29
7	20.76	Psi, psi.-Carotene, 1,1',2,2'-tetrahydro-1,1'-dimethoxy	$C_{42}H_{64}O_2$	600	3.03
8	21.59	2,3-dihydroxypropyl palmitate	$C_{19}H_{38}O_4$	330	5.09
9	25.02	3-(tetradecanoyl oxy)-2-[(trimethylsilyl)oxy]propyl myristate	$C_{34}H_{68}O_5Si$	584	1.08
10	25.24	4'-apo-á,.psi.-carotenoic acid	$C_{35}H_{46}O_2$	498	1.02
11	25.96	Lanosta-7,9(11)-dien-18-oic acid, 22,25-epoxy-3,17,20-trihydroxy-, ç-lactone, (3á)	$C_{30}H_{44}O_5$	484	1.49
12	26.71	Trimethylsilyl (13E)-9-(methoxyimino)11,15-bis[(trimethylsilyl)oxy]prost-13-en-1-oate	$C_{30}H_{61}NO_5Si_3$	599	2.61
13	27.00	Sarreroside	$C_{30}H_{42}O_{10}$	562	1.35
14	28.08	4H-Cyclopropa[5',6']benz[1',2':7,8]azuleno[5,6-b]oxiren-4-one,8,8a-bis(acetyloxy)-2a-[(acetyloxy)methyl]-1,1a,1b,1c,2a,3,3a,6a,6b,7,8,8a-dodecahydro-3,3a,6b-trihydroxy-1,1,5,7-tetramethyl	$C_{26}H_{34}O_{11}$	522	1.27
15	29.09	9,12,15-Octadecatrienoic acid, 2,3-bis[(trimethylsilyl)oxy]propyl ester, (Z,Z,Z)	$C_{27}H_{52}O_4Si_2$	496	1.06
16	29.86	(5á)Pregnane-3,20á-diol,14à,18à-[4-methyl-3-oxo-(1-oxa-4-azabutane-1,4-diyl)]-,diacetate	$C_{28}H_{43}NO_6$	489	4.08
17	30.61	9,10-Secocholesta-5,7,10(19)-triene-1,3-diol, 25-[(trimethylsilyl)oxy]-, (3á,5Z,7E)	$C_{30}H_{52}O_3Si$	488	8.56
18	31.78	9-Octadecenoic acid, (2-phenyl-1,3-dioxolan-4-yl)methyl ester, cis	$C_{28}H_{44}O_4$	444	5.92
19	33.41	Octasiloxane, 1,1,3,3,5,5,7,7,9,9,11,11,13,13,15,15-hexadecamethyl	$C_{16}H_{50}O_7Si_8$	578	17.04
20	33.69	1-Monolinoleoylglycerol trimethylsilyl ether	$C_{27}H_{54}O_4Si_2$	498	9.33

MF: Molecular formula, M.Wt: Molecular weight, RT: Retention time

Table 3: GC-MS profiling of PDSE

No.	RT (min)	Name	MF	M.Wt	Peak area %
1	3.38	Trimethylsilyl cyclopentanecarboxylate	$C_9H_{18}O_2Si$	186	1.06
2	4.13	Glycine, N-acetyl-, trimethylsilyl ester	$C_7H_{15}NO_3Si$	189	3.49
3	15.79	1-Hexadecanol, 2-methyl	$C_{17}H_{36}O$	256	1.11
4	16.77	Hexadecanoic acid, trimethylsilyl ester	$C_{19}H_{40}O_2Si$	328	31.92
5	17.83	Phosphoric acid, dioctadecyl ester	$C_{36}H_{75}O_4P$	602	5.31
6	17.93	D-Glucopyranoside, methyl 2 (acetylamino)-2-deoxy-3-O (trimethylsilyl), cyclic methylboronate	$C_{13}H_{26}BNO_6Si$	331	1.21
7	18.32	2,3-Dihydroxynaphthoic acid	$C_{11}H_8O_4$	204	2.36
8	18.95	Trans-9-Octadecenoic acid, trimethylsilyl ester	$C_{21}H_{42}O_2Si$	354	2.17
9	19.04	9,12-Octadecadienoic acid (Z,Z)-trimethylsilyl ester	$C_{21}H_{40}O_2Si$	352	12.37
10	19.30	Linolenic acid, trimethylsilyl ester	$C_{21}H_{38}O_2Si$	350	24.30
11	21.01	Trimethylsilyl-9,11,15 tris (trimethylsilyl) oxy prosta 5,13-dien-1-oate	$C_{32}H_{66}O_5Si_4$	642	1.45
12	23.77	3',8,8'-Trimethoxy-3-piperidyl-2,2'-binaphthalene-1,1',4,4'-tetrone	$C_{28}H_{25}NO_7$	487	3.06

MF: Molecular formula, M.Wt: Molecular weight, RT: Retention time

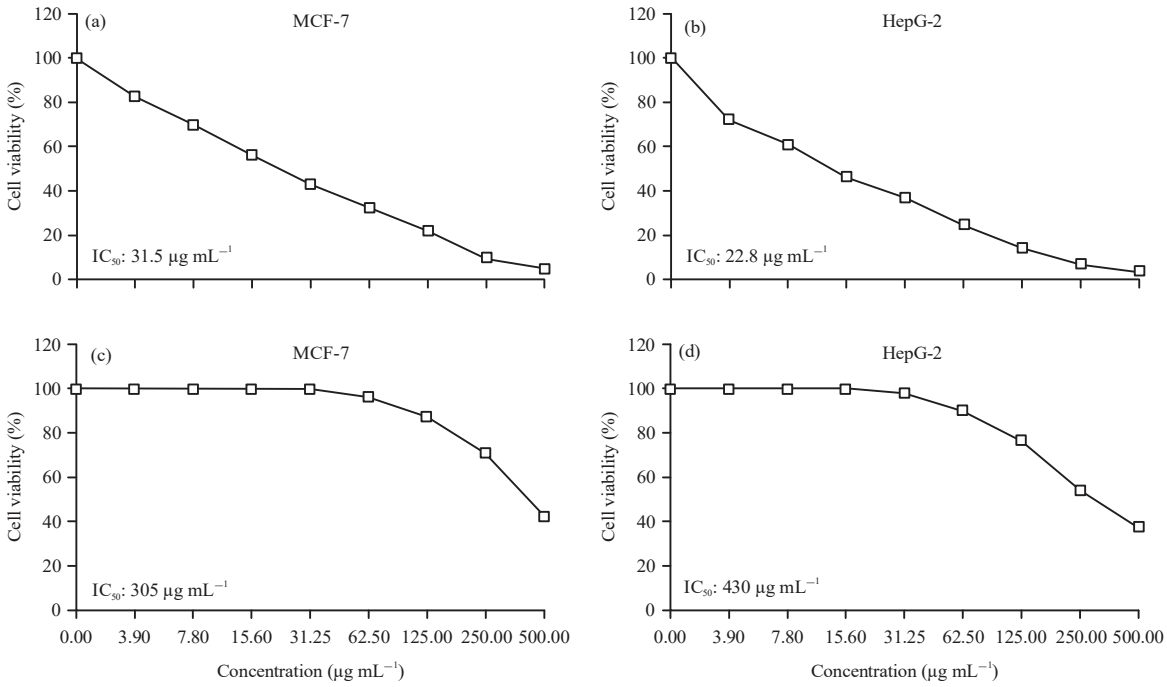

Fig. 1(a-d): Effect of the *in vitro* treatment with PASE and PDSE on MCF-7 and HepG-2 viability

***In vitro* cytotoxicity assays:** After GC-MS analysis of both extracts, we further tested the anticancer activity against human breast (MCF-7) and hepatocellular (HepG-2) cancer cell lines. The results showed that the IC_{50} of PASE were 31.5 and 22.8 µg mL^{-1} against MCF-7 and HepG-2 cell lines, respectively. While in PDSE the IC_{50} were 305 and 430 µg mL^{-1} against the 2 cancer cell lines under the same conditions, respectively (Fig. 1).

***In vivo* antitumor activities:** The study was further extended to address the efficacy of both extracts as antitumor agents *in vivo*. To test the efficacy of these extracts on tumor model, EAC-cells were inoculated (2×10^6/mouse) in different group of mice. The Group 1-5 were treated by normal saline, Cis (2 mg kg^{-1}) or with 100 mg kg^{-1} of both seeds extract from day 1-6. After 14 days, all groups were sacrificed to estimate the extracts antitumor efficacy. The results showed that the tumor volume and the tumor cells count were decreased significantly in the group of mice which was treated with PASE (100 mg kg^{-1}) when compared to their control. Unlike the effect of PASE on tumor bearing mice, PDSE did not show any antitumor activity (Table 4).

Total body weight changes: The change in the total body weight (TBW) was monitored as an indirect index for tumor progression in our model. As shown in Fig. 2, the change in the TBW in the group of EAC-bearing mice which was treated with PASE (Group 4) was decreased when compared to their control (EAC-bearing mice). On the other hand, an increase in the TBW change was observed in the group of EAC-bearing mice that was treated with PDSE (Group 5) as shown in Fig. 2. The group of mice inoculated with EAC-cells alone (Group 2) showed the highest change in the TBW, while the group of mice which was inoculated with EAC-cells and treated with Cis (Group 3) showed the lowest change in the total body weight.

Hematological and biochemical assessments: Treatment with both extracts led to significant increase in the total white blood cells (WBCs) when compared to control group. The number of monocytes cells was increased in concomitant with the increase of total WBCs in the group of mice which was treated with both seed's extracts (Group 4 and 5). Tumor bearing mice showed a significant decrease in the total WBCs when compared to the control group of mice (Table 5).

Biochemically, the treatment with PASE led to enhance the liver and kidneys functions indicated by the levels of aspartate transaminase (AST), alanine transaminase (ALT), urea and creatinine when compared to the group of mice which was inoculated with tumor alone (Group 2) and tumor bearing mice that was injected with Cis alone (Group 3). The levels of hepatic SOD and CAT were significantly increased in the group of mice which treated with PASE in concomitant with a decrease in the level MDA. Tumor bearing mice treated with

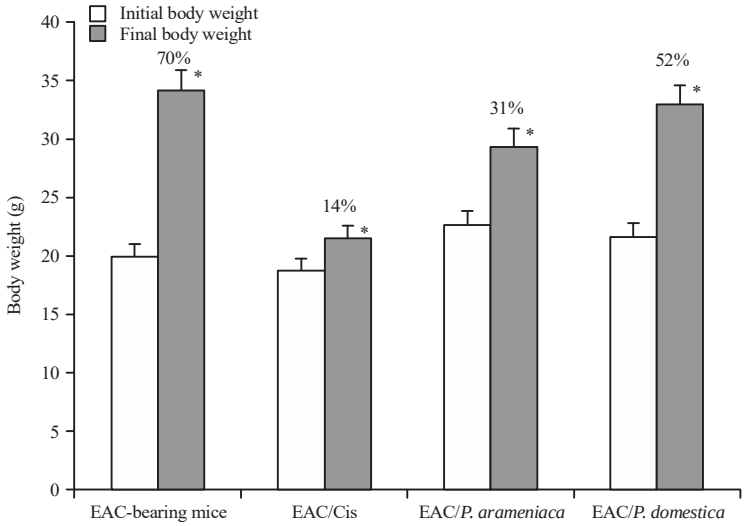

Fig. 2: Total body weight changes after treatment with both extracts in the tumor bearing group of mice
*p<0.05

Table 4: Tumor profile of the different groups under study

Groups	Total volume (×10⁶)	Percentage	Total count (×10⁶)	Percentage	Live cells (×10⁶)	Percentage	Dead cells (×10⁶)	Percentage
EAC-bearing mice	11.00±1.5[a]	-	693.00±5.3[a]	-	629.00±4.3[a]	-	64.00±3.8[b]	-
EAC-bearing mice/Cis	2.50±0.9[c]	85	215.00±3.4[d]	97	162.00±2.5[d]	74	53.00±1.9[c]	-53
EAC-bearing mice/*P. armeniaca*	6.75±0.8[b]	-14	384.00±4.3[c]	45	336.00±3.8[c]	100	48.00±2.3[c]	-71
EAC-bearing mice/*P. domestica*	9.25±1.7[a,b]	11	642.00±4.2[b]	7	568.00±2.9[b]	31	74.00±2.5[a]	100
F-value	24.77		7898.78		11695.63		54.71	
p-value	0.000		0.000		0.000		0.000	

Different letters show significant difference among all treatments

Table 5: Complete blood count in the different groups under study

Groups	Platelet (×10³ µL⁻¹)	Hb (g dL⁻¹)	RBCs (×10⁶ uL⁻¹)	WBCs (×10³ uL⁻¹)	Differential count: Neut. (%)	Lymph. (%)	Mon. (%)
Naïve control	980.00±35[b]	14.40±2.8	8.70±0.9	4.30±2.0[b]	10.00±1.6[d]	84.50±3.1[a]	11.00±1.5[d]
EAC-bearing mice	999.00±41[b]	10.20±1.7	6.70±0.8	12.20±1.8[a]	33.30±2.5[b]	39.00±2.6[c]	33.00±2.8[b]
EAC-bearing mice/Cis	760.00±33[c]	11.20±1.9	7.40±1.3	13.10±1.5[a]	40.30±2.7[a]	30.60±3.0[d]	22.00±3.7[c]
EAC-bearing mice/*P. armeniaca*	842.00±52[c]	11.60±2.4	8.10±1.2	9.10±2.3[a,b]	14.50±2.1[d]	69.50±3.7[b]	45.00±2.8[a]
EAC-bearing mice/*P. domestica*	1363.00±58[a]	11.50±2.6	8.10±1.9	11.20±2.7[a]	20.60±1.9[c]	44.00±2.5[c]	44.00±3.1[a]
F-value	79.79	1.37	1.08	8.36	101.00	168.99	77.31
p-value	0.000	0.312	0.416	0.003	0.000	0.000	0.000

Different letters show significant difference among all treatments, Neut.: Neutrophils, Lymph.: Lymphocytes, Mon.: Monocytes

Table 6: Serum aspartate transaminase (AST), alanine transaminase (ALT), urea and creatinine. hepatic superoxide dismutase (SOD), catalase (CAT) and malondialdehyde (MDA) levels in the different group under study

Groups	AST (µ L⁻¹)	ALT (µ L⁻¹)	Urea (mg dL⁻¹)	Creatinine (mg dL⁻¹)	SOD (IU mg⁻¹ wet liver tissue)	CAT (µM of decomposed H_2O_2 min⁻¹ mg⁻¹ wet liver tissue)	MDA (nmol g⁻¹ wet liver tissue)
Naïve control	87.40±2.9[e]	25.90±0.9[d]	20.30±1.1[d]	0.37±0.07[c]	11.60±0.46[a]	51.00±2.9[a]	118.9±2.8[d]
EAC-bearing mice	129.80±3.5[b]	49.20±1.2[b]	41.50±1.9[b]	0.68±0.09[b]	5.10±0.28[d]	12.00±1.8[c]	310.3±3.9[b]
EAC-bearing mice/Cis	189.10±2.7[a]	82.70±3.3[a]	88.20±1.5[a]	0.94±0.08[a]	3.20±0.24[e]	8.00±1.9[c]	406.7±4.4[a]
EAC-bearing mice/*P. armeniaca*	101.70±2.1[d]	35.80±2.3[c]	33.30±2.1[c]	0.43±0.10[c]	8.50±0.39[b]	30.00±2.8[b]	220.4±2.9[d]
EAC-bearing mice/*P. domestica*	121.20±2.6[c]	53.10±2.7[b]	39.60±1.8[b]	0.52±0.11[b,c]	6.60±0.29[c]	25.00±1.9[b]	252.1±3.2[c]
F-value	584.68	271.16	676.06	18.93	267.34	162.69	2799.1
p-value	0.000	0.000	0.000	0.000	0.000	0.000	0.000

Different letters show significant difference among all treatments

PDSE did not show amelioration in regard to the levels of SOD or CAT in liver tissues when compared to the group of mice which was inoculated with tumor alone. Treatment tumor bearing mice with PDSE led to a decrease in the levels of SOD, CAT and increase the level of MDA when compared to their control (Table 6).

DISCUSSION

This study was conducted to evaluate the phytochemical compositions of PASE and PDSE by qualitative, quantitative and GC-MS analysis. Furthermore, the study was extended to address the anticancer efficacy of both seeds extract *in vitro* and *in vivo* using MCF-7, HepG-2 cell lines and EAC-bearing mice model, respectively. According to these findings, the results indicated that the total phenolics, flavonoids and saponin contents were higher in PASE than those in PDSE. Also, the total antioxidant capacity (TAC) and DPPH scavenging activity were higher in PASE than their levels in PDSE. Our data agreed with previous study reported that there was a significant positive correlation between the secondary metabolites such as phenolics, flavonoids and saponins with the TAC[5]. Based on our finding, PASE was found to be rich with some important phytochemicals' constituents (secondary metabolites) could be potential candidates as anticancer agents.

Plants secondary metabolites such as phenols, flavonoids and glycosides were characterized by gas chromatography and mass spectrum (GC-MS) analysis[23]. The present study revealed that by GC-MS analysis, PASE contains several bioactive compounds including octasiloxane, linoleate, palmitate and pregnane. Such these compounds having the nature of phenolic, flavonoids and fatty acids could have potential effects as antimicrobial, anti-inflammatory, antioxidant and anticancer agents[24].

Screening the antitumor efficacy *in vitro* and *in vivo* showed that of PASE has a potent antitumor activity than of PDSE against MCF-7 and HepG-2 cell lines *in vitro* and against EAC-bearing mice *in vivo*. The potent anticancer activity of PASE could be due to their phytochemical contents and the presence of active chemical ingredients having anticancer properties. These finding agreed with another study which showed that the MK615, extracted from Japanese apricot has been shown a potent effect against cancer cell lines *in vitro*[25].

Several studies reported that the natural compounds present in some medicinal plants have a potent antioxidant [26] and anticancer effects and could ameliorate the side effects of chemotherapy. It has been demonstrated that apricot-feeding led to cardio and hepato-protective effect due to its antioxidant phenolic levels in rats[27]. Furthermore, another study showed that the treatment with apricot extract could protect against the kidney injury and oxidative stress[28]. It has found also that treatment with apricot extracts have anti-inflammatory, antiparasitic, antiaging and reno-protective effects due to their contents of essential vitamins and fibers[29]. Upon treating tumor bearing mice with PASE, the levels of liver function enzymes (ALT and AST) as well as kidney function parameters (urea and creatinine) were significantly diminished when compared with tumor bearing mice treated with Cis alone which induce liver and kidneys functions impairment that indicate the improvement of liver and kidneys functions by PASE. Interestingly, the antioxidant enzymes (SOD and CAT) were increased, while the level of lipid peroxidation end product (MDA) was decreased as compared to Cis-treated group of mice that showed high oxidative stress. This could be due to the presence of many active components which act as antioxidants able to scavenge free radicals resulted from the growing of tumor cells in mice. In conclusion, PASE showed a potent *in vitro* and *in vivo* anticancer activity along with improvement of liver and kidneys functions as well as antioxidants enzymes *in vivo* due to the presence of high levels of potent secondary metabolites such as phenolics, flavonoids, saponin and other chemical constituents.

SIGNIFICANT STATEMENT

This study discovers the possible antitumor effect of PASE and PDSE seed extracts that can be beneficial due to their phytochemicals and antioxidant constituents. This study will help in using herbal medicine in cancer treatment.

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REFERENCES

1. Cragg, G.M. and D.J. Newman, 2005. Plants as a source of anti-cancer agents. J. Ethnoharmacol., 100: 72-79.
2. Balunas, M.J. and A.D. Kinghorn, 2005. Drug discovery from medicinal plants. Life Sci., 78: 431-441.
3. Iqbal, J., B.A. Abbasi, T. Mahmood, S. Kanwal, B. Ali, S.A. Shah and A.T. Khalil, 2017. Plant-derived anticancer agents: A green anticancer approach. Asian Pac. J. Trop. Biomed., 7: 1129-1150.
4. Huang, A., M. Ma, B. Jin and B. Han, 2016. Chemotherapy-induced leukopenia as a prognostic factor in patients with metastatic non-small cell lung cancer treated with platinum-based chemotherapy. Int. J. Clin. Exp. Med., 9: 5241-5248.

5. El-Naggar, S.A., I.B. Abdel-Farid, H.A. Elgebaly and M.O. Germoush, 2015. Metabolomic profiling, antioxidant capacity and *in vitro* anticancer activity of some compositae plants growing in Saudi Arabia. Afr. J. Pharm. Pharmacol., 9: 764-774.
6. Conklin, K.A., 2004. Chemotherapy-associated oxidative stress: Impact on chemotherapeutic effectiveness. Integr. Cancer Ther., 3: 294-300.
7. El-Naggar, S.A., A.A. Alm-Eldeen, M.O. Germoush, K.F. El-Boray and H.A. Elgebaly, 2015. Ameliorative effect of propolis against cyclophosphamide-induced toxicity in mice. Pharm. Biol., 53: 235-241.
8. Noble, R.L., 1990. The discovery of the vinca alkaloids-chemotherapeutic agents against cancer. Biochem. Cell Biol., 68: 1344-1351.
9. Einhorn, L.H. and J. Donohue, 2002. *Cis*-diamminedichloroplatinum, vinblastine and bleomycin combination chemotherapy in disseminated testicular cancer. J. Urol., 167: 928-932.
10. Slimestad, R., E. Vangdal and C. Brede, 2009. Analysis of phenolic compounds in six Norwegian plum cultivars (*Prunus domestica* L.). J. Agric. Food Chem., 57: 11370-11375.
11. Durmaz, G. and M. Alpaslan, 2007. Antioxidant properties of roasted apricot (*Prunus armeniaca* L.) kernel. Food Chem., 100: 1177-1181.
12. Yigit, D., N. Yigit and A. Mavi, 2009. Antioxidant and antimicrobial activities of bitter and sweet apricot (*Prunus armeniaca* L.) kernels. Braz. J. Med. Biol. Res., 42: 346-352.
13. Minaiyan, M., A. Ghannadi, M. Asadi, M. Etemad and P. Mahzouni, 2014. Anti-inflammatory effect of *Prunus armeniaca* L. (Apricot) extracts ameliorates TNBS-induced ulcerative colitis in rats. Res. Pharm. Sci., 9: 225-231.
14. Kalia, S., V.K. Bharti, A. Giri and B. Kumar, 2017. Effect of *Prunus armeniaca* seed extract on health, survivability, antioxidant, blood biochemical and immune status of broiler chickens at high altitude cold desert. J. Adv. Res., 8: 677-686.
15. Hwang, H.J., P. Kim, C.J. Kim, H.J. Lee and I. Shim *et al*., 2008. Antinociceptive effect of amygdalin isolated from *Prunus armeniaca* on formalin-induced pain in rats. Biol. Pharm. Bull., 31: 1559-1564.
16. Nayudu, S.T. and K. Sowjanya, 2017. Anti-diabetic activity of methanolic extract of *Prunus domestica*. Int. J. Recent Innovat. Trends Comput. Commun., 5: 213-220.
17. Savić, I.M., V.D. Nikolić, I.M. Savić-Gajić, T.D. Kundaković, T.P. Stanojković and S.J. Najman, 2016. Chemical composition and biological activity of the plum seed extract. Adv. Technol., 5: 38-45.
18. Singleton, V.L., R. Orthofer and R.M. Lamuela-Raventos, 1999. Analysis of total phenols and other oxidation substrates and antioxidants by means of Folin-Ciocalteu reagent. Methods Enzymol., 299: 152-178.
19. Zhishen, J., T. Mengcheng and W. Jianming, 1999. The determination of flavonoid contents in mulberry and their scavenging effects on superoxide radicals. Food Chem., 64: 555-559.
20. Prieto, P., M. Pineda and M. Aguilar, 1999. Spectrophotometric quantitation of antioxidant capacity through the formation of a phosphomolybdenum complex: Specific application to the determination of vitamin E. Anal. Biochem., 269: 337-341.
21. Blois, M.S., 1958. Antioxidant determinations by the use of a stable free radical. Nature, 181: 1199-1200.
22. Ebrahimzadeh, H. and V. Niknam, 1998. A revised spectrophotometric method for determination of triterpenoid saponins. Ind. Drugs, 35: 379-381.
23. Lewis, K. and F.M. Ausubel, 2006. Prospects for plant-derived antibacterials. Nat. Biotechnol., 24: 1504-1507.
24. Kumar, P.P., S. Kumaravel and C. Lalitha, 2010. Screening of antioxidant activity, total phenolics and GC-MS study of *Vitex negundo*. Afr. J. Biochem. Res., 4: 191-195.
25. Adachi, M., Y. Suzuki, T. Mizuta, T. Osawa and T. Adachi *et al*., 2007. The "Prunus mume Sieb. et Zucc" (Ume) is a rich natural source of novel anti-cancer substance. Int. J. Food Propert., 10: 375-384.
26. Kan, T., M. Gundogdu, S. Ercisli, F. Muradoglu and F. Celik *et al*., 2014. Phenolic compounds and vitamins in wild and cultivated apricot (*Prunus armeniaca* L.) fruits grown in irrigated and dry farming conditions. Biol. Res., Vol. 47. 10.1186/0717-6287-47-46.
27. Raj, V., A.K. Mishra, A. Mishra and N.A. Khan, 2016. Hepatoprotective effect of *Prunus armeniaca* L. (Apricot) leaf extracts on Paracetamol induced liver damage in Wistar rats. Pharmacogn. J., 8: 154-158.
28. Vardi, N., H. Parlakpinar, F. Ozturk, B. Ates and M. Gul *et al*., 2008. Potent protective effect of apricot and β-carotene on methotrexate-induced intestinal oxidative damage in rats. Food Chem. Toxicol., 46: 3015-3022.
29. Miyazawa, M., H. Utsunomiya, K.I. Inada, T. Yamada, Y. Okuno, H. Tanaka and M. Tatematsu, 2006. Inhibition of *Helicobacter pylori* motility by (+)-Syringaresinol from unripe Japanese apricot. Biol. Pharm. Bull., 29: 172-173.