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Phenolic composition, antioxidant and antibacterial properties, and *in vitro* anti-HepG2 cell activities of wild apricot (*Armeniaca Sibirica* L. Lam) kernel skins

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ABSTRACT

The polyphenols profiles of the methanol extracts of bitter apricot [*Armeniaca Sibirica* (L.)] kernel skins (AKS) were analysed by liquid chromatography-electrospray ionization mass spectrometry. The antioxidan, anticancer effect on HepG2 cell and antibacterial properties of the AKS polyphenol extracts were further characterized *in vitro*. Polyphenol compounds (35), including nine phenolic acids, thirteen anthocyanins and thirteen flavonoids, were identified in AKS for the first time. The content of apigenin 7-*O*-glucoside, (cyanidin 3-(4″-acetylrutinoside), 3- (6″-acetylglucoside)-5-glucoside and salicylic acid was relatively high than the others. The AKS polyphenols strongly reduced Fe^{3+} and exhibited good scavenging activity towards 2,2′-azino-bis(3-ethylbenzothiazoline-6-sulphonic acid) free radicals, 1,1-diphenyl-1-picrylhydrazyl free radicals, hydroxyl radicals, superoxide anions and hydrogen peroxide. The AKS polyphenols could regulate oxidant stress in HepG2 cells by downregulating reduced glutathione, upregulating oxidative glutathione, malondialdehyde and advanced oxidation protein products, and reduced cell viability to induce apoptosis of HepG2 cells *in vitro*. The AKS polyphenols showed strong antibacterial activity against *Escherichia coli*, *Staphylococcus aureus*, *Bacillus subtilis*, *Acetobacter aceti* and *Bacillus cereus*. Therefore, the antioxidant, inhibitory effect on HepG2 cells and antimicrobial activity of the AKS polyphenols were distinct and worthy of further consideration for medical industry applications.

1. Introduction

Apricot (*Prunus* sp.) is an important fruit crop worldwide, belonging to a large family, the Rosaceae. At present, apricot is grown in the Mediterranean Basin and moderate regions including ex-Soviet Union countries, Iran, China, Japan, South Africa and the United States (Hansakon et al., 2019). More than 3.8 million tons of apricots were produced in 2012, as disclosed by the Food and Agricultural Organization Statistics Database (FAOSTAT) in 2013 (Galiñanes et al., 2015). Due to the significant amounts of nutrients such as oils, proteins, amino acids, carbohydrates, soluble sugars, minerals, vitamins, and fibres in the apricot, apricot kernel exhibits a wide range of biological activity and is typically used in a variety of foods as well as in the cosmetics industry (Lee, 2014; Rai et al., 2016). In the apricot kernel processing industry, removing the apricot kernel skin and debitterizing are the two important steps to improve the quality and commercial value of the processed products, and to debitterize the high content of amygdalin (potentially to a xigenic compound) in apricot kernels (Zhang et al., 2016) Numerous studies have shown that the blanching and debitterizing water used during the previous two steps contains highly valuable compounds such as proteins, reducing sugars, polysaccharides, phenolics and amygdalin (Garrido et al., 2010), and the radical-scavenging capacities of this water were highly correlated with these identified phenolic compounds (Han et al., 2013; Yiğit et al., 2009; Zhang et al., 2018); It has been reported that apricot kernels has much higher antioxidant activity and phenolic content than the flesh fruit

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(Soong and Barlow, 2004). The phenolic compounds of apricot kernels possess a wide range of health benefits, such as free-radical scavenging property, anticancer activity, prevention of coronary heart diseases and antimicrobial properties (Dulf et al., 2017; Korekar et al., 2011; Pistollato et al., 2015). However, compared to sweet almond, the chemical composition and activity of apricot kernel skin are less commonly reported (Han et al., 2013). Almond skins have been proposed as a source of bioactive polyphenols. Flavonoids and phenolic acids, including flavonols, flavanols, flavanones and simple phenolic acids, were identified in almond skins and their antioxidant and free-radical scavenging activity has been reported (Lu et al., 2018; Mandalari et al., 2010). To increase the value of by-products and to reduce economic and environmental issues, the bioactive compounds in apricot kernels skins should be evaluated, extracted and used as beneficial ingredients in the apricot processing industry, as well as for their economic potential.

Wild apricot [*Armeniaca Sibirica* (L.) Lam, syn. Siberian apricot] is one kind of bitter apricot that belongs to the Armeniaca genus of the Rosaceae family. Compared to the sweet kernels, the use of bitter apricot kernels for human nutrition is limited because of their content of the toxic, cyanogenic glycoside amygdalin. Consequently, as a traditional oriental medicine, bitter apricot kernels has been widely used to cure respiratory disorders (coughing, wheeze, asthma, emphysema, and bronchitis) and skin diseases (acne vulgaris, dandruff, and furuncle) (Geng et al., 2016)for its wide range of biological activity including antihyperlipidaemia, anti-inflammatory, anticancer, antioxidant, antimicrobial, antiasthmatic, analgesic, preventing heart disease, atherosclerotic, etc (Chang et al., 2006; Jeong-Su et al., 2006; Korekar et al., 2011). Therefore the functional compounds contained in bitter apricot kernels skins and their medicinal effect demand for thorough investigation to develop their production potential and specific nutritional and medicinal qualities. In this article, the phenolic composition of wild apricot kernel skins (AKSs) was analysed to identify compounds with liquid chromatography-electrospray ionization mass spectrometry (LC-ESI/MS). The antioxidant, antimicrobial activity and the effect on $HepG_2$ cells of these polyphenols were investigated to understand the potential for application as a human antioxidant and medicine from the AKS polyphenols.

2. Materials and methods

2.1. Materials

Wild apricots [*Armeniaca Sibirica* (L.) Lam] were purchased from Chifeng, Inner Mongolia in China, in 2016 and stored in the dark (4 °C) in the Key Laboratory of Synthetic and Natural Functional Molecular Chemistry of the Ministry of Education (No: AK20160510), Northwest University. Apricot kernel skin was isolated as described by (Monagas et al., 2007) and dried naturally.

2.2. Extraction of polyphenol fraction

AKS mixtures (5 g) were extracted twice with 50% ethanol (130 mL) in a microwave extractor (Scientz-IIDM, Ningbo Xinzhi Biotechnology Co., Ltd., Ningbo, Zhejiang, China) (540 W) for 89 s. After filtration, the filtrate samples were combined and evaporated using a rotary evaporator. The residue was dissolved in 20 mL of distilled water and extracted four times with 20 mL of ethyl acetate. The organic phases were combined and dried with anhydrous sodium sulphate for 5 h and then evaporated to remove the solvent. The residue from the AKS was dissolved in methanol and used for component analysis and detection of antioxidant, antibacterial and cellular activity.

2.3. Determination of total phenolic content

The total polyphenol content of AKS was determined colourimetrically by the Folin Ciocalteu method as described by Feng (Feng et al., 2017). Gallic acid was used as a reference compound to obtain the standard curve equation: $Y = 0.05193 + 0.09855X$ ($R^2 = 0.9995$). Total phenol content was expressed as mg of gallic acid equivalents (GAE)/100 g of AKC sample fresh weight (FW). Each determination was performed in triplicate and repeated at least three times.

2.4. LC-ESI/MS analysis of phenolic compounds

Composition and level of phenolic compounds in the AKS extracts were determined using the liquid chromatography-electrospray ionization mass spectrometer (LC-ESI/MS) (Thermo, Ultimate 3000 LC, Orbitrap Elite) with DL-*o*-chlorophenylalanine as the internal standard. A Phenomenex reversed-phase C_{18} column (Alltech, Licosphere, United States) (100 × 4.6 mm, 3 μm I.D.) was used for the separation of bioactive compounds. The mobile phase consisted of two solvents: water containing 0.1% formic acid (solvent A) and acetonitrile containing 0.1% formic acid (solvent B). The gradient elution was carried out as follows: 0–5 min, 15% B; 5–10 min, 15–20% B; 10–20 min, 20–25% B; 20–30 min, 25–35% B; 30–40 min, 35–50% B; 40–50 min, 80% B and 50–55 min, 15% B with a flow rate of 0.3 mL/min, and the temperature was set at 40 °C. The eluents then were analysed well by ESI-MS/MS using an electron spray ionization tandem mass spectrometer operating in the negative mode. The operating conditions included the following: desolvation temperature 300 °C, sheath gas flow 45 arb, aux gas flow 15 arb, sweep gas flow 1 arb, capillary voltage 3.2 kV, capillary temperature 350 °C, and S-lens RF level 60%. Spectra were recorded in the ESI negative mode between 50 and 1000 m/z. The injection volume was 4 μL, under the automatic injector temperature of 4 °C. LC/MS detection data were converted to the common data format (CDF) by Xcalibur software (Thermo). The converted data were extracted by R software, edited in Excel 2010 and expressed as a two-dimensional data matrix including retention time, m/z, compound name, ID and compound content.

2.5. Measurement of antioxidant activity of AKS polyphenols

2.5.1. Total reduction capacity

The reducing power of the AKS polyphenols was determined as described by (Khaled-Khodja et al., 2014) with slight modifications. The extract solutions (2 mL) at different concentrations (20, 30, 40, 50, 60 μg/mL) were mixed with 2.5 mL sodium phosphate buffer (pH 6.6, 0.2 M) and 2.5 mL potassium ferricyanide (1%, w/v) in test tubes. The mixture was vortexed and incubated at 50 °C for 30 min. After the incubation period, 2.5 mL trichloroacetic acid (10%, w/v) was added into the tubes and mixed thoroughly for 10 min. The solution (2.5 mL) was transferred to another set of tubes and mixed with 2.5 mL of deionized water and 0.5 mL of 0.1% ferric chloride solution. The antioxidants present in the extracts formed a coloured complex with TCA, potassium ferricyanide, and ferric chloride, whose absorbance was recorded at 700 nm by the 1780 UV-Vis spectrophotometer (Shimadzu, Japan). Ascorbic acid was used as the standard radical scavenger at the concentration of 20, 30, 40, 50, 60 μg/mL.

2.5.2. ABTS radical-scavenging activity

Radical-scavenging activity of the AKS polyphenol extracts was determined spectro-photometrically (Shimadzu 1780 UV-Vis spectrophotometer) with 2, 2′-azino-bis(3-ethylbenzothiazoline-6-sulphonic acid) (ABTS) decolourisation assay (Galiñanes et al., 2015; Luisi et al., 2019). ABTS, generated by reacting with potassium persulphate (2.5 mM) for 16 h, was used as the free-radical provider. Before use, the solution was diluted with ethanol (50%) to obtain an absorbance of 0.75 ± 0.02 at 734 nm. Then, 8 mL of ABTS solution was added to 2 mL of the AKC polyphenol extracts (20, 30, 40, 50, 60 μg/mL) and mixed vigorously. The absorbance was monitored at 734 nm after 10 min to ensure reaction. Ascorbic acid (vitamin C) was used as positive control at the same centration range as the extracts.

2.5.3. DPPH radical-scavenging assay

The electron donation ability of the AKS polyphenols was measured by bleaching of the purple-coloured solution of 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical according to the method of (Giusti et al., 2017; Trampetti et al., 2019). The extracts (20,30,40,50,60 g/mL) were prepared in ethanol/water (v/v). An aliquot of 2 mL of the extract was added to 2.0 mL of DPPH solution in methanol (1×10^{-4} mol/L). The mixture was shaken vigorously and reacted in the dark at room temperature for 30 min. The absorbance of the solution was then measured at 517 nm by a 1780 UV-Vis spectrophotometer (Shimadzu, Japan). Ascorbic acid was used as a positive control at the same concentration range as the extracts. The percent of inhibition was calculated using the following formula:

$$\text{Percentage reduction (\%)} = [1-(A_1-A_2)/A_0]$$

where A_0 indicates the average absorbance of the DPPH solution with distilled water; A_1 indicates the absorbance of the reacted sample; A_2 indicates the absorbance of the negative control.

Additionally, $OH^{\cdot}$ scavenging activity was determined by the deoxyribose assay (Ningappa et al., 2008). H_2O_2 scavenging activity was determined according to the method of Sarma (Sarma et al., 2016). Ascorbic acid was used as the control in the assays.

2.6. Cytotoxicity assay of AKS polyphenols

2.6.1. Cells culture

The inhibitory effect of AKS polyphenol extracts on human hepatocellular carcinoma (HepG2) was investigated *in vitro*. HepG2 cells derived from human liver tissue with a well-differentiated hepatocellular carcinoma were obtained from the Medical Department of Xi'an Jiaotong University (Shaan xi, Xian, China). Cells were routinely cultured in DMEM (Dulbecco's modified Eagle's medium) supplemented with 10% FBS (fetal bovine serum), 1% penicillin/streptomycin, in a monolayer culture, and incubated at 37 °C in a humidified atmosphere containing 5% CO_2. The experiment was conducted when the cells were in the logarithmic growth phase.

2.6.2. Antioxidant analyses in HepG2 cells

The antioxidant of AKS polyphenol extracts on HepG2 cells were evaluated in 96-well culture plates (200 μL per well) at a density of 1×10^6 Hep G2 cells/well. The plates were incubated at 37 °C for 24 h. Then, the HepG2 cells were exposed to different concentrations of the AKS polyphenol extracts (0, 50, 200 μg/mL) for 24 h, 48 h or 72 h. Gallic acid (GA) and quercetin (QC) were used as controls under the same conditions. Reduced glutathione (GSH) and oxidized glutathione (GSSG) and malondialdehyde (MDA) were measured by commercial kit from Nanjing Jiancheng. Advanced oxidation protein products (AOPP) was measured by commercial kit from MLBIO. Experiments were performed following manufacturer's instructions.

2.6.3. Cell viability by the MTT assay

The effect of AKS polyphenols on the HepG2 cell viability was determined using the MTT [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide] assay (Notarnicola et al., 2010; Zengin et al., 2019) The cells were plated in 96-well culture plates (200 μL per well) at a density of 1×10^4 cells/well. After incubateing at 37 °C for 24 h, the HepG2 cells were treated with different concentrations of the extracts (50, 100, 200, 400, 500, 800, 1000 μg/mL) for 24 h, 48 h or 72 h. Subsequently, a volume of 20 μL of 5 mg/mL MTT was added to each well and incubated in the dark at 37 °C for 4 h. After removal of the MTT, the intracellular formazan products in each well were dissolved in 150 μL DMSO, and the absorbance was measured at 510 nm using a microplate reader. Gallic acid (GA) and quercetin (QC) were used as controls under the same conditions. Each experiment was performed in triplicate and repeated 5 times. Cell viability was expressed as percentage relative to control cells.

2.6.4. Apoptosis analysis by Annexin V-FITC/PI (fluorescein isothiocyanate and propidium iodide)

HepG2 cell apoptosis was detected by flow cytometry using Annexin V-FITC/PI double staining. Briefly, the cells were plated in 24-well culture plates (1 mL per well) at a density of 1×10^4 cells/well. After incubateing at 37 °C for 24 h, the cells were exposed to different concentrations of AKS polyphenol extracts (50, 100, 200, 400, 600, 800, 1000 μg/mL) for 24 h. The cells were washed with PBS, detached with trypsin, harvested, gently suspended in 400 L binding buffer followed by staining with Annexin V-FITC/PI (5 μL) for 15 min in the dark at room temperature. Then, a volume of 10 μL of 1 PI staining solution was added and incubated for 5 min under the same conditions. The apoptotic cells were observed using a flow cytometer within 30 min.

2.7. Antibacterial activity

The *in vitro* antibacterial activities of the AKS polyphenol samples were tested against Gram-positive bacteria (*Staphylococcus aureus* ATCC25923, *Bacillus cereus* CHCC63301, *Bacillus subtilis* ATCC6633), Gram-negative bacteria (*Escherichia coli* ATCC25922, *Acetobacter aceti* ATCC15973) and *Aspergillus niger* (CMCC98003) using the agar diffusion method as described by (Metrouh-Amir et al., 2015). All of these test organisms were collected from the Medical Department of Xi'an Jiaotong University, Xi'an, China. *Escherichia coli*, *Bacillus subtilis*, and *Bacillus cereus* were cultivated in Luria-Bertani (LB) medium at 37 °C for 24 h. *Staphylococcus aureus* and *Aspergillus niger* were incubated in Baird-Parker (BP) medium and Czapek–Dox medium nutrient at 37 °C for 24 h, respectively. *Acetobacter aceti* was cultivated in Acetobacter medium at 30 °C in a shaker for 24 h.

In the agar well diffusion assay, the dry sterilized filter paper discs (6 mm in diameter) contain 50 μL/disc of the AKS polyphenol extractives (1000 g/mL), which were placed on nutrient agar media of a Petri dish that was consistently seeded with the test organisms. Then, the plates were incubated at 37 ± 2 °C over 24 h for bacterial strains, while *Aspergillus niger* was cultivated for 48 h. The zone of inhibition that appears was measured (in mm) as an indication of the antibacterial activity of the AKS extracts. The minimum inhibitory concentration (MIC) of the extract at different concentrations (1000,500,250,125,62.5,31.25,15.63,7.8,3.9,1.95,0.98 g/mL) was evaluated according to the method described under the same conditions. Methanol was used as the negative control, and ampicillin and tetracycline hydrochloride (THC) were used as positive controls.

2.8. Statistical analyses

All experiments were performed at least three times. The results were expressed as the mean values ± standard deviations. Radical scavenging activity was analysed by origin 8.0 (OriginLab Corporation, USA). The IC_{50} value was calculated using IBM SPSS19.0. The rate of cell apoptosis was analysed using NovoExpress. Colume graphs were prepared by GraphPad PRISM 7.0, and statistical differences between two groups with two factors were determined by two-way ANOVA. $P < 0.05$ was defined for significance.

3. Results and discussion

3.1. Total polyphenol content of AKS

Polyphenols have received considerable attention for their potential beneficial effects on human health. They have been reported to show various types of bioactivity, including anti-inflammatory, anticancer, and antioxidant properties. The phenolic content in *AKS* extracts, measured by the Folin-Ciocalteu method, was 874.49 ± 6.75 mg GAE per 100 g FW, which was higher than the phenolic content of almond

Table 1
Polyphenol compounds identified in ethanol extract of apricot kernel skins by LC-ESI/MS.

No.	Compounds	RT (min)	$[M-H]^-$ (*m/z*)	Mw	Formula	Content (mg/100 g)
Flavones						
1	Apigenin 7-O-glucoside	9.7	431.0984	432.1056	$C_{21}H_{20}O_{10}$	60.47 ± 1.08
2	Luteolin 7-xyloside	7.49	417.0829	418.09	$C_{21}H_{22}O_9$	4.60 ± 0.02
3	Apigenin	17.23	269.0455	270.0528	$C_{15}H_{10}O_5$	0.22 ± 0.01
4	Tricetin 3′-xyloside	5.07	433.0777	434.0849	$C_{20}H_{18}O_{11}$	1.08 ± 0.01
	Total flavones					66.37 ± 1.12
Flavonols						
5	Quercitrin	5.83	447.0934	448.1006	$C_{21}H_{20}O_{11}$	19.23 ± 0.12
6	Quercetin	12.54	301.0354	302.0427	$C_{15}H_{10}O_7$	4.31 ± 0.07
7	Kaempferol	17.85	285.0406	286.0477	$C_{15}H_{10}O_6$	5.44 ± 0.12
8	Rutin	5.41	609.1455	610.1534	$C_{27}H_{30}O_{16}$	3.77 ± 0.05
9	(±)Taxifolin	3.85	303.0512	304.0583	$C_{15}H_{12}O_7$	2.22 ± 0.02
10	Quercetin 3-(3″-sulfatoglucoside)	30.59	543.0485	544.0523	$C_{25}H_{20}O_{14}$	0.83 ± 0.03
	Total flavonols					35.80 ± 0.41
dihydroflavone						
11	Isoliquiritigenin	29.63	255.0662	256.0736	$C_{15}H_{12}O_4$	9.08 ± 0.22
Dihydrochalcones						
12	Phloretin	18.01	273.0771	274.0841	$C_{15}H_{14}O_5$	1.39 ± 0.01
Flavanones						
13	(−)-Naringenin	16.1	271.0612	272.0685	$C_{15}H_{12}O_5$	3.15 ± 0.1
Phenolic acids						
14	Salicylic acid	6.39	137.0248	138.0317	$C_7H_6O_3$	38.92 ± 0.26
15	Gentisic acid	1.32	153.0197	154.0266	$C_7H_6O_4$	31.34 ± 0.03
16	Caffeic Acid	7.35	179.0346	180.0423	$C_9H_8O_4$	19.33 ± 0.58
17	Ferulic acid	3.73	193.0508	194.0579	$C_{10}H_{10}O_4$	10.69 ± 0.11
18	Vanillic acid	1.24	167.0353	168.0423	$C_8H_8O_4$	7.23 ± 0.06
19	m-Coumaric acid	3.00	163.0404	164.0473	$C_9H_7O_3$	7.08 ± 0.05
20	Gallic acid	1.15	169.0146	170.0215	$C_7H_6O_5$	1.47 ± 0.02
21	Homovanillic acid	7.5	181.051	182.0579	$C_9H_{10}O_4$	1.40 ± 0.03
22	Syringic acid	1.45	197.046	198.0528	$C_9H_{10}O_5$	0.71 ± 0.01
	Total phenolic acids					118.17 ± 1.15
Anthocyanins						
23	Cyanidin 3-(4″- acetylrutinoside)	14.44	635.1611	636.169	$C_{29}H_{32}O_{16}$	56.71 ± 1.13
24	Cyanidin3-(6″-acetylglucoside)-5-glucoside	11.58	651.1561	652.1639	$C_{29}H_{32}O_{17}$	11.34 ± 0.16
25	Petunidin 3-galactoside	6.63	477.1037	478.1111	$C_{22}H_{22}O_{12}$	6.61 ± 0.05
26	Cyanidin 3-rutinoside	5.01	593.1504	594.1585	$C_{27}H_{30}O_{15}$	4.47 ± 0.09
27	Cyanidin 3-O-galactoside	5.84	448.0968	449.1084	$C_{21}H_{21}O_{11}$	4.13 ± 0.05
28	Petunidin 3-rutinoside	17.54	623.1725	624.169	$C_{28}H_{32}O_{16}$	2.80 ± 0.05
29	Petunidin	19.34	315.0511	316.0583	$C_{16}H_{12}O_7$	2.79 ± 0.03
30	Pelargonidin 3-*p*-coumarylglucoside	1.58	577.135	578.1424	Unknown	2.00 ± 0.01
31	Malvidin 3-glucoside-pyruvate	4.84	559.1243	560.1166	$C_{27}H_{28}O_{13}$	1.45 ± 0.01
32	Pelargonidin 3-lathyroside	2.95	563.1402	564.1479	Unknown	1.21 ± 0.03
33	Cyanidin 3-glucogalactoside	5.41	610.1489	611.1612	$C_{27}H_{31}O_{16}$	1.12 ± 0.03
34	Cyanidin 3-(6-acetylgalactoside)	12.85	489.1040	490.1111	$C_{23}H_{22}O_{12}$	0.44 ± 0.02
35	Pelargonidin 3-arabinoside	14.66	401.0880	402.0951	Unknown	0.17 ± 0.01
	Total anthocyanins					95.24 ± 1.67
Total of phenolic compound						329.21 ± 4.68

Results are indicated as mean ± standard deviation (SD) of three replicates.
RT: retention time; Content (mg/100 g): the results were expressed as milligrams of gallic acid equivalents (GAE)/100 g of sample fresh weight (FW).

(*Amygdalus pedunculata* Pall) skins recorded as 781.83 ± 4.81 mg GAE/100 g, but lower than the phenolic content of the natural skins by the freeze-thaw methods of *A. communis* L. (3474.1 ± 239.8 GAE/100 g) (Mandalari et al., 2010), showing that the phenolic content of apricot or almond kernel skins differs because of inherent genetic characteristics and extraction methods (Nile et al., 2017).

3.2. Phenolic composition of AKS

Phenolic compounds in the methanol extracts of AKS were analysed by LC-ESI/MS. Table 1 summarizes the phenolic compounds characterized in the extracts, including retention times, experimental m/z, and molecular formula and the identified compounds. Overall, 35 phenolic compounds were identified, including phenolic acids, flavones, flavonols and anthocyanins. As the most abundant phenolic compounds in the AKS extracts, the content of phenolic acids was 118.17 ± 1.1 mg/100 g. A total of nine phenolic acids consisting of 4-hydroxycinnmic acids (caffeic acid, *m*-coumaric acid and ferulic acid) and 5-hydroxybenzoic acids (gallic acid, gentisic acid, homovanillic acid, salicylic acid, syringic acid and vanillic acid) were characterized in this study. Within the group of phenolic acids, salicylic acid (38.92 ± 0.26 mg/100 g) and gentisic acid (31.34 ± 0.03 mg/100 g) were quantitatively the largest portion of the total phenolic acids. The content of caffeic acid, ferulic acid, vanillic acid and *m*-coumaric acid was 19.34 ± 0.58 mg/100 g, 10.69 ± 0.11 mg/100 g, 7.23 ± 0.66 mg/100 g and 7.08 ± 0.0 mg/100 g, approximately 69, 14.6, 4.8 and 2.15 times higher than the content of these acids found in the methanol extracts of the *Amygdalus pedunculata* Pall seed coat (APSC) (Lu et al., 2018), indicating that AKSs are more nutritious or valuable than APSC. Hydroxybenzoic acids (such as protocatechuic, *p*-hydroxybenzoic, chlorogenic, vanillic and trans-*p*-coumaric acids) were also identified in the almond (*Amygdalus communis* L.) skin samples (Mandalari et al., 2010). Phenolic acids are widely distributed among various parts of the plants including roots, leaves, fruits and vegetables (Pan et al., 2015). Salicylic acid, a plant hormone and analgesic, antipyretic, is an anti-inflammatory drug precursor compound to aspirin. Gentamic acid is a metabolic oxidation product of salicylic acid. The caffeic acid is the most common type of phenolic acid found widely in the fruits, while the

ferulic acid is found in the cell walls of the seed coat, the bran and the fruits in esterified form (Jin and Mumper, 2010). Plant phenolic acids have formed an integral part of our diet, thus making them a prime focus of increased interest. These phenolic compounds are known to exhibit potent anticancer activities as well as combatting various diseases associated with oxidative stress (Anantharaju et al., 2016). Numerous studies have shown that the antitumour activity exerted by plant extracts could be due to the presence of phenolic acids (Anantharaju et al., 2016) and phenolic acids, i.e., benzoic and cinnamic acid derivatives with higher hydroxyl substitutions can be considered as potential candidates for preventing the cancer cell proliferation (Eleni et al., 2014; Seidel et al., 2014). The main function of ferulic acid in the superficial layer of grains might be to protect the kernel from the oxidative effects of the inferior layers (Luthria and Memon, 2012), and high concentrations of *p*-coumaric acid were detected as contributing to the high antioxidant capacities of the maize samples (Luthria and Memon, 2012). The antioxidant capacity of phenolic acids has been reported to relate to the structure of the phenolic acids and increases with the increasing degree of hydroxylation of the phenolic structure, which is referred to as the structure-activity relationship (Llano et al., 2015).

Compare to phenolic acids, anthocyanins (ACNs), flavones, flavanols, etc., are classified as complex phenolic compounds, known as flavonoids. Anthocyanins are glycosides and acylglycosides of anthocyanidins. The six anthocyanidins most commonly found in fruits and vegetables are pelargonidin, cyanidin, delphinidin, petunidin, peonidin, and malvidin. Cyanidin was found to be the most widely distributed aglycone, which was found in almost every food, but the concentrations varied considerably (Wu et al., 2006). 3-Monoglycosides, 3-diglycosides, 3,5-diglycosides, and 3-diglycoside-5-monoglycoside, as well as nonacylated or acylated ACNs, are the more known glycosidic variations among these pigments, glucose being the most common conjugated sugar Speciale et al. (2014). In this study, 14 anthocyanins were identified in the methanol extracts of AKS, with the content of 95.24 ± 1.67 mg/100 g (Table 1). Cyanidins occur as pigments in 6 of thirteen anthocyanins. The content of cyanidin 3-(4″-acetylrutinoside), cyanidin 3-(6″-acetylglucoside)-5-glucoside were found to be the highest in obtained ACNs as 56.71 ± 1.13 mg/100 g and 11.34 ± 0.16 mg/100 g. The percentages of both acylated ACN content in total anthocyanin accounted for 71.45%. In most foods, acylated ACNs are generally minor ACNs, while acylated ACNs comprised a majority of the ACNs with percentages > 50%, e.g., concord grape (50%), red onion (77%), red cabbage (85%), and red radish (100%) (Wu et al., 2006). The acylated groups may significantly affect the bioavailability, stability, and other biological effects of ACNs (Kurilich et al., 2005). Except for cyanidin 3-(6″-acetylglucoside)-5-glucoside, the other anthocyanins are considered monoglycosides. Petunidin 3-galactoside, cyanidin 3-rutinoside, cyanidin-3-o-galactoside, and petunidin 3-rutinoside were quantified as 6.61 ± 0.05 mg/100 g, 4.47 ± 0.09 mg/100 g, 4.13 ± 0.05 mg/100 g, 2.8 ± 0.05 mg/100 g, respectively. As the only detected pigment, the content of petunidin was 2.79 ± 0.03 mg/100 g. The levels of the other ACNs detected were lower than the levels of the anthocyanins mentioned above. Pelargonidin 3-*p*-coumarylglucoside and pelargonidin 3-lathyroside were first identified in AKS.

As shown in Table 1, flavone compounds of apigenin 7-*O*-glucoside, luteolin 7-xyloside, tricetin 3′-xyloside and apigenin were identified in AKS extracts. As the most abundant identified polyphenol, the content of apigenin 7-*O*-glucoside was 60.47 ± 1.08 mg/100 g, which accounted for 52.24% of the total flavonoids in the plant. Quercitrin, quercetin, kaempferol, rutin and (±) taxifolin were the major flavonol compounds quantified, having concentrations of 19.23 ± 0.12, 4.31 ± 0.07, 5.44 ± 0.12, 3.77 ± 0.05 and 2.22 ± 0.02 mg/100 g, respectively. Isoliquiritigenin, phloretin and naringenin as the only dihydroflavone, dihydrochalcone and flavanone compound was quantitated. The above-mentioned flavonoids were also analysed in APSC (Lu et al., 2018). The content of apigenin 7-*O*-glucoside, isoliquiritigenin and phloretin in AKS was 1.75, 18.5 and 3.3 times higher than the content of APSC under the same conditions (Mandalari et al., 2010). The most represented flavonoids present in almond (*Amygdalus communis* L.) skins are (+)-catechin, (−)-epicatechin, quercetin-3-O-rutinoside, quercetin-3-O-galactoside, quercetin-3-O-glucoside, kaempferol-3-O-rutinoside, isorhamnetin-3-O-rutinoside, kaempferol-3-O-glucoside, isorhamnetin-3-O-glucoside (Mandalari et al., 2010). The antioxidant capacity of the above-mentioned flavonoids is largely reported in the literature (Milbury et al., 2006). However, as far as we are aware, no reports about these polyphenols in skins of *Armeniaca Sibirica* (L.) Lam have previously been published. Six phenolic compounds including protocatechuic aldehyde, procyanidin B_1, epigallocatechin, protocatechuic acid, catechin and chlorogenic acid, were identified in the sample of blanching water concentrate and debitterizing water concentrate by the HPLC analysis, indicating that the polyphenol composition of AKS is more abundant and has advantages in nutrition and oxidation resistance.

3.3. Antioxidant activity of AKS polyphenols

Phenolic compounds are known to be the main bioactive compounds in plants with antioxidant capacities to scavenge free radicals, participate in regeneration of other antioxidants and protect cell constituents against oxidative damage. In this study, the total antioxidant capacity of the AKS extracts was determined using the following in-vitro assays such as reducing power, DPPH, ABTS, hydroxyl radical scavenging and the $O_2^{\cdot-}$-scavenging activity assay. The results showed that the reducing activity, DPPH, $OH^{\cdot-}$, $O_2^{\cdot-}$ and H_2O_2 radical-scavenging activity of AKS polyphenol extracts and their controls (Vc solution) were positively correlated with the concentrations of samples at the tested concentrations (Fig. 1 a, c, d, e, f). The results agreed with previous studies that reported higher polyphenolic yields are positively correlated to higher antioxidant activity in extracts (Bolzon et al., 2017; Galiñanes et al., 2015), and confirmed the ability of the compounds to act as a proton donor that might similarly be affected by the concentration of different compounds present in the extracts (Shah et al., 2018). The ABTS scavenging activity of AKS polyphenols was significant lower at 20–30 μg/mL concentration range, while showed no significant difference in 40–60 μg/mL concentration range than the control treatment (Vc) (Fig. 1b,$p < 0.0001$). The ABTS scavenging activity of AKS polyphenols was between 73% and 90% and showed little difference within the concentration range (20–60 μg/mL). This revealed that AKS polyphenols exhibited strong scavenging activity towards ABTS free radicals at a minimum concentration of 20 μg/mL.

Compared with the control treatment (Vc), the AKSs polyphenols extracts showed stronger reducing activity and H_2O_2 scavenging activity at the same corresponding concentration (Fig. 1 a, f,$p < 0.0001$). This indicated that AKS polyphenols extracts had strong antioxidant capacity and scavenging activity towards H_2O_2. The DPPH and $O_2^{\cdot-}$ scavenging capacities of AKSs polyphenols extracts were significantly lower than the control treatment (Fig. 1 d, e,$p < 0.0001$) at the same corresponding concentration. Except for the treatment at a concentration of 20 μg/mL, the scavengeing activity for $OH^{\cdot-}$ radicals was little different between AKS polyphenols extracts and Vc (Fig. 1 b). The antioxidant activity of the AKS polyphenols for different free radicals or oxidants exhibited a certain difference, which may be the result of the synergistic effects of the phenolic hydroxyl groups of polyphenol molecules in the AKS extract on inhibition abilities for free radicals.

The IC_{50} value (half maximal inhibitory concentration) indicates the free radical inhibitory strength (low IC_{50} values mean stronger free radical inhibition at low concentrations). As observed from the IC_{50} values in Table 2, the reducing activity, ABTS scavenging capacity, and H_2O_2 radical scavenging activities of AKS polyphenols were significantly higher compared with the activity of their corresponding controls (ascorbic acid) ($p < 0.01$), with IC_{50} values approximately

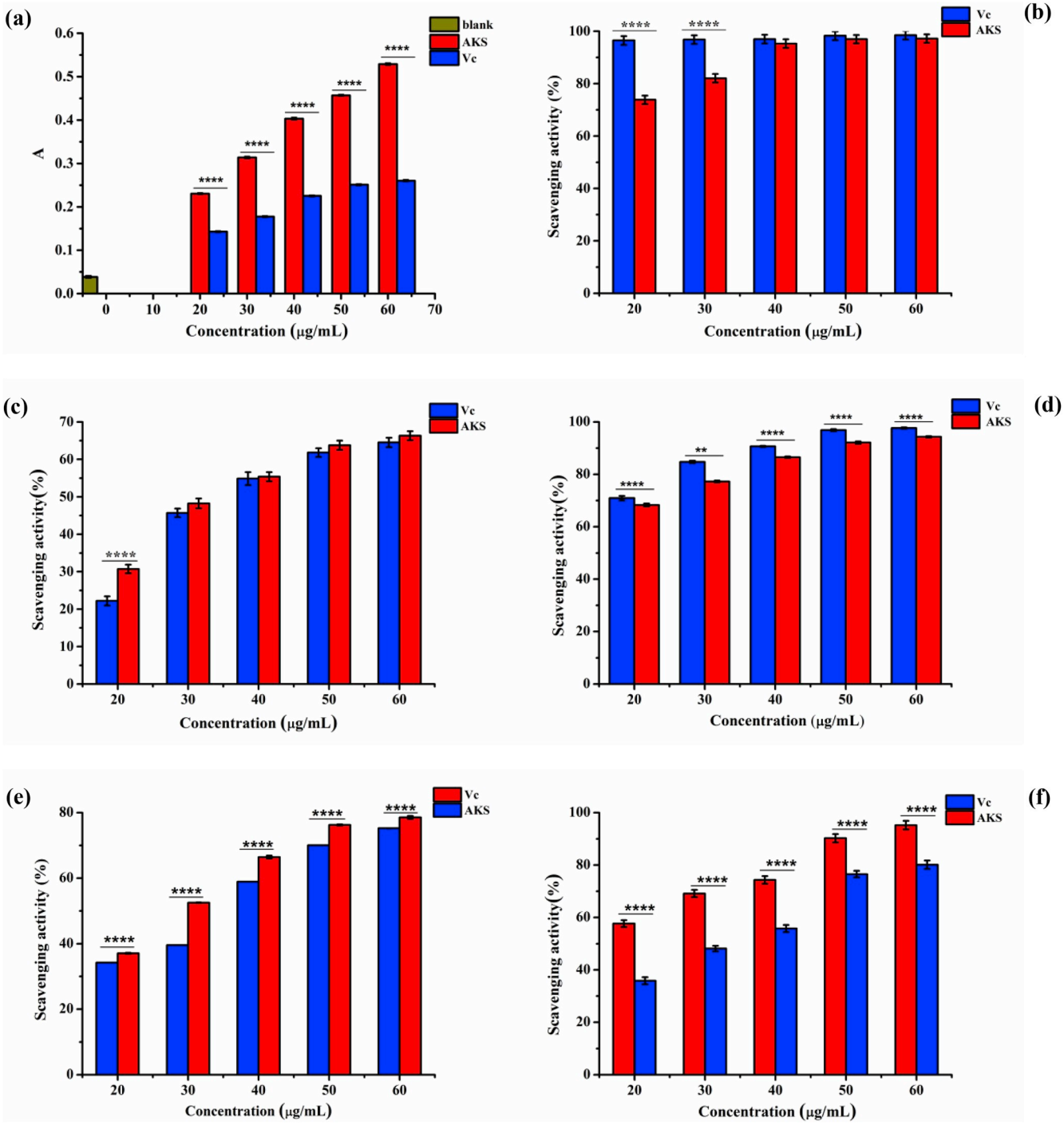

Fig. 1. Antioxidant activity of AKS polyphenols against Fe^{3+} (a), ABTS free radical (b), OH- (c), DPPH free radical (d), O_2·- (e) and H_2O_2 (f). A: absorbance value (Fig. 1a). Significant differences as compared with the control group were established at **p < 0.01 and ****p < 0.0001, respectively.

Table 2
IC_{50} values of AKS polyphenols on antioxidant activity (mg/mL) (The control was ascorbic acid).

	Fe^{3+}	ABTS free radical	OH^- free radical	DPPH free	O_2^- free radical	H_2O_2
AKC	3.05 ± 0.78	0.24 ± 0.23 b	37.64 ± 1.77	13.77 ± 0.98	32.46 ± 1.62	18.71 ± 1.03 b
Control (Vc)	5.08 ± 1.88	14.68 ± 1.05 a	34.16 ± 1.57	14.23 ± 1.90	27.37 ± 1.13	29.79 ± 1.25 a

Results are indicated as mean ± standard deviation (SD) of three replicates. Means not sharing a common single letter in each line for each measurement were significantly different at p < 0.05.

3.05 ± 0.78 μg/mL, 0.24 ± 0.23 μg/mL and 18.71 ± 1.03 μg/mL, respectively. The AKS polyphenols had litter difference than the control treatment for the reducing activity and radical scavenging capacity to reduce the stable DPPH, OH^{-} and $O_2^{\cdot-}$ radicals (Table 2).

The antioxidant activity of AKS polyphenols may be the result of the synergistic effects of different compounds. The high antioxidant activity of these extracts can be attributed to the structural characteristics of the polyphenols, including the presence of multiple hydroxyl groups, the arrangement of these hydroxyl groups, the presence of additional substituents such as double bonds, conjugation, and glycosylation, where they act as hydrogen donors, reducing agents, singlet oxygen quenchers, and free radical scavengers (Rahmat Ali et al., 2012). Apigenin 7-*O*-glucoside was found to be the most active among the flavonoid constituents (Lee et al., 2005) and to be the most potent for the ability to inhibit free radical-induced microsomal lipid peroxidation in 35 phenolic compounds (Cholbi et al., 1991). In this study, apigenin 7-*O*-glucoside was the most abundant polyphenol in the identified polyphenols of AKS (18.64%), which may be one of the major contributors to the antioxidant properties of the extracts analysed. Anthocyanins have a wide range of bioactivity study fields, including antioxidant, anticancer and anti-inflammatory properties (Chikhoune et al., 2017). As the second abundant polyphenol in the AKS polyphenol extract, anthocyanins may be attributed to antioxidants in this study. Many flavonoids and phenolic acids such as salicylic acid, gentisic acid, caffeic acid, quercitrin, kaempferol, ferulic acid, and gallic acid of the AKS polyphenols have been reported to show strong antioxidant activity for DPPH free radicals, hydroxyl radicals, superoxide radicals, ABTS free radicals, and hydrogen peroxide. In addition, we have observed a relatively high IC50 value, thus we need to optimize the effect by isolating single effective compound from AKS extract. A stronger bioactivity may be available from isolated compound. Therefore, this study demonstrates that the AKS polyphenol extracts could be an effective natural antioxidant-resource in foods and the medical industry.

3.4. Inhibitory effect of AKS polyphenols on HepG2 cells

3.4.1. Antioxidant of AKS polyphenol extracts on HepG2 cells

Lipid peroxidation is a mechanism of oxidative cell injury by chemicals (Han et al., 2013). MDA, as one of the main products of lipid peroxidation (María Angeles et al., 2008), has been found elevated in various diseases thought to be related to free radical damage. MDA has been widely used as an index of lip peroxidation in biological and medical sciences (Suttnar et al., 2001). AOPP are recognized as markers of oxidative damage to proteins, the intensity of oxidative stress and inflammation (Agnieszka, 2010). Compared with control treatment, the concentration of AOPP and MDA in HepG2 cells was increased at the different dosage of the AKS polyphenols extracts, QC and GA, respectively (Fig. 2 a, b). It indicated that they could stimulate the oxidative stress and disturbance the normal redox state of HepG2, which cause toxic effects and inhibition of HepG2 cells growth through the production of peroxides and free radicals to damage all components of the cell, including proteins, lipids, and DNA (Valko et al., 2005). The concentration of AOPP and MDA in HepG2 cells at different dosage of AKS polyphenols, GA, and QC exhibited increase in a concentration and time-dependent manner (Fig. 2 a, b). At the same concentration and treated time, the concentrations of AOPP and MDA in HepG2 cells induced by QC, GA and AKS were: QC > AKS polyphenols > GA, indicating that AKS promoted oxidative stress in HepG2 cells more strongly than GA, but weaker than QC. However, there was no significant change in the induced concentration of AOPP and MDA in HepG2 cells between AKS polyphenols and the control treatment, such as QC or GA ($p < 0.05$).

Glutathione exists in both reduced (GSH) and oxidized (GSSG) states. GSH is one of the major endogenous antioxidants produced by the cells, participating directly in the neutralization of free radicals and reactive oxygen compounds, as well as protecting cellular protein thiol groups and maintaining exogenous antioxidants such as vitamins C and E in their reduced (active) forms (Gerlinde et al., 2003). Therefore, GSH is critical to fight against oxidative stress (Martin et al., 2008). With donating an electron, glutathione itself becomes reactive and readily reacts with another reactive GSH athione to form GSSG. In this study, compared with the control treatment, the GSH level in HepG2 cells treated by AKS polyphenols, GA, or QC was decreased in a concentration and time-dependent manner (Fig. 2 c), while the yield of the corresponding product GSSG was significantly increased (Fig. 2 d). This seemed that the scavenging effect on the free radicals of GSH in the HepG2 cells was reduced by polyphenols. It indicated that the protective effect of GSH on HepG2 cells was weakened, which maybe leads to its sensitivity to drugs or inhibition to its activities.

At the same condition, there was no significant change in GSH concentration of HepG2 cells between AKS polyphenols and the control treatment, GA ($p < 0.05$). However, the concentration of GSH in HepG2 cells treated by AKS polyphenols was significantly lower than its control treatment, QC ($p < 0.0001$). This indicated that the AKS polyphenols could strongly decrease the level of GSH in HepG2 cells (Fig. 2c). It could be seen that AKS polyphenols has a strong scavenging effect on GSH in HepG2 cells and showed strong anti-cancer effect on HepG2 cells. So it should have a positive effect on inhibiting the cellular viability of HepG2 cells.

3.4.2. Inhibitory effect of AKS polyphenols on HepG2 cells viability

Cellular viability is affected by oxidative stress, since the production of reactive species causes damage to the mitochondrial membranes permeability transition pores, thereby inducing apoptosis (Sas et al., 2007). In this study, the AKS polyphenols, GA, and QC exhibited strong inhibitory properties against HepG2 cells, with the ratio of inhibition of HepG2 cells increased in a concentration and time-dependent manner (Fig. 3). After incubating for 24 h, the HepG2 cell inhibition rates of AKS polyphenols, GA, and QC at the concentration of 50 μg/mL and 1000 μg/mL increased from 16.52% to 65.36%, 26.42%–85.26%, and 28.90%–89.67%, respectively. The ratio of inhibition of HepG2 cells in the samples increased from 24 h to 72 h at each concentration. When the sample concentration was 1000 μg/mL, the HepG2 cells inhibition rates of AKS polyphenols, GA, and QC increased from 65.36% to 75.53%, 85.26%–91.21%, and 89.67%–95.54% from 24 h to 72 h, respectively. The results showed QC has the strongest inhibition compared to the other two samples and indicated that flavonoids (quercetin, gallic acid, etc.) may be attributed to the inhibition of mutagenesis in human cells, which agreed with previous studies (Ramos et al., 2008). Phenolic compounds isolated from plant sources have been demonstrated to inhibit or retard the proliferation of cancer cells (Jaganathan et al., 2013; Pandey and Rizvi, 2009). Both cinnamic and benzoic acid derivatives possess potent anti-proliferative activity as evident by the low IC_{50} values exhibited by them on several cancer cell lines (Anantharaju et al., 2016; Faried et al., 2007). The AKS polyphenols showed strong inhibition of HepG2 cells, which may be attributed to the presence of bioactive compounds such as phenolics and flavonoids. Further research is necessary for identification and characterization of active compounds present in AKS extracts, which are responsible for the above mentioned biological activities.

3.4.3. Effect of AKS polyphenols on HepG2 cells apoptosis

Cell apoptosis is an evolutionarily conserved process that plays varied and essential roles in tissue homeostasis and organism development. The cells undergoing apoptosis exhibit caspase-mediated cell death through transforming procaspases into active caspases (Schultz and Jr, 2003). The major players during apoptosis are cysteine aspartic acid-specific proteases (caspases), B-cell lymphoma-2 family protein (BCL-2), and inhibitor of apoptosis proteins (IAPs) (Curti et al., 2017). The effects of AKS polyphenols, GA and QC on HepG2 cells apoptosis are shown in Table 3. The apoptotic rates of HepG2 cells induced by AKS polyphenols, GA and QC increased with concentration. At the

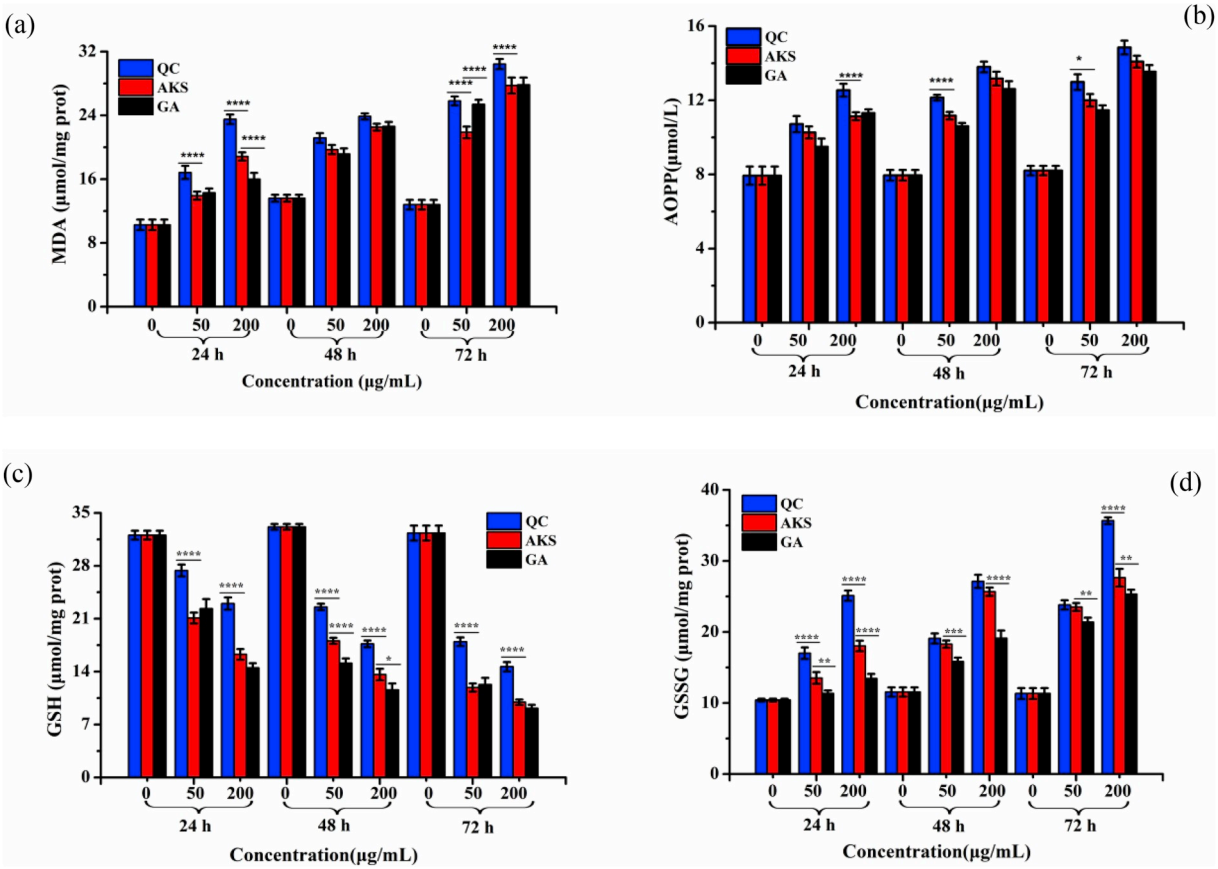

Fig. 2. The effect of AKS polyphenols, Gallic acid (GA) and querceti (QC) on malondialdehyde (MDA)(a), advanced oxidation protein products (AOPP) (b), reduced glutathione (GSH)(c) and on oxidized glutathione (GSSG)(d) in HepG2 cells with 24 h, 48 h or 72 h treatment. Significant differences as compared with the control group were established at * $p < 0.05$, ***$p < 0.001$ and ****$p < 0.0001$, respectively.

concentration of 50 μg/mL, the apoptotic rates of HepG2 cells induced by AKS polyphenols, GA, and QC were 7.93%, 10.77% and 12.90% respectively (Table 3). When the concentration was 1000 μg/mL, the apoptotic rates of HepG2 cells induced by AKS polyphenols, GA, and QC were 56.38%, 60.42%, 65.57%, respectively (Table 3). Compared with AKS polyphenols and GA, QC has the strongest ability to induce the apoptosis of HepG2 cells at each concentration. Numerous studies have shown that QC has a wide range of biological effects, such as anti-inflammatory (Kim et al., 2006), antioxidant, antitumour, anti-ulcer, immunomodulatory and vasodilatory effects. The apoptosis experiments showed that AKS polyphenols GA and QC have good anticancer activity. Induction of cell apoptosis is one of the most effective methods of inhibiting the proliferation of cancer cells. Many studies have shown that the induction of apoptosis is a major phenomenon exhibited by phenolic compounds. For example, Prasad (Prasad et al., 2011) confirmed the induction of apoptosis by caffeic acid by the morphological changes and the acridine orange and ethidium bromide staining methods. Ferulic acid could upregulate Bax and downregulate Bcl-2 to induce apoptosis in osteosarcoma cells and induced the expression of Bax, caspase-3 and -9 in fibrosarcoma cells (Umut et al., 2016). The anticancer activity of AKS polyphenols may be attributed to its bioactive phenolics and flavonoids such as apigenin 7-*O*-glucoside, kaempferol, gallic acid, caffeic acid and ferulic acid.

In summary, this study has shown that polyphenols may induced oxidative stress in HepG2 cells and decreased its GSH levels, which may lead to the accumulation of large amounts of Reactive oxygen species (ROS)(Sohal, 2002). ROS could damage the activity of HeGP2 cells and promote its apoptosis. At the same time, polyphenols as an antioxidant can directly scaveng a variety of free radicals and participate in the defense mechanism of normal cells, which could reduce the oxidative stress damage caused by HepG2.

3.5. Antibacterial activity

3.5.1. Antimicrobial screening

The results of testing for antibacterial activity are presented in Table 3. The AKS polyphenol extracts were observed to be significantly active against *Escherichia coli*, *Staphylococcus aureus*, *Bacillus subtilis*, *Acetobacter aceti* and *Bacillus cereus,* with zones of inhibition of 13.0 mm, 16.3 mm, 18.6 mm, 14.6 mm, and 14.3 mm, respectively. However, AKS polyphenols did not show an obvious inhibitory effect on *Aspergillus niger* even under the maximum experimental concentrations. The results also suggested that the AKS extract displayed a more effective antimicrobial impact against Gram-positive (*Staphylococcus aureus*, *Bacillus subtilis* and *Bacillus cereus*) bacteria than against Gram-negative bacteria (*Escherichia coli, Acetobacter aceti*), which is consistent with the conclusions of many studies that Gram-positive bacteria are more susceptible to the polyphenols than Gram-negative bacteria (Arakawa et al., 2004), possibly due to the variation in the cell wall composition of Gram-positive and Gram-negative bacteria. The presence of an outer membrane permeability barrier in the Gram-negative microorganism cell wall could limit the access of the antimicrobials to their targets in the bacterial cells. Therefore, Gram-negative microorganisms are generally more resistant to antimicrobial agents than Gram-positive bacteria (Meriem et al., 2015).

In comparison with positive controls (ampicillin and THC), AKS polyphenols and ampicillin showed higher potential against *Bacillus subtilis*, while THC showed the stronger inhibitory activity against *Bacillus cereus*. The negative control group did not show antibacterial activity against the test microorganisms in this experiment, which

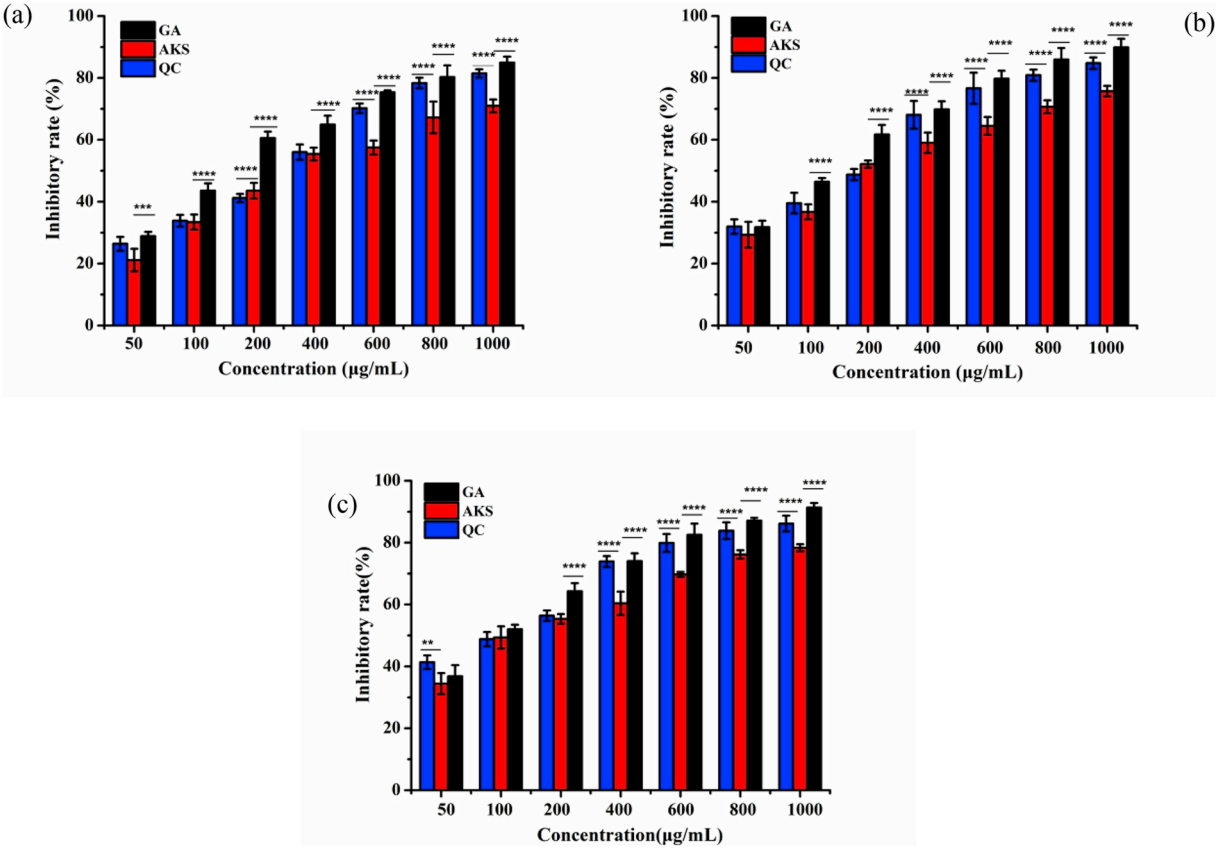

Fig. 3. The effect of AKS polyphenols, Gallic acid (GA) and querceti (QC) on oxidized glutathione (GSSG) in HepG2 cells with 24 h(a), 48 h(b) or 72 h(c) treatment. Significant differences as compared with the control group were established at * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ and **** $p < 0.0001$, respectively.

Table 3
Rate of HepG2 cells apoptosis induced by AKS polyphenols extracts, Quercetin (QC) and Gallic acid (GA).

Concentration (mg/mL)	Apoptosis rate (%)		
	AKS polyphenols	QC	GA
50	7.93 ± 2.17 b	10.77 ± 1.93 b	12.9 ± 2.41 a
100	13.85 ± 2.36 b	17.42 ± 2.39 b	21.12 ± 2.24 a
200	18.30 ± 0.63 b	24.62 ± 1.22 a	28.92 ± 1.28 a
400	26.30 ± 1.05 c	30.42 ± 1.28 b	36.74 ± 1.38 a
600	36.54 ± 1.24 c	42.40 ± 1.33 b	46.72 ± 1.37 a
800	48.26 ± 1.28 c	55.36 ± 1.36 b	58.24 ± 1.45 a
1000	56.38 ± 1.33 c	60.42 ± 1.54 b	65.57 ± 1.62 a

Results are indicated as mean ± standard deviation (SD) of three replicates. Means not sharing a common single letter in each line for each measurement were significantly different at $p < 0.05$.

indicated that the antibacterial activity of AKS polyphenols was possible from the component compounds of the polyphenols such as quercitrin, kaempferol, ferulic acid or gallic acid.

3.5.2. Determination of MIC

Minimum inhibitory concentration (MIC) is the lowest concentration that kills 99.9% of microorganisms. The MIC of the AKS polyphenols against the test microorganisms are shown in Table 4. The results showed that the polyphenol extract had a lowest MIC for *Bacillus subtilis* at 31.25 μg/mL followed by *Acetobacter aceti at* 62.5 μg/mL, *Staphylococcus aureus* at 150 μg/mL, *Bacillus cereus* and *Escherichia coli* at 250 μg/mL, respectively, indicating greater antimicrobial potency to *Bacillus subtilis* (G^+) and *Acetobacter aceti* (G^-). This result was slightly different from the results from the zones of the inhibition assay, showing Gram-negative bacteria *Acetobacter aceti* was more vulnerable to the polyphenols of the AKS. Compared to the positive controls (ampicillin and THC), the MIC of the AKS polyphenols against the test microorganisms was higher, which indicates that the inhibitory activity of ampicillin and THC was stronger than the inhibitory activity of the AKS extract. Ampicillin showed stronger inhibitory activity for *Escherichia coli, Bacillus subtilis* and *Acetobacter aceti* than THC, with lower MICs, while the inhibitory activity of THC against *Bacillus cereus* was stronger than that of ampicillin. Only ampicillin showed obvious inhibitory activity against the fungus *Aspergillus niger* in the test with the MIC of 1000 g/mL. We could conclude from our results that the AKS extract exhibited potent bactericidal activity against the pathogenic microorganisms, probably due to its high content of functional components such as polyphenols, flavonoids, anthocyanins, etc. (Balasundram et al., 2006; Duda-Chodak, 2012). Numerous research results indicate plant polyphenols have strong antiviral and antibacterial properties against foodborne pathogens (Maddox et al., 2010). Dietary phenolics (flavonols, flavan-3-ols, flavones, and anthocyanins) could lead to more potent microbial-inhibitory compounds (Balasundram et al., 2006) that selectively influence intestinal bacterial species (Mokhtar et al., 2017). Some polyphenolic acids such as gallic acid, cinnamic acid, etc., produce irreversible changes in membrane properties through changes in hydrophobicity and occurrence of local rupture or pore formation in the cell membranes with consequent leakage of essential intracellular constituents (Mokhtar et al., 2017). Wu (Wu et al., 2013) showed positive correlations between the antibacterial activities of 11 flavonoids, including kaempferol and quercetin, and their rigidification of membrane. Polyphenols can bind to bacterial cell membranes and destroy the membrane proteins of bacteria and cause metabolic disorder in bacteria, which can inhibit bacterial growth or kill bacteria. However, the cell membrane structure varies between types of bacteria, leading to differences in the growth inhibition of different bacteria by polyphenols. Promising antibacterial

Table 4
Bacteriostatic activity and minimum inhibitory concentration (MIC) of AKS polyphenols.

Test microorganism	Diameter of bacteriostatic circle (mm)				MIC (mg/mL)		
	AKC	Ampicillin	THC	Control group	AKC	Ampicillin	THC
Escherichia coli	13.0 ± 1.4 c	36.3 ± 1.4 a	27.3 ± 1.4 b	–	250	1.95	3.90
Staphylococcus aureus	16.3 ± 1.4 b	38.6 ± 0.8 a	37.0 ± 0.0 a	–	125	< 1.95	1.95
Bacillus subtilis	18.6 ± 0.8 c	39.6 ± 0.8 a	35.3 ± 1.8 b	–	31.25	< 1.95	1.95
Bacillus cereus	14.6 ± 0.8 c	31.0 ± 1.4 b	40.3 ± 1.4 a	–	250	1.95	< 1.95
Aspergillus niger	–	13.6 ± 0.8	–	–	–	> 1000	–
Acetobacter aceti	14.3 ± 0.7 c	34.6 ± 1.1 a	31.2 ± 0.9 b	–	62.5	< 1.95	1.95

Results are indicated as mean ± standard deviation (SD) of three replicates. Means not sharing a common single letter in each line for each measurement were significantly different at $p < 0.05$.

activity of the AKS extracts was exhibited due to the presence of phenolic acids (118.17 mg/100 g), flavonoids and their glycosides (113.66 mg/L)and glycosides of anthocyanins (91.42 mg/100 mL). The polyphenolic compounds in AKS are possible as a potential functional food with characteristic bactericidal properties against bacterial infections in humans from wild apricot.

4. Conclusions

In conclusion, the results obtained suggest that AKS extracts contain a significant amount of phenolic compounds with different biological activities including antioxidant and antibacterial effects and activities that inhibit proliferation of and induce apoptosis of HepG2 cells. Based on this research, we confirmed that AKS polyphenols might be used against various disorders and diseases associated with free radical or reactive oxygen species-generated stress, superoxide dismutase, and cell cytotoxic studies. AKS polyphenols may be a good source of antioxidants, antiseptics and anticancer agents in the medical industry. However, further *in vivo* and clinical studies must be carried out for identification and characterization of these active AKS polyphenols that are responsible for these biological properties.

Author contributions

Fangling Qin, Lu Yao, Cairui Lu, Cong Li and Yehua Shen designed the experiments. Yanyan Zhou and Bang Chen searched for relevant literature. Fangling Qin, Lu Yao and Cairui Lu performed the experiments. Yanyan Zhou assisted in the extraction of experimental data. Fangling Qin analysed the experimental data and wrote the manuscript. Chencan Su was involved the supplementary experiments and revision for the article. Cong Li and Yehua Shen guided the manuscript preparation.

Conflict of interest

The authors declare no conflicts of interest.

Declaration of interests

NO.

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