UPLC experiment conditions

Comprehensive metabolomics analysis of loquat leaves extracts was achieved using ultrahigh-performance liquid chromatography coupled with triple quadrupole tandem mass spectrometry (UHPLC-QqQ-MS/MS) through electrospray ionization-mass spectrometry (ESI-MS) positive and negative ion acquisition mode carried out on a XEVO QqQ triple quadruple instrument (Waters Corporation, Milford, MA, USA). The UPLC system encompassed a Waters Acquity QSM pump, a LC-2040 (Waters Corporation) autosampler, degasser and Waters Acquity CM detector. Samples were separated using a Waters Acquity UPLC BEH C18 column (1.7 μm particle size – 2.1 × 50 mm). A binary mobile phase was prepared by filtration using 0.2 μm filter comprising a membrane disc and degassed by sonication before injection. The mobile phase consisted of water + 0.1% (v/v) formic acid (A) and methanol + 0.1% (v/v) formic acid (B). The mobile phase was pumped at 0.2 mL/min into the UPLC system with injection volume of 5 μL and programmed as gradient elution through 32 min performed as the following sequences: 0.0–2.0 min, 10% B; 2.0–5.0 min, 30% B; 5.0–15.0 min, 70% B; 15.0–22.0 min, phase 90% B; 22.0– 25.0 min, 90% B; 26.0 min, 100% B; 26.0–29.0 min, 100% B; 29.0–30.0 min, 10% B.

ESI-MS conditions

For LC/MS analysis, a triple quadrupole (QqQ) mass spectrometer was coupled to the UPLC instrument via an ESI interface. Ultra-high-purity helium (He) was used as the collision gas and high purity nitrogen (N_2) as the nebulizing gas. The mass spectrometer was monitored in both negative and positive ionization modes over 50–1200 *m/z* mass range. The optimized detection parameters were as follows: temperature 150 °C, cone voltage 30 V, capillary voltage 3 kV, desolvation temperature 440 °C, cone gas flow 50 L/h, and

desolvation gas flow 900 L/h. The analysis process run time lasted for 32 min. Regarding the automatic MS/MS fragmentation process of the precursor ions that have been filtered by the first quadrupole (Q1), then in the second quadrupole (Q2) the mass fragmentation was performed through collision-induced dissociation (CID) energy that was ramped from 30 to 70 eV utilizing Ultra-high purity helium as collision gas. Eventually, the third quadrupole mass analyzer (Q3) filtered the daughter ions produced from CID, which consequently related to the molecular structure of the precursor ions**.**

Annotation of UPLC-MS/MS metabolites

The raw UPLC–MS data were pre-processed using Maslynx 4.1 software. Tentative assignment of metabolites was established via comparing their retention times relative to external standards, interpreting tandem mass spectra (quasi-molecular ions as well as diagnostic MS/MS fragmentation profiles) combined with our in-house comprehensive database that was set up covering all compounds previously reported in the literature in different onion cultivars including Dictionary of Natural Products (https://dnp.chemnetbase.com/), Puchem and Massbank (https://massbank.eu/MassBank/) to provide high confidence level of annotation.

2.6. Antioxidant activity

2.6.1. DPPH radical scavenging assay

For this study, the DPPH method was chosen as an easy and rapid method for assay. The DPPH method is one of the most frequently used methods to evaluate the ability of compounds to scavenge free radicals or to donate hydrogen, and to assess the antioxidant capacity of various plant extracts at a time. In brief, DPPH method depends on the reduction of the DPPH radical

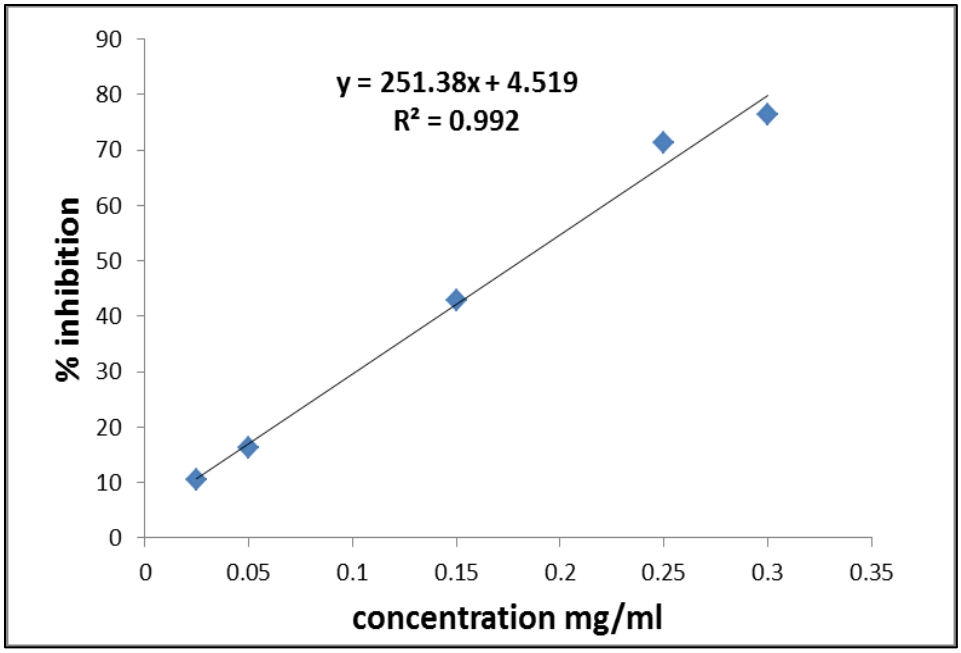
(purple colour) by an antioxidant, which changes its color to yellow. This change can be monitored and quantified using spectrophotometer at 515– 520 nm. The higher the extent of decolorization, the higher the antioxidant capacity (1). The DPPH radical is stable and does not need to be generated for hours before the assay, as in other free radical scavenging methods (2). DPPH (4 mg) was accurately weighed, transferred into 100 ml volumetric flask, dissolved in methanol and the volume adjusted with the same solvent to prepare 0.04 mg/ml solution. Ten microliters of each sample, standard solutions or methanol (negative control) were added in the microplate in triplicate, then 190 µl of DPPH solution was added to each well. Then the microplate was incubated at room temperature for 30 min and absorbance was measured at 517 nm using BIOTEK microplate reader. Control of each sample (using methanol instead of DPPH solution) was used to measure the sample solutions' background absorbance (3). DPPH radical scavenging activity was calculated as % DPPH inhibition according to the following equation:

[1- (Abs $_{\textbf{extract}}$- Abs $_{\textbf{positive control}}$**)** / **(**Abs $_{\textbf{negative control}}$ - Abs $_{\textbf{positive control}}$**)**] x 100 Where A_{ext} is the absorbance of the extract, $A_{\text{negative control}}$ is the absorbance of negative control (containing all reagents except the compound to be tested) and $A_{\text{positive control}}$ is the absorbance of positive control (the gallic acid concentration that gives 100% DPPH inhibition). The activity was expressed as mg gallic acid equivalent per gram of dried plant weight (mg GAE g^{-1} dry plant weight).

2.6. 2. Total polyphenolic content

The total phenolic content of the different extracts was determined by Folin- Ciocalteu method. The Folin- Ciocalteu's assay is one of the oldest methods used for the determination of the total phenolic content in medicinal plants or foods. The method is based on the generation of phenolate anions under alkaline conditions, which are able to the reduce Folin- Ciocalteu reagent and convert its yellow color to blue color of molybdenum oxide, which has maximum absorbance at 630 nm.

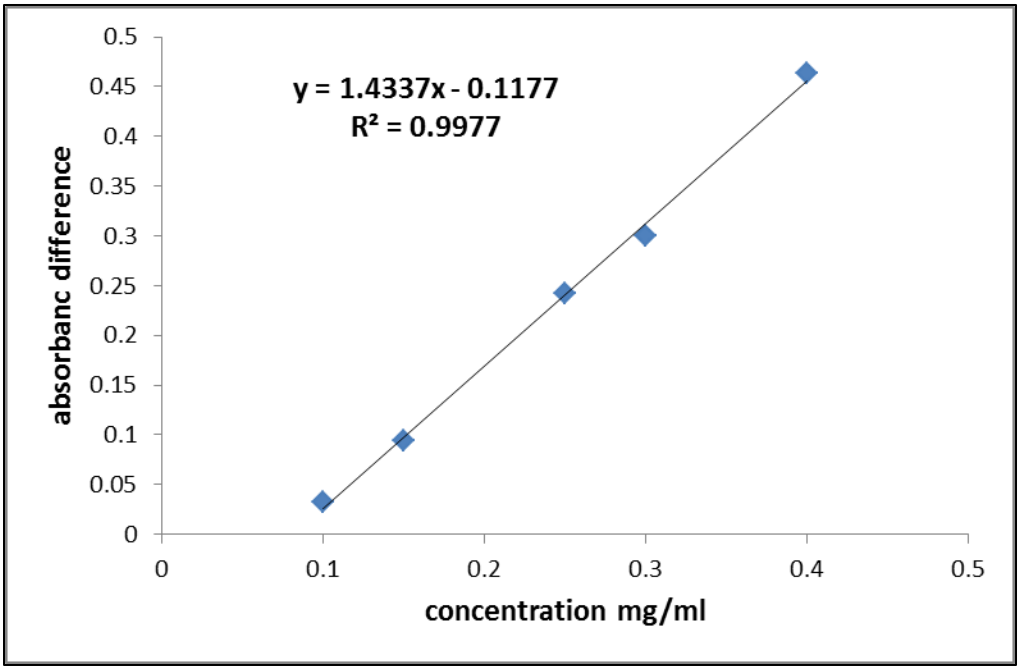
The greater the quantity of phenolic compounds in the sample, the more intense color produced (4). Twenty microliters of each extract, gallic acid standard solutions, methanol (blank) were added to a 96-well microplate, each in triplicate followed by the addition of 100 µl of Folin- Ciocalteu reagent and allowed to stand for 5 min. Then, 80 µl of Na_2CO_3 (7.5% w/v) was added to each mixture. Finally, the microplate was incubated for 1h in the dark and the absorbance was measured at 630 nm. Control of samples (using 180 µl distilled water instead of Folin- Ciocalteu reagent and Na_2CO_3) was used to measure sample solutions' background absorbance (5,6). The total phenolic content of each extract was expressed as mg gallic acid equivalents per gram of dried plant weight (mg GAE g^{-1} dry plant weight).



Concentration (mg/ml)	**0.025**	**0.05**	**0.015**	**0.25**	**0.3**
Absorbance*	0.319	0.298	0.203	0.102	0.084
% inhibition	10.393	16.292	42.977	71.348	76.404

*Absorbance values are the mean of three determinations

Figure S.1. Calibration curve (% inhibition versus concentration of gallic acid), y= DPPH percentage inhibition, x= gallic acid equivalent, R= correlation coefficient



Concentration(mg/ml)	**0.1**	**0.15**	**0.25**	**0.3**	**0.4**
Absorbance*	0.094	0.156	0.304	0.365	0.526
Absorbance difference	0.032	0.094	0.242	0.3	0.464

*Absorbance values are the mean of three determinations

Figure S.2. Calibration curve (absorbance difference versus concentration) of gallic acid, y= absorbance difference, x= gallic acid equivalent, R= correlation coefficient

Table S.1. Geographical locations and time of collection of the collected *Eriobotrya japonica* samples

Cultivar	Geographical origin	Season	Date of collection
Golden Nuggets	Eva grow farm, Cairo, Alexandria Desert Road, Kilo 84	Fruiting	March 2018
		Flowering	December 2019
		Post-fruiting	July 2019
Zekeim & Emanwil	Moustafa El Lebeidy plantation, El Mansoureya, Giza	Fruiting	April 2018
		Flowering	January 2019
		Post-fruiting	July 2019

Table S.2. The DPPH free radical scavenging activity as (mg GAE g^{-1} extract and mg GAE g^{-1} dry plant weight) of the fractions of three examined *E. japonica* cultivars at different seasons

Season of sample collection	Fraction	Golden Nuggets		Zekeim		Emanwil	
		mg GAE g^{-1} extract	mg GAE g^{-1} dry wt	mg GAE g^{-1} extract	mg GAE g^{-1} dry wt	mg GAE g^{-1} extract	mg GAE g^{-1} dry wt
Fruiting	Pet. ether	14.4 ± 0.42	0.319 ± 0.016	5.48 ± 0.31	0.085 ± 0.001	10.2 ± 0.43	0.255 ± 0.015
	CH_2Cl_2	22.29 ± 0.72	0.424 ± 0.02	27.18 ± 0.45	0.841 ± 0.057	26.79 ± 0.55	0.388 ± 0.018
	EtOAc	22.69 ± 0.66	0.26 ± 0.02	22.5 ± 0.69	0.269 ± 0.001	25.57± 0.79	0.359± 0.02
	Butanol	26.43± 0.57	0.24 ± 0.014	18.04 ± 0.47	0.591± 0.021	24.26 ± 0.71	0.674 ± 0.07
Flowering	Pet. ether	8.34 ± 0.43	0.109 ± 0.001	7.39 ± 0.34	0.159 ± 0.012	5.76 ± 0.23	0.14 ± 0.001
	CH_2Cl_2	17.51 ± 0.55	0.181 ± 0.013	17.36 ± 0.59	0.796 ± 0.05	27.47± 0.46	1.099 ± 0.09
	EtOAc	26.43 ± 0.63	0.201 ± 0.016	17.7 ± 0.67	0.216 ± 0.017	26.45± 0.83	0.736 ± 0.13
	Butanol	27.82 ± 0.71	0.595 ± 0.025	19.5 ± 0.81	0.856 ± 0.048	26.17 ± 0.51	1.244 ± 0.22
Post-fruiting	P. ether	5.42 ±0.11	0.074 ± 0.001	10.65± 0.22	0.217 ± 0.001	13.8± 0.39	0.228 ± 0.002
	CH_2Cl_2	17.85 ± 0.47	0.147± 0.01	20.55 ± 0.66	0.27 ± 0.02	27.52 ± 0.71	0.215± 0.013
	EtOAc	22.05± 0.56	0.154 ± 0.013	16.57 ± 0.47	0.126 ± 0.012	27.02± 0.61	0.124 ± 0.011
	Butanol	18.71 ± 0.43	0.339 ± 0.018	17.02 ± 0.34	0.339 ± 0.022	27.82± 0.59	0.179 ± 0.012

* Results are the average of three determinations ± SD.

Table S.3. Total polyphenolic content as (mg GAE g^{-1} extract and mg GAE g^{-1} dry plant weight) of various leaves extracts of the three examined *E. japonica* cultivars at different seasons

Season of sample collection	Fraction	Golden nuggets		Zekeim		Emanwil	
		mg GAE g^{-1} extract	mg GAE g^{-1} dry wt	mg GAE g^{-1} extract	mg GAE g^{-1} dry wt	mg GAE g^{-1} extract	mg GAE g^{-1} dry wt
Fruiting	Pet. ether	17.7± 0.53	0.393 ± 0.01	31.92 ± 0.9	0.494 ± 0.015	17.38 ± 0.51	0.435 ± 0.013
	CH_2Cl_2	21.43 ± 0.82	0.407± 0.014	42.81± 1.22	1.325 ± 0.026	17.94± 0.47	0.26 ± 0.01
	EtOAc	92.96 ± 2.35	1.065 ± 0.06	146.77 ± 2.5	1.757 ± 0.029	91.25 ± 2.48	1.282 ± 0.05
	Butanol	52.62 ± 1.23	0.478 ± 0.02	43.64± 0.85	1.431 ± 0.02	61.78 ± 1.53	1.717 ± 0.065
Flowering	Pet. ether	33.11 ± 0.69	0.434 ± 0.07	39.95 ± 0.77	0.857 ± 0.018	56.01 ± 1.34	1.364 ± 0.03
	CH_2Cl_2	21.11 ± 0.71	0.218 ± 0.011	35.48 ± 1.13	1.627± 0.023	52.67 ± 1.56	2.107 ± 0.06
	EtOAc	83.16 ± 1.68	0.631 ± 0.05	187.58 ± 3.5	2.288 ± 0.06	152.63 ± 3.11	4.247 ± 0.1
	Butanol	54.84 ± 1.63	1.172 ± 0.024	57.03 ± 1.15	2.504 ± 0.045	45.76 ± 1.24	2.175± 0.08
Post-fruiting	Pet. ether	25.89 ± 0.59	0.352± 0.012	27.08 ± 0.78	0.551 ± 0.022	43.92 ± 1.55	0.725 ± 0.018
	CH_2Cl_2	22.16 ± 0.66	0.182 ± 0.001	62.16 ± 1.41	0.817± 0.03	65.68 ± 1.73	0.512 ± 0.014
	EtOAc	123.85 ± 2.44	0.866 ± 0.02	174.33 ± 3.88	1.33 ± 0.04	101.74 ± 2.75	0.467 ± 0.012
	Butanol	12.29 ± 0.76	0.223 ± 0.01	72.76 ± 2.12	1.449 ± 0.027	30.7 ± 1.68	0.197 ± 0. 01

* Values are expressed as mean ± SD of three determinations.

Table S.4. XO inhibitory activity expressed as (percentage inhibition) of methylene chloride and ethyl acetate fractions of the leaves of the three examined *E. japonica* cultivars at a concentration of 2.5 mg/ml at different seasons

Season of sample collection	Fraction	Golden Nuggets	Zekeim	Emanwil
Fruiting	CH_2Cl_2	96.89 ± 1.56	24.54 ± 0.54	8.65 ± 0.27
	EtOAc	97.15 ± 1.87	99.18 ± 1.88	98.14 ± 2.03
Flowering	CH_2Cl_2	14.73 ± 0.42	17 ± 0.59	31.63 ± 0.63
	EtOAc	54.46 ± 0.96	97.48 ± 1.92	96.23 ± 2.13
Post-fruiting	CH_2Cl_2	62.85 ± 0.79	86.1 ± 1.57	95.96 ± 1.71
	EtOAc	66.67 ± 0.86	81.21 ± 1.64	75.46 ± 1.33

* Data are expressed as mean ± SD of three determinations

Table S.5. XO inhibitory activity expressed as (percentage inhibition) of petroleum ether and butanol fractions of the leaves of the three examined *E. japonica* cultivars at a concentration of 5 mg/ml at different seasons

Season of sample collection	Fraction	Golden Nuggets	Zekeim	Emanwil
Fruiting	Pet. ether	17.14 ± 0.44	3.09 ± 0.03	83.36 ± 1.24
	Butanol	82.12± 1.53	45.84 ± 0.41	22.73 ± 0.63
Flowering	Pet. ether	4.42 ± 0.11	2.68 ± 0.008	99.43 ± 2.15
	Butanol	3.95 ± 0.08	68.39 ± 0.71	83.36 ± 1.69
Post-fruiting	Pet. ether	62.26 ± 0.81	3.39 ± 0.031	4.44 ± 0.025
	Butanol	3.71 ± 0.05	3.13 ± 0.01	3.8 ± 0.034

* Data are expressed as mean ± SD of three determinations

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