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Changes in the phenolic profile of Argentinean fresh grapes during production of sun-dried raisins

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ABSTRACT

Changes in the phenolic profile of 'Arizul', 'Sultanina', 'Superior', and 'Flame' grapes from the Province of San Juan (Argentina) caused by sun drying were evaluated. Our main goal was to propose that the obtained raisins are a good source of bioactive antioxidants. The 'Flame' red variety had the highest amount of total phenols when compared to white raisins (TSP = 201 ± 13 and 154 ± 28 mg gallic acid equivalent/100 g DW raisins, respectively). The sun drying of fresh grapes produced an increased amount of phenolic acids and flavonoids (rutin, kaempferol-hexoside, quercetin and isoquercitrin). Multiple regression analysis (MRA), principal components (PC) and factor analysis (FA) showed a high correlation between the phenolic profile and the antioxidant activity (AA) of raisins ($r \geq 0.90$, $p < 0.05$). The 'Flame' variety showed the highest AA, which was linked to the amount of gallic acid, astilbin, quercetin-3-*O*-glucuronide, isorhamnetin, and isorhamnetin-hexoside present in this variety. On the other hand, the AA in the 'Arizul' variety was better correlated with the content of (+)-catechin, caftaric and fertaric acids, whereas the 'Sultanina' variety was correlated with resveratrol. Multi-elemental analyses showed that raisins are rich in K (639–883 mg/100 g), Ca (51–121 mg/100 g) and Mg (28–42 mg/100 g). These findings support the potential health properties of raisins as health-promoting food.

1. Introduction

Consumers are increasingly making decisions about their daily food intake based on the food's nutritive values as well as the presence or absence of contaminants and agrochemicals (Fang et al., 2010). Grape (genus *Vitis*) consumption has received considerable attention because these fruits are rich in phenolic compounds whose antioxidant capacity and health benefits have been well described (Karadeniz et al., 2000; Cantos et al., 2002; Pasinetti and Ho, 2010). Dried grapes, or raisins, are produced worldwide, with the United States of America (USA) the largest raisin-producing and -consuming country (28%), followed by Turkey (26%). Argentina is the 7th largest producer, with 3.4% of world production (INV, 2011). The Province of San Juan, located in the west central region of Argentina, is the main raisin producer and exporter, with 91% of the total amount exported by Argentina. The arid climatic conditions in San Juan (dry atmosphere, altitude, high radiation and temperature) enable the production of high quality raisins, with 'Arizul' and 'Sultanina' (Thompson Seedless) the most important raisin varieties being produced and exported there.

Sun drying is the oldest process used to obtain raisins from fresh grapes. Under this method, grape bunches are traditionally spread on a rocky-sandy soil and exposed to the sun and natural air for 2–3 weeks. A more recent method used to obtain raisins from fresh grapes involves an oven-drying step, followed by the addition of sulfur dioxide (for golden raisins) (Fadhel et al., 2005; Moreno et al., 2008). Among the dried fruits, raisins have a mineral profile that is beneficial for human health (USDA, 2012), as they are a good source of nutritive elements, such as potassium, iron, calcium, magnesium (Fang et al., 2010). They are also a good source of boron, which is recognized as an essential trace element that may have an

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important role in bone health (Bin and Clifford, 2008). Conversely, consumers should be aware that some contaminants, such as heavy metals, might be transmitted to raisins during sun-drying processes. Therefore, the multi-elemental composition of raisins can help evaluate both the presence of nutritional elements and the absence of inorganic pollutants. Furthermore, in addition to their high content of soluble and insoluble fibers (Fang et al., 2010), raisins are high in sugar content, which accounts for the characteristic sweet flavor and high energy levels.

On the other hand, drying methods have a significant impact on the phenolic profile of grapes. Thus, polyphenols are usually less abundant in fresh grapes than in raisins (on a per dry-weight basis), mainly because they are concentrated and partially modified during the dehydration process (Williamson and Carughi, 2010). Berli et al. (2011) showed that the amount of phenolics in grapes skin increased as levels of UV-B radiation was increased. Mencarelli et al. (2010) and Bonghi et al. (2012) attributed these changes to both the variations in the temperature used during the drying process and grape genotypes, because modifications in the phenyl-propanoids pathways occur in the berry skins. Furthermore, some polyphenols like caffeic acid, quercetin and catechin are commonly found in raisins, regardless of the grape variety (Serratosa et al., 2008; Peinado et al., 2010; Meng et al., 2011). On the other hand, Karadeniz et al. (2000) reported that flavonol and hydroxycinnamic compounds were not influenced by the drying process. These authors reported that procyanidins and flavan-3-ols were instead completely degraded when grapes were transformed into raisins (*Vitis vinifera* L. cv. sultanina). In a similar fashion, Serratosa et al. (2008) observed an increase in the concentration of phenolic compounds during the production of sun-dried raisins (cv. Pedro Ximenez), which can be essentially explained by the water lost during the drying process. Moreover, Peinado et al. (2013) reported that Pedro Ximenez grapes, exposed to sunlight, presented a higher antioxidant capacity than fresh grapes. Thus it is reasonable to infer that both UV radiation and temperature bring about changes in the phenolic profile when fresh grapes are processed into raisins by sun drying.

To our knowledge, there are no previous reports of the dynamics of the changes that occur in the phenolic profile of either 'Superior' or 'Flame' grapes during the sun-drying process to produce raisins (40–45 °C). Additionally, there are no previous reports on the multi-elemental composition of Argentinean raisins to consider nutritional quality and food safety. The main goals of this study were: a) to evaluate changes in the phenolic profile of four grapes varieties ('Arizul', 'Sultanina, 'Superior' and 'Flame') during the sun-drying process, and b) to verify if raisins can be considered a good source of bioactive compounds, and demonstrating that raisins are much more stable than grapes. In addition, the multi-element composition of Argentinean raisins is reported here for the first time, providing more complete nutritional information on this valuable product.

2. Materials and methods

2.1. Reagents

Ultra-pure water (≤0.056 μS/cm, containing ≤5 μg/L TOC) was obtained from a water purification system Arium 126 61316-RO, in tandem with an Arium 611 UV unit (Sartorius AG, Goettingen, Germany). Methanol (HPLC grade) and formic acid (puriss p.a. for mass spectroscopy) were obtained from J. T. Baker (State of México, México) and Fluka (Steinheim, Germany), respectively. Commercial Folin–Ciocalteu (FC) reagent, HNO_3 (63%) and HCl (37%) were purchased from Merck Química Argentina (Buenos Aires, Argentina). 2,2-Diphenyl-1-picrylhydrazyl (DPPH), gallic acid (GA), caffeic acid, rutin, quercetin, myricetin, malvidin-*O*-glucoside, resveratrol and kaempferol were purchased from Sigma Aldrich (Buenos Aires, Argentina). A commercial standard of (+)-catechin was used (Extrasynthese, Genay, France). Inductively coupled plasma multi-element standard solution, Merck VI CertiPUR®, was obtained from Merck Química Argentina (Buenos Aires, Argentina). The composition and concentration of the Merck VI standard was as described in the accompanying certificate of analysis. Nitric acid (63.7%), ultra-pure grade, was prepared from analytical grade acid using a sub-boiling distiller (Figmay Sub-boiling distiller, Córdoba, Argentina). The purity of the nitric acid was verified by ICP-MS before use. NIST 1548a Typical Diet was used as the certified reference material (CRM) (NIST, Gaithersburg, MD, USA) to verify the accuracy during multi-elemental analysis. All other chemicals were of analytical grade.

2.2. Samples

Fresh grape and raisin samples (white varieties: 'Arizul', 'Sultanina and 'Superior'; red variety: 'Flame') were supplied by Héctor Paños S.R.L., a food-processing plant located in the "9 de Julio" Department (Tulum Valley), Province of San Juan, Argentina. This establishment has its own plantation where the grapes are grown, harvested, sun-dried, and processed (washed, dried and polished with glycerine) to produce raisins from different varieties. The sampling area is situated on both sides of the San Juan River between 31° and 32° south latitude. The altitude varies from 650 to 750 m above sea level. The climate is continental with hot summers (temperatures up to 40 °C) and cold winters. Rainfall is scarce (≤90 mm per year), requiring additional irrigation with either surface water (rivers formed by melting ice) or groundwater.

Fresh grapes were randomly harvested after reaching the appropriate ripeness and packed in black polyethylene bags. Three independent samples (×4 varieties × 600 g/sample) were used for the analyses. The raisins were collected and put into black polyethylene bas at the end of the sun-drying process (2–3 weeks), and three independent samples (×4 varieties × 600 g/sample) were used for multi-elemental content, polyphenols analysis, and antioxidant assays. All values were calculated as the means ± SD of three individual determinations (each performed in triplicate). All samples were stored in the dark at 4–8 °C until analysis within 30 days. Dry matter (for fresh grapes and raisins) was determined according to AOAC (2000) methods, and expressed as a percentage (w/w).

2.3. Sample preparation

Both fresh grapes and raisin samples were homogenized in a food grinder (TECNODALVO, Buenos Aires, Argentina), weighed (ca. 1.00 g) and extracted by sonication (40 kHz, 45 min, 25 °C, ultrasound bath model TB02TACA, TESTLAB S.R.L, Buenos Aires, Argentina) using 10 mL of acidified methanol (0.1% HCl, v/v) ($MeOH\text{-}H^+$), according to Meng et al. (2011) with slight modifications. The homogenate was then centrifuged at 10,000 × *g* during 10 min using a Biofuge 28RS Heraeus Sepatech Centrifuge (Heraeus Instruments, Hanau, Germany). The supernatant was separated, filtered (0.45 μm) and used for further analyses.

2.4. Total soluble phenolic content

The total soluble phenolic (TSP) content of acidified methanolic extracts was determined by the Folin-Ciocalteu method (Heldrich, 1990). An extract dilution (1 g/L) was first oxidized using Folin-Ciocalteu reagent (125 μL), and then neutralized with sodium carbonate (20% w/v). After 30 min, the absorbance of the resulting blue solution was measured at 765 nm using a Shimadzu Multi-Spec-1501 spectrophotometer (Shimadzu Corporation, Kyoto,

Japan, equipped with a holder for multiple cells and temperature control). TSP were determined by linear regression from a calibration plot constructed using gallic acid (0–250 mg/mL), and expressed as mg of gallic acid equivalents (GAE) per 100 g of grapes or raisins on a fresh weight (FW) (mg GAE/100 g FW) and on a dry weight (DW) (mg GAE/100 g DW).

2.5. Identification and quantification of phenolics by HPLC-PDA-ESI-QTOF MS

Phenolic compounds were analyzed by HPLC-PDA-ESI–MS/MS, using an Agilent Series 1200 LC System (Agilent, Santa Clara, CA, USA), coupled to a PDA detector (Agilent Series 1200) in tandem with an ESI source, connected to a MicroQTOF II (Bruker Daltonics, Billerica, MA, USA) mass spectrometer (MS and MS/MS). The HPLC system was equipped with a binary gradient pump, solvent degasser and autosampler (Agilent Series 1200L, Santa Clara, CA, USA) (Fabani et al., 2013).

HPLC analyses were performed on a LUNA (Phenomenex, Torrance, CA, USA) C18 column (5 μm, 250 mm × 4.60 mm i.d.), at 35 °C and 0.4 mL/min flow rate, using 0.5% formic acid (solvent A), and 0.5% formic acid in methanol (solvent B). The gradient program started with 20% B and changed to 50% B along 3 min, held for 5 min, followed by a second ramp to 70% B along 7 min, held for 5 min, and a third ramp to 80% B along 1 min, remaining in this last condition for 9 min (stabilization) before the next run. The injection volume of properly diluted samples was 40 μL. UV–vis analyses were carried out in the range of 200 and 600 nm (PDA). MS spectra were recorded (80 to 1500 *m/z*) in both negative (for analyses of phenolic acids, stilbenes, flavonols and flavanols) and positive modes (for the analysis of anthocyanins). The working conditions for the ESI source were as follows: capillary voltage, 4500 V; nebulizer gas pressure, 4.0 bars; drying gas flow, 8.0 L/min and drying gas temperature 180 °C. Nitrogen and argon were used as nebulizer and collision gases, respectively. The MS detector was programmed to perform an MS/MS scan of the three most abundant ions, using collision energy of 13.0 eV. Data acquisition and processing were performed using Compass (V. 3.1, BrukerDaltonics, Billerica, MA, USA) and Data Analysis (V. 4.0, BrukerDaltonics, Billerica, MA, USA) software, respectively.

Polyphenols present in samples were identified according to their retention times, UV/vis spectra, high-resolution MS and MS/MS spectra, in comparison with pure compounds, when available, or with compounds reported in the literature. MS analysis was used for quantification of the polyphenols with external calibration plots, constructed by linear regression from available phenolic standards. Limits of detection (LOD) and limits of quantification (LOQ) of the compounds studied were experimentally evaluated considering a signal-to-noise ratio of 3 and 10, respectively. Instrumental LOQ ranged from 0.0013 to 0.05 mg/L.

2.6. Antioxidant capacity

2.6.1. Free radical scavenger assay

Free radical scavenging effects were assessed according to the procedure described by Brand-Williams et al. (1995) with slight modifications to reduce the test time (Tapia et al., 2004). Extracts were assayed at concentrations 6.25, 12.5, 25 and 50 mg/mL. Scavenging activities were evaluated at 517 nm in an UV–vis spectrophotometer (MultiSpec-1501, Shimadzu Corporation, Kyoto, Japan,). Quercetin was used as the reference compound. The loss of color (fade percentage) indicated the free radical scavenging efficiency of the substances. DPPH antioxidant capacity was expressed as% of DPPH discoloration using the equation:

$$\%\ \text{Scavenging effect} = [1 - (A_{sample} - A_{blanck})/A_{DPPH}] \times 100$$

The extract concentration providing 50% of radicals scavenging activity (EC_{50}) was calculated by plotting the inhibition percentage (A_{517}) against the extract concentration.

2.6.2. Ferric-reducing antioxidant power assay (FRAP)

The iron-reducing power of the samples was tested using the assay reported by Oyaizu (1986). The absorbance was read at 700 nm using an UV–vis spectrophotometer (MultiSpec-1501, Shimadzu Corporation, Kyoto, Japan,). Catechin was used as the reference compound. Results are expressed as the sample concentration that has the same activity as a 50 μM catechin solution.

2.7. Multi-elemental composition

Samples were prepared for multi-elemental analysis as follows: 20 g of raisins were milled, and a small portion (0.2 g) was introduced into quartz vessels, followed by the addition of 8 mL concentrated nitric acid (sub-boiling grade). After fumes were released (2–3 h), vessels were closed with PTFE caps, mineralized in a microwave oven (Anton Paar Multiwave 3000; Graz, Austria), and heated using the following power sequence: starting with a 15 min ramp until reaching 600 W, holding for 45 min (maximal T = 169 °C; max pressure = 75 bar), and a final 15 min step disabling the power to reach atmospheric pressure. Mineralized samples were quantitatively transferred to 25 mL volumetric flasks, completing the volume with ultrapure water, followed by filtration using 0.45 mm filters. A certified reference material (CRM: NIST 1548 a – typical diet) was analyzed using the same procedure for quality assurance (QA) and quality control (QC). Recovery of elements measured from CRM was between 70% and 110% of certified values (See Supplementary material, Table S3 for certified *vs.* measured concentrations of selected metals).

Multi-elemental content was analyzed according to Fabani et al. (2013). Twenty-nine elements were quantified in the raisins: Li, Be, B, Na, Mg, Al, K, Ca, V, Cr, Mn, Fe, Co, Ni, Cu, Zn, Ga, As, Se, Rb, Sr, Mo, Ag, Cd, Te, Ba, Tl, Pb and Bi. Multi-elemental analyses were carried out on a Quadrupole Inductively Coupled Plasma Mass Spectrometer (Q-ICPMS) (Agilent Technology 7500 cx Series, Santa Clara, CA, USA), equipped with an ASX-500 series autosampler (Agilent). The concentration for each element was calculated by linear regression from a calibration plot constructed from serial dilutions of the multi-elemental standard solution. Samples were diluted tenfold using HNO_3 (2% in ultrapure water) before ICP-MS measurements. Standards and blanks were prepared using the same mixture (HNO_3 2%).

2.8. Statistical analysis

Results were analyzed by one-way ANOVA test, and Duncan's test was used to compare the significant differences of the mean values ($p < 0.05$). The statistical package InfoStat (Di Rienzo et al., 2014) and STATISTICA 10 from StatSoft Inc. (2010) were used for statistical analyses.

2.8.1. Stepwise multiple regression analysis (MRA)

MRA was used to assess the relationship between the polyphenolic profile and the antioxidant activity of studied samples. The regression (*Beta*) coefficients were analyzed to evaluate key variables for the prediction of antioxidant activity in studied samples. The magnitude of these *Beta* coefficients allows comparing the relative contribution of each independent variable (a particular polyphenol in this case) to the prediction of the dependent variable (the antioxidant capacity in this case).

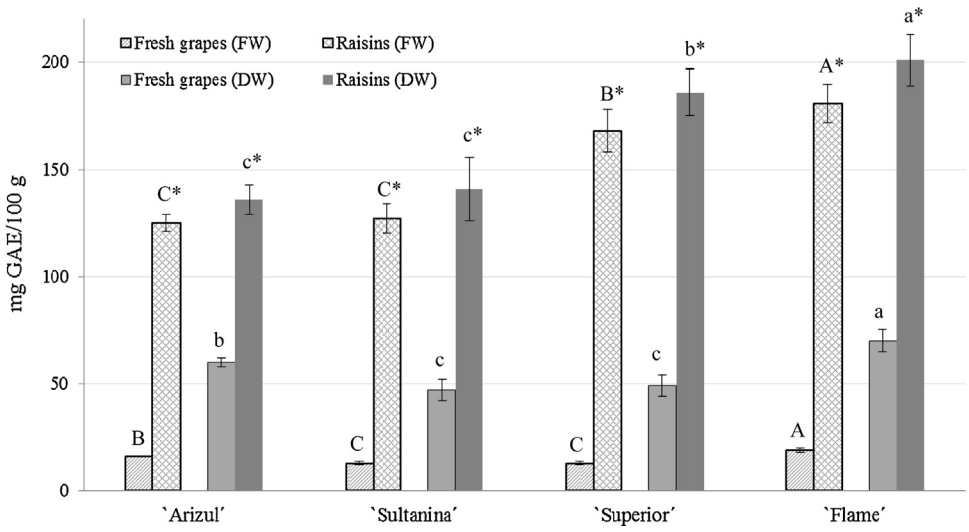

Fig. 1. Total soluble phenolics (mg GAE/100 g) expressed as mg of gallic acid equivalents (GAE) per 100 g of fresh grapes or raisins on a fresh weight (FW) (mg GAE/100 g FW) and on a dry weight (DW) (mg GAE/100 g DW). Different letters in each column indicate significant differences among fresh grape and raisin varieties (Duncan, $p < 0.05$) (n = 3, analysed in triplicate).

2.8.2. Multivariate exploratory techniques

Principal components (PC) and factor analysis (FA) were applied to the complete dataset, involving phenolic compounds (phenolic acids, stilbene, flavonols, flavanols and flavanonol) and antioxidant activity (DPPH and FRAP). Thus, we looked to verify differences among the antioxidant capacity of different raisin varieties.

3. Results and discussion

3.1. Changes in the phenolic composition from fresh grapes to raisins

Fig. 1 shows the total soluble phenolic (TSP) content of both fresh grape and raisin samples, expressed as fresh weight (FW) and dry weight (DW). Results were transformed from a fresh weight basis to a dry weight basis to avoid differences arising from the moisture content between fresh grapes and raisins (Table 1) (Karadeniz et al., 2000).

In grapes, TSP values ranged from 47 ± 5 to 70 ± 7 mg GAE/100 g DW, while in raisins, from 136 ± 7 to 201 ± 13 mg GAE/100 g DW, showing significant differences between varieties (Fig. 1). 'Flame' (red variety) had the major TSP content, followed by 'Arizul', 'Superior' and 'Sultanina' (white varieties). Among the studied raisins, 'Flame' presented the highest amount of TSP, whereas 'Arizul' had the lowest content (Fig. 1). It is worth mentioning that TSP values were higher in raisins than in fresh grapes. The rate between TSP raisins/TSP fresh grapes was calculated for each

Table 1
Dry matter (w/w), phenolic compounds identified and quantified in fresh grapes and raisins.

	Arizul		Sultanina		Superior		Flame	
	Fresh grapes	Raisins	Fresh grapes	Raisins	Fresh grapes	Raisins	Fresh grapes	Raisins
Dry matter (w/w)	28 ± 3 a	92 ± 1 A	29 ± 4 a	90.0 ± 0.7 A	27.6 ± 0.2 a	90.3 ± 0.8 A	29 ± 1 a	90 ± 1 A
Phenolic compounds	μg/100 g DW	mg/100 g DW	μg/100 g DW	mg/100 g DW	μg/100 g DW	mg/100 g DW	μg/100 g DW	mg/100 g DW
Phenolic Acids								
Gallic acid	7 ± 3 a	0.23 ± 0.03 B	7 ± 1 b	0.160 ± 0.02 BC	8 ± 3 b	0.12 ± 0.04C	31 ± 6 a	0.50 ± 0.02 A
Caftaric acid	171 ± 14 a	19 ± 3 A	42 ± 6 b	7.2 ± 0.6 B	41.6 ± 0.5 b	3.264 ± 0.002 B	157 ± 5 a	15.6 ± 0.5 A
Fertaric acid	333 ± 51 a	1.2 ± 0.4 A	188 ± 9 b	0.6 ± 0.2 B	151 ± 5 b	0.53 ± 0.08 B	209 ± 33 b	1.05 ± 0.08 AB
Coutaric acid	nd	2.5 ± 0.5 A	nd	1.0 ± 0.3 B	nd	0.644 ± 0.006 B	20.1 ± 0.4	3.5 ± 0.7 A
μg/100 g DW								
Stilbenes								
trans-resveratrol	nd	nd	2.6 ± 0.5 a	27 ± 8	3.8 ± 0.2 a	nd	nd	nd
Flavonoids								
Flavonols								
Quercetin	1.7 ± 0.3 b	12.9 ± 0.8 B	3.1 ± 0.2 a	98 ± 15 A	0.8 ± 0.3 c	27 ± 3 B	3.3 ± 0.1 a	97.25 ± 0.02 A
Quercetin-3-*O*-rutinoside	117 ± 25 a	nd	98 ± 2 a	260 ± 27A	75 ± 1 a	109 ± 27 B	140 ± 40 a	206 ± 42 A
Quercetin-3-*O*-glucuronide	4.5 ± 0.5 b	3.4 ± 0.7C	28 ± 2 a	11 ± 2 B	13.7 ± 0.3 b	3.5 ± 0.6C	32 ± 9 a	41.9 ± 0.2 A
Isoquercitrin	31 ± 4 a	39 ± 6 B	37 ± 3 a	121 ± 16 A	40 ± 4 a	58 ± 5 B	35 ± 5 a	119 ± 7 A
Kaempferol	1.8 ± 0.3 b	26.6 ± 0.5 A	2.36 ± 0.03 b	49 ± 19 A	0.6 ± 0.1 c	30 ± 4 A	3.3 ± 0.3 a	44 ± 12 A
Kaempferolhexoside	35 ± 8 a	198 ± 12 A	41 ± 6 a	213 ± 36 A	55 ± 4 a	81 ± 18 B	41 ± 11 a	135 ± 10 B
Isorhamnetin	nd	nd	nd	3.2 ± 0.9 B	1.2 ± 0.4 a	10.8 ± 0.4 A	0.72 ± 0.0 a1	17 ± 5 A
Isorhamnetin-hexoside	nd	2.4 ± 0.3C	1.8 ± 0.4 b	8 ± 2C	9 ± 2 a	23 ± 3 B	6 ± 1 a	43 ± 2 A
Flavan-3-ols								
(+)-catechin	28 ± 3 b	158 ± 1 A	20 ± 2 c	27 ± 5C	29.8 ± 0.8 b	15 ± 3C	38 ± 1 a	57 ± 7 B
(−)-epicatechin	15 ± 2 a	15 ± 5 A	1.6 ± 0.2 b	nd	14 ± 2 a	nd	11 ± 3 a	27 ± 2 A
Procyanidin dimer	5 ± 1 a	nd	5 ± 1 a	nd	4.0 ± 0.1 a	nd	6 ± 2 a	nd
Flavones								
Astilbin	2.9 ± 0.4 a	12 ± 4 B	0.3 ± 0.1 b	5 ± 2C	2.6 ± 0.2 a	0.8 ± 0.2C	3 ± 1 a	27 ± 2 A

Abbreviations. nd. Not detected. DW: dry weight. Results are expressed as mean ± SD (standard deviations) (n = 3, analysed in triplicate). Different letters indicate significant differences (Duncan, $p < 0.05$) in each sample type (fresh grapes and raisins) among the four varieties studied. Instrumental LOQ ranged from 0.0013 to 0.05 mg/L.

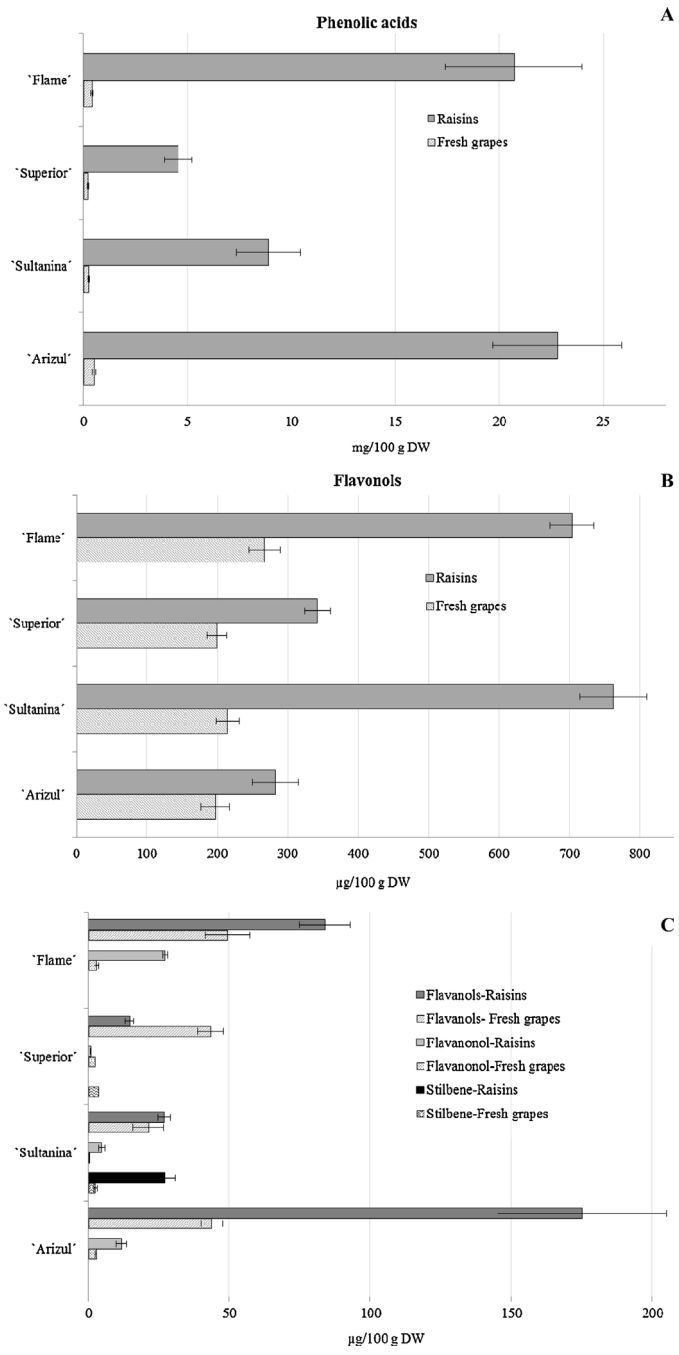

Fig. 2. Changes in the main phenolic families caused by the sun-drying process. A: phenolic acids': flavonols. C: flavanols, flavanonol and stilbene (n = 3, analysed in triplicate).

studied variety, giving the following values: 'Arizul' = 2.27; 'Sultatina' = 3; 'Superior' = 3.8 and 'Flame' = 2.87. When the effect of the drying process was evaluated, the highest TSP rate was observed for 'Superior' variety (3.8). Regarding the phenolic concentrations reported for other grapes, our current values are similar to those measured in currants (Corinthian raisin, *Vitis vinifera* L.) (151–246 mg GAE/100 g DW; Chiou et al., 2007). However, TSP values found during this work were lower than the corresponding values for raisins produced in the Xinjiang Province (300–447 mg GA/100 g DW; Meng et al., 2011).

Results of the HPLC-PDA-ESI–MS and MS/MS assays on fresh grapes and raisins are summarized in Table 1. A total of 17 compounds, belonging to the families of phenolic acids, stilbenes and flavonoids (flavonols, flavan-3-ols and flavanonols) were identified and quantified in all studied varieties. Additionally, five anthocyanins were identified and quantified in the 'Flame' variety (See Supplementary material, Tables S1–S2 for compound identification parameters; Figs. S1, S2 and S3 for chromatograms of compounds identified in fresh grapes and raisins).

Fig. 2A–C shows dynamic changes in the phenolic profile of fresh grapes during the sun-dried raisin production. Fig. 2A and B shows values for phenolic acids and flavonols, quantified in fresh grapes and raisins, respectively. Fig. 2C shows the levels of flavanols, flavanonol and stilbene for the varieties that were analysed.

3.1.1. Phenolic acids

Phenolic acids were the most abundant polyphenols in fresh grapes and raisins. Four of them – gallic, caftaric, fertaric and coutaric acids – were identified and quantified. The main compounds found in fresh grapes were fertaric and caftaric acids; 'Arizul' was the variety with the greatest concentration of these acids. Conversely, coutaric acid was only found in 'Flame' fresh grapes (Table 1). Regarding raisins, caftaric acid was the main compound among identified hydroxycinnamic acids (ranging from 3 to 19 mg/100 g DW), representing 72–83% of the total phenolic acid content in studied raisins. The contents of trans-caftaric acid in 'Arizul' and 'Flame' are in agreement with values previously reported by Breksa et al. (2010) (153 mg/kg DW, A95-15). Coutaric acid was the second most abundant phenolic acid in raisins (from 0.6 to 4 mg/100 g DW); 'Arizul' and 'Flame' were the varieties presenting the highest concentrations (Table 1).'superior' was the variety with the lowest level of phenolic acids in both fresh grapes and raisins. This last result is in agreement with Breksa et al. (2010), who reported that caftaric acid was the predominant phenolic compound in 16 raisin samples from Florida (USA). Also Kelebek et al. (2013) reported similar results in Turkish raisin varieties. The differences observed in the behavior of cinnamic acids throughout different grapes varieties have also been reported by Bonghi et al. (2012). The importance of hydroxycinnamic acids (caftaric and fertaric) on human health is related to their antioxidant activities (Teixeira et al., 2013). Additionally, gallic acid is an important free radical scavenger (Yilmaz and Toledo, 2004).

3.1.2. Flavonoids

3.1.2.1. Flavonols. Nine flavonols were detected and quantified. Rutin (quercetin-3-*O*-rutinoside) was the main flavonoid identified in fresh grapes, ranging from 75 to 140 µg/100 g DW (Table 1). The amount of this flavonol was variable and dependent on the variety (Table 1). However, this compound was not detected in 'Arizul' raisins. Rutin levels found in the analyzed raisin samples are in agreement with values reported by Kelebek et al. (2013) (from 0.46 to 2.70 mg/kg). Kaempferol-hexoside was the second most abundant flavonol in both fresh grapes and raisins. Isoquercitrin (quercetin-3-*O*-glucopyranoside) was present in fresh grapes, with similar concentrations throughout analyzed varieties (31–55 µg/100 g DW). It is worth noting that isoquercitrin presented higher concentrations in raisins in comparison to fresh grapes (Table 1). This flavonol exhibits a broad range of positive *in vitro* and *in vivo* biological effects, particularly potential antioxidant, anti-inflammatory, anticarcinogenic, cardioprotective, antidiabetic, anti-allergic, and neuropharmacological activities (Valentová et al., 2014). Quercetin was present mainly in 'Sultanina' and 'Flame' raisins (median 98 µg/100 g DW), whereas its content in fresh grapes was considerably lower (between 0.8 and 3.3 µg/100 g DW). Quercetin-3-*O*-glucuronide was identified in all varieties of fresh grapes and

raisins studied (Table 1). Price et al. (1995) have shown that the content of quercetin in grapes is dependent on exposure to sun. In addition, Soleas et al. (1997) mentioned that the water status of the plant and the grape variety could affect the content of quercetin. Differences in the UV radiation and dehydration process for the studied grapes varieties could account for the variations observed in levels of quercetin and isoquercitrin during this work.

The content of kaempferol was similar to quercetin in fresh grapes (Table 1). The presence of quercetin and kaempferol glycosides was previously reported in white grapes (Karadeniz et al., 2000). Other flavonoids, like isorhamnetin and isorhamnetin-hexoside, were quantified in variable concentration, depending on the grape variety (Table 1).

3.1.2.2. Flavononols. Astilbin levels (dihydroquercetin-3-rhamnoside) were lower in fresh grapes than in raisins, with the exception of the 'Superior' variety. This natural flavononol shows properties as aldose reductase inhibitor and antioxidant. It has been clinically used to treat a variety of diseases such as leptospiriosis, syphilis, and acute and chronic nephritis (Tang et al., 2013). After ingestion, (poly)phenol glycosides are modified in the digestive tract; their absorption is associated with hydrolyzing activity. It is becoming increasingly evident that metabolites of dietary phenols are much more bioavailable than previously suggested (Rodriguez-Mateos et al., 2014). Thus, the presence of astilbin in raisins is of great importance to promote human health and, accordingly, raisins containing astilbin could be considered a healthful food.

3.1.2.3. Flavan-3-ols. The highest level of flavan-3-ols was detected in the 'Arizul' variety, followed by 'Flame', 'Superior' and 'Sultanina' (Table 1). The concentration of (+)-catechin was higher than (−)-epicatechin in all analyzed samples (Table 1), presenting a variable behavior according to the grape variety considered (Table 1). (−)-Epicatechin was not quantified in all fresh grapes, but only in the 'Flame' and 'Arizul' raisins. This behavior could be related to the degradation of flavanols during the sun-drying process (Karadeniz et al., 2000), which depends on the grape variety considered (Yilmaz and Toledo, 2004). In this respect, our current results are in accordance with those reported by Kelebek et al. (2013). The catechin and epicatechin monomers as well as their polymers have an even more effective antioxidant activity than vitamin E (Rice Evans et al., 1997). Thus, many reports suggest that catechins might prevent chronic diseases on humans (Breksa et al., 2010). In our case, a procyanidin dimer was detected only in fresh grape extracts. This compound appears to be degraded during the sun-drying process, probably due to enzymatic oxidation, in agreement with results reported by Karadeniz et al. (2000) during their study of Thompson seedless grapes and raisins. On the other hand, Williamson and Carughi (2010) attributed the probable degradation to the limitations in the extraction and analytical methods used to detect this dimer. Moreover, Bonghi et al. (2012) suggested that the increase in flavonol concentrations in raisins can be seen as one of the main metabolic events, characterizing grape berries undergoing postharvest dehydration, due to the fact that the genotype affects their content (Moreno et al., 2008; Mencarelli et al., 2010).

3.1.2.4. Stilbenes. The compound *trans*-resveratrol, a recognized antioxidant and antiproliferative compound (Ider et al., 2000), was identified in the 'Arizul' variety of both fresh grapes and raisins (median 2.6 ± 0.5 μg/100 g DW). In addition, this compound was detected in 'Superior' grapes (Table 1), whereas in the other varieties, levels of this compound were below the detection limit. Our current findings are in agreement with previous reports (Iacopini et al., 2008).

3.1.2.5. Anthocyanins. These phytochemicals have been reported as being involved in the prevention of chronic diseases (Butkhupl et al., 2010). They are the pigments responsible for the red, blue and purple color in berries, and are present only in the fruit skin of *Vitis vinifera* species. Five anthocyanins were identified and quantified in the red variety 'Flame'. The predominant anthocyanin was peonidin-3-glucoside (588.3 ± 0.8 μg/100 g DW), in agreement with a previous report for red table grape cultivars from Murcia (Spain; Cantos et al., 2002). Other abundant anthocyanins found were: cyanidin-3-glucoside > malvidin-3-glucoside > petunidin-3-glucoside. Furthermore, the acylated anthocyanin peonidin-3-*trans*-coumaroylglucoside was identified in raisins.

Fig. 3 shows changes in the anthocyanin content due to the sun-drying process. Our current results indicate that the concentration of anthocyanins was lower in raisins than in fresh grapes. The degradation observed for these compounds in the production of raisins could probably be attributed to the high temperature (~40–45 °C) during the natural sun-drying process of fresh grapes (two-three weeks) (Rein, 2005). Thus, only peonidin-3-glucoside and cyanidin-3-glucoside were identified in raisins, in smaller amounts with respect to the corresponding fresh grapes (Fig. 3). Mencarelli et al. (2010) reported a decrease in anthocyanins after dehydration of Aleatico grapes at 30 °C. This drop in the content of anthocyanins was attributed to the peroxidase activity that, in turn, attacks oxidizable substrates such as anthocyanins.

According to Serratosa et al. (2008) and Peinado et al. (2013), the content of individual phenolic compounds increases with the drying process, mainly due to the concentration effect, but also as the consequence of the hydrolysis of polymerized phenolic compounds In this work, the TSP varied widely among different fresh grapes and raisins, whereas all grape varieties studied presented a similar qualitative phenolic profile, and the differences observed were mainly related to the quantity of each compound (quantitative profile), highlighting phenolics acids (mainly caftaric and coutaric acids) and flavonoids (rutin, kaempferol- *O*-hexoside, quercetin and isoquercitrin). Moreover, the phenolic profile of raisins was similar to that observed for fresh grapes. However, a common pattern in the quantitative profile of the main flavonoids of fresh grapes and raisins was not found. Some compounds were concentrated from grapes to raisins, others partially modified, and few were degraded during the sun-drying process at 40–45 °C.

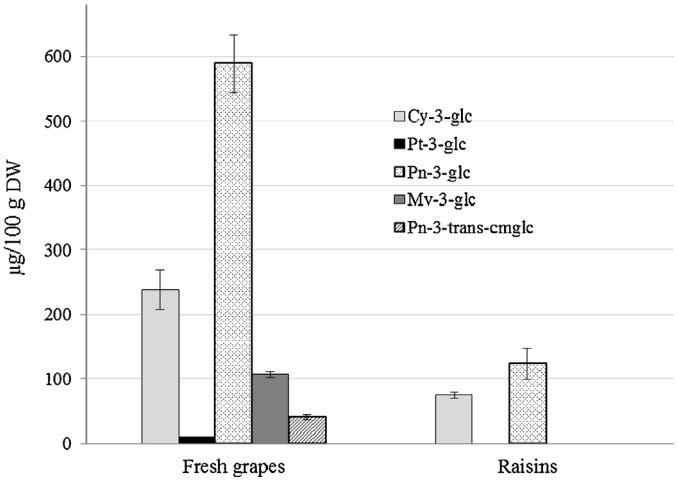

Fig. 3. Changes in 'Flame' anthocyanin content due to dehydration of fresh grapes. Abbreviations: Cy, cyanidin; Pt, petunidin; Pn, peonidin; Mv, malvidin; glc, glucoside; cm, coumaroyl; Anthocyanin compounds were quantified as malvidin-3-glucoside (n = 3, analysed in triplicate).

These results suggest that changes in the phenolic profile from grapes to raisins are mainly driven by the grape variety rather than the dehydration process, which is in accordance with the data reported by Iacopini et al. (2008) for ten *V. vinifera* genotypes from Italy. In our case, the variety 'Flame' had the highest content of phenolic compounds with regards to anthocyanin content, and the variety 'Superior' was the highest among white varieties. Moreover, these results are also in agreement with those published by Bonghi et al. (2012), who cited that postharvest berry dehydration selectively affects specific phenylpropanoid pathways, which may be associated with stress adaptation, inducing the synthesis of phenolics during the sun-drying of grapes to produce raisins. Furthermore, Berli et al. (2011) proved that the solar UV-B radiation is involved in the phenol metabolism of *Vitis vinifera* L., increasing the biosynthesis of berry skin polyphenols. In this study, the dehydration of fresh grapes was carried out at higher temperatures (40–45 °C) than reported previously. According to Mencarelli et al. (2010), temperature affects the content of phenolic compounds.

So far, raisins can be considered an important source of health-promoting polyphenols, acting as a "reservoir" of these bioactive compounds in view of the greater stability of raisins in comparison with fresh grapes, mainly due to lower water content.

3.2. Antioxidant activity in raisins

The DPPH free radical scavenging effect of extracts based on the EC_{50} values was calculated. Differences for DPPH were observed between raisin varieties; 'Flame' presented the lowest EC_{50} value 7.1 ± 0.1 mg/mL (highest antiradical capacity value), followed by 'Arizul' (8.95 ± 0.07 mg/mL), while the 'Sultanina' and 'Superior' varieties exhibited the lowest scavenging capacity, 9.3 ± 0.1 and 10.3 ± 0.1 mg/mL, respectively. With respect to FRAP, 'Superior' (0.8 ± 0.2 μg/mL) and 'Sultanina' (1.0 ± 0.2 μg/mL) had the highest reducing power, followed by 'Flame' (1.2 ± 0.4 μg/mL) and 'Arizul' (1.3 ± 0.3 μg/mL), respectively. In addition, a significantly negative correlation between the values obtained for DPPH and FRAP assays was observed. This is because the FRAP assay measures the reducing power of the extract, while DPPH evaluates the ability for quenching free radicals. Thus, each test measures different routes for the antioxidant action of polyphenols.

3.3. Correlation between antioxidant capacity and phenolic profile

Simple correlation analysis was used to explore the relationships between the antioxidant activity (AA) (DPPH and FRAP) and TSP measured in raisin samples. The Pearson's correlation ($p < 0.05$) was low, in concordance with results reported by Moreno-Montoro et al. (2015) for Spanish commercial grape juices, and by Iacopini et al. (2008) in skins and seeds of ten *Vitis vinifera* varieties. These authors indicated that AA could not be simply predicted by the content of TSP. According to previous reports, the AA of different samples is a function of several factors, like the interaction between different phenolic compounds, or the interaction between phenolics with other components of the food matrix (Rohn et al., 2004; Baroni et al., 2012).

Consequently, Multiple Regression Analysis (MRA) was used to predict the AA of raisin samples, taking into account their phenolic profile. For all samples, stepwise multiple regression analysis was used to correlate FRAP and DPPH assays with the phenolic profile, clustered by family. MRA showed a high correlation between AA and the phenolic profile of grapes (r> than 0.90, $p < 0.05$). According to β values, (+)-catechin, (−)-epicatechin, caftaric acid, quercetin-3-*O*-glucuronide and kaempferol-hexoside contributed negatively to the FRAP assay, while isoquercitrin contributed positively. On the other hand, (−)-epicatechin, gallic acid and astilbin show a positive influence on DPPH analysis. In addition, principal components (PC) and factor analysis (FA) were further used to demonstrate the association between phenolic profile and AA.

Fig. 4A (biplot graphic) shows that the phenolic profile of 'Flame' was closely linked to the amount of gallic acid, astilbin, quercetin-3-*O*-glucuronide, isorhamnetin-hexoside, isorharmnetin and DPPH, in concordance with the results given in Table 2 and by MRA. The variables that positively contribute to the activity of DPPH were, as expected, in highest concentration in 'Flame', since this is the variety that has higher DPPH activity. By contrast, the 'Superior' variety had the lowest amount of these compounds. Also, Fig. 4B shows an association between the content of (+)-catechin, caftaric and fertaric acid in the 'Arizul' variety. On the other hand, resveratrol presented a similar association in the

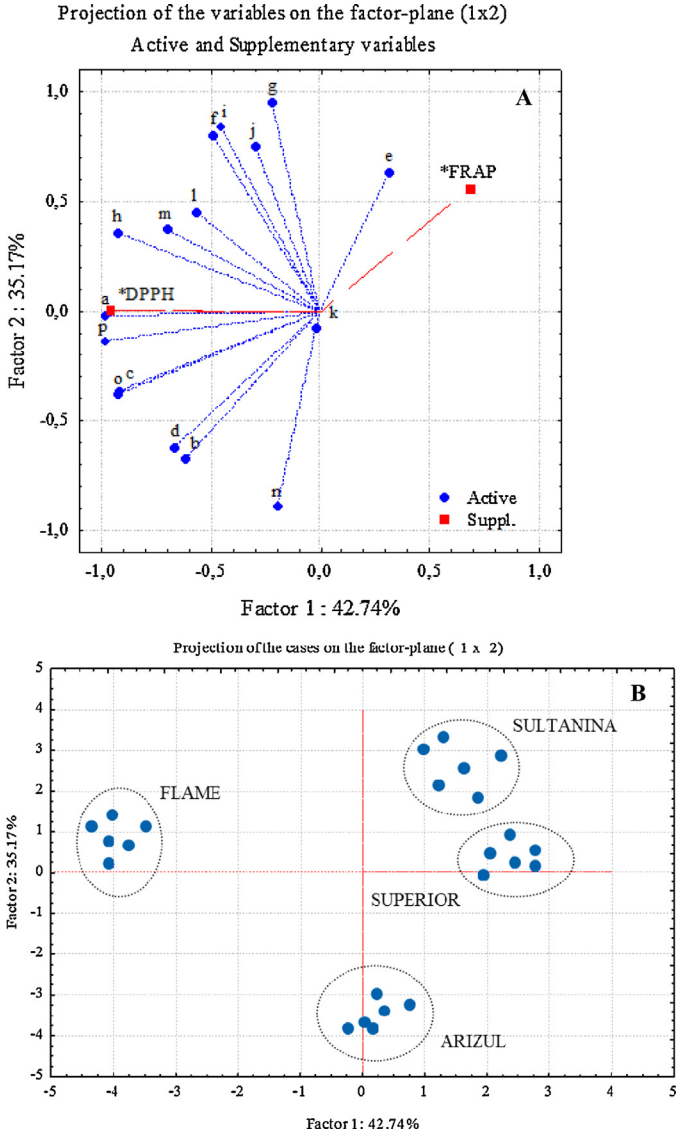

Fig. 4. Biplot graphics summarize the association between content of phenolic compounds with the four raisin varieties studied. A. Projection of variables on the factor plane (1 × 2) corresponding to factor analysis (FA) of raisins. a gallic acid, b caftaric acid, c coutaric acid, d fertaric acid, e resveratrol, f quercetin, g rutin, h quercetin-3-*O*-glucoronide, i isoquercitrin, j kaempferol, k kaempferol-hexoside, l isorhamnetin, m isorhamnetin-hexoside, n (+)-catechin, o (−)-epicatechin, p astilbin. B. Projection of the cases (samples) on the factor plane (1 × 2) corresponding to factor analysis (FA) of raisins (n = 3, analysed in triplicate).

Table 2
EC_{50} (mg/mL), FRAP value (μg/mL), multielement composition and the contribution of 40 g (1/4 cup) of ingested raisins to DDA of nutritional elements.

	Arizul		Sultanina		Superior		Flame	
EC_{50} (mg/mL)	8.95 ± 0.07		9.3 ± 0.1		10.3 ± 0.1		7.1 ± 0.1	
FRAP (μg/mL)	1.3 ± 0.3		1.0 ± 0.2		0.8 ± 0.2		1.2 ± 0.4	
Element a	mg/100 g	Contribution to DDA (%)	mg/100 g	Contribution to DDA (%)	mg/100 g	Contribution to DDA (%)	mg/100 g	Contribution to DDA (%)
K b	746 ± 81 bc	8.5	686 ± 47 c	7.8	872 ± 92 a	10.0	800 ± 83 ab	9.1
Ca b	77 ± 18 b	3.9	109 ± 12 a	5.5	58 ± 7 c	2.9	84 ± 13 b	4.2
Mg b	37 ± 4 a	2.1	37 ± 5 a	2.1	32 ± 4 b	1.8	35 ± 3 ab	2.0
Na b	8 ± 2 b	0.2	17 ± 4 a	0.5	5 ± 1 c	0.1	0.8 ± 0.1 d	0.02
Fe b	0.8 ± 0.2 a	2.1	nd		0.5 ± 0.1 b	1.3	0.3 ± 0.1 c	0.8
Cu b	0.24 ± 0.05 c	3.2	0.31 ± 0.06 b	4.1	0.4 ± 0.1 a	5.3	0.29 ± 0.06 bc	3.9
Mn b	0.25 ± 0.04 ab	2.5	0.27 ± 0.02 a	2.7	0.19 ± 0.03 c	1.9	0.21 ± 0.06 bc	2.1
Zn b	0.18 ± 0.03 c	0.5	0.49 ± 0.08 b	1.3	0.03 ± 0.01d	0.1	0.7 ± 0.2 a	1.9
B	3.2 ± 0.4 b		5 ± 1 a		2.6 ± 0.3 b		2.5 ± 0.5 b	
Sr	0.44 ± 0.09 b		0.6 ± 0.1 a		0.14 ± 0.03 c		0.44 ± 0.05 b	
Rb	0.12 ± 0.02 b		0.15 ± 0.05 b		0.9 ± 0.2 a		0.13 ± 0.03 b	
Li	0.05 ± 0.01 b		0.05 ± 0.01 b		0.069 ± 0.008 a		0.03 ± 0.04 c	

Abbreviations. DDA: Daily douse allowance. nd. Not detected. Results are reported as mean ± SD (mg/100 g raisins DW) (n = 3, analysed in triplicate). [a] Limit of detection (LOD) (mg/100 g): Fe (0.03), Cr (0.056), Mo (0.0065), Se (0.003), Be (0.001), Ag (0.0002), As (0.003), Bi (0.001), Cd (0.001), Co (0.001), Ga (0.0006), Ni (0.04), Pb (0.001). Te (0.007), Tl (0.044) and V (0.0005). [b] Mineral nutrients in daily diet. Different letters in the same line indicate significant difference (Duncan, $p < 0.05$) between raisins varieties.

'Sultanina' variety. Several compounds contribute negatively to the FRAP assay. These compounds were found in higher concentrations in both 'Arizul' and 'Flame' varieties. In summary, there was a correlation between the phenolic profile and AA. Overall, from Fig. 4, a clear separation of two varieties ('Flame' and 'Arizul') along Factor 1 (x-axis) (42.74%) was observed, whereas Factor 2 (y-axis) (35.17%) allowed a further separation between the 'Sultanina' and 'Superior' varieties.

3.4. Multi-elemental composition

Twenty-nine elements were analyzed and quantified in the raisin varieties to characterize their multi-elemental composition, evaluating potential differences between them.

3.4.1. Macro, micro and trace elements

Results are shown in Table 2. Raisins presented high levels of K (639–883 mg/100 g raisins), Ca (51–121 mg/100 g raisins) and Mg (28–42 mg/100 g raisins). Conversely, studied raisins presented lower values of Na (0.8–21 mg/100 g raisins). The median content of micro and trace elements decreases as follows: Fe > Cu > Mn > Zn > V, while Be, Cr, Mo, and Se were not detected (Table 2). Raisins are among the 50 major food contributors of dietary boron (B), with values ranging from 2.0 to 5.4 mg/100 g boron in the varieties studied in this paper; 'Sultanina' showed the highest levels of boron (Table 2).

The pulp of studied raisins was rich in K and Ca. Their concentrations varied with the nature of the soil, viticulture practices, grape variety, and climatic conditions (Cabanis, 2003). The contents of K and Ca in raisins were significantly different (Duncan's, $p < 0.05$) within the studied varieties (Table 2). This could be attributed to the selectivity process within the vegetable/fruit, leading to different bioaccumulation of diverse trace elements for different fruit varieties (Anderson and Smith, 2005). Potassium is the major intracellular cation in the body, and is thus important for normal cellular function. On the other hand, Ca is an essential nutrient that is quantitatively the most abundant element in the body as well as being a vital electrolyte (Segura et al., 2006). Mg is a natural element in grapes. We did not observe significant differences for Mg among the raisins studied (Table 2). Mg is the most abundant intracellular divalent cation and an essential cofactor for more than 300 enzymatic reactions (Segura et al., 2006). A low-Na, high-K diet, high in Ca and Mg is currently recommended to maintain a good health. Our current results show that levels of Na, Fe and Zn were significantly different among the four studied raisin varieties. Furthermore, Li, Cu and Rb presented the highest concentrations in the 'Superior' variety, whereas 'Flame' and 'Arizul' had similar lower values. In addition, 'Sultanina' showed the highest content of V, Mn, Sr and Ba (Table 2).

Concentrations of measured elements were similar to the pattern generally observed in raisins (USDA, 2012). Furthermore, the average content of Na, Mg, K, F and Ca was similar to that reported for five Tunisian varieties of raisins (Ghrairi et al., 2013). On the other hand, Chinese raisins produced in the Province of Xinjiang showed higher values than those found in this work for trace elements (Fang et al., 2010). Additionally, considering that more consumers are basing their daily food intake decisions upon the nutritive value and health-promoting aspects of the food, the contribution of inorganic nutrients (minerals) in a serving portion of raisins (40 g; 1/4 cup) was calculated and compared to their daily dose allowance (DDA) (Seiler et al., 1994). Results showed that a daily intake of 40 g of raisins represents between 0.1% and 8.9% of the DDA (Table 2).

3.4.2. Harmful elements

Few researchers, with the exception of Fang et al. (2010), have determined the concentration of the heavy metals in raisins that serve as an indicator of environmental contamination. As, Cd and Pb have harmful effects when ingested above recommended intake levels. We thus decided to evaluate levels of toxic elements in the studied raisins (Ag, Al, As, Bi, Cd, Co, Ga, Ni, Pb, Te and Tl). The content of ten elements was below the detection limit (<LOD; Table 2). Only Al was above the quantification limit (LOQ) (from 0.6

to 2.9 mg/100 g raisins), but within the mean dietary intakes suggested by the World Health Organization (WHO, 1997; 2.5–6.3 mg/day). These results indicate that raisins analyzed were safe for consumption in terms of toxic elements.

4. Conclusions

Changes in the phenolic profile of four grape varieties ('Arizul', 'Sultanina, 'Superior' and 'Flame') after sun-drying were evaluated. In addition, the antioxidant activity and multi-element composition of raisins were analyzed. The results support that the raisins studied could be considered reservoirs for health-promoting phenolics with antioxidant capacity, as well as for mineral content, mainly related to important levels of K, Ca and Mg. Thus, phenolic compounds and their glycosides, identified and quantified, together with reports on bioavailability, bioactivity and health impact of a diet rich in flavonoids and related compounds, contribute to considering raisins as a health-promoting food. These findings also support the use of raisins as a stored food, with longer storage periods than fresh grapes.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.jfca.2017.01.006.

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