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Comprehensive metabolite profiling of *Solanum tuberosum* L. (potato) leaves by HPLC-ESI-QTOF-MS

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ABSTRACT

The objective of this work was to study the non-targeted metabolite profiling of potato leaves using high performance liquid chromatography coupled to quadrupole-time of flight mass spectrometry (HPLC-ESI-QTOF-MS). The mass accuracy, true isotopic pattern in both MS and MS/MS spectra provided by QTOF-MS made possible the tentative identification of 108 compounds present in potato leaves, including organic acids, amino acids and derivatives, phenolic acids, flavonoids, iridoids, oxylipins and other polar and semi-polar compounds. Among them, 32 compounds have been found for the first time in potato leaf and in the Solanaceae family. Quinic acid and its derivatives represented more than 45% of the bioactive compounds quantified in the extract. Derivatives of hydroxybenzoic acid and gentisic acid were also founded at considerable concentrations.

This study shed light on the composition of potato leaf extract and will serve as a base for further research into activities of the various compounds found in this matrix which has demonstrated a potential use as functional ingredients.

1. Introduction

Potato (*Solanum tuberosum* L.) is one of the most commonly cultivated commercial plants which represent an important crop worldwide. According to the latest report from the Food and Drug Administration (FAO), the total world potato production was estimated in 381,682 thousand tons in 2014 (FAOSTAT, 2017). In fact, potato is now the world's third-most consumed food (Ortiz & Mares, 2017). Globally, the nutritional composition of potatoes comprises proteins (up to 4.2 g/100 g), fiber (up to 3.67 g/100 g), essential amino acids, vitamins (thiamin, riboflavin, niacin, folic acid, vitamin B6, vitamins E and C and carotenoids), and minerals such as potassium, among others (Burlingame, Mouillé, & Charrondière, 2009). The global utilization of potato is moving from fresh to processed potato products e.g. chips or ready meals (Akyol, Riciputi, Capanoglu, Caboni, & Verardo, 2016). The high value of potato cultivar and the increase demand for processed potato products generate large amount of by-products from a variety of sources i.e. peel, leaves and stems.

Regarding potato leaves composition, earlier studies revealed the presence of organic acids i.e. sucrose, glucose, fructose, glycoalkaloids and malic, citric and ascorbic acids as well as minerals such as potassium, phosphorus, calcium, magnesium or sodium (Brown, McDonald, & Friedman, 1999; Kolbe & Stephan-Beckmann, 1997). Furthermore, several studies including protein profile, MicroRNAs and terpenes characterization (Lakhotia et al., 2014; Lim et al., 2012; Szafranek & Synak, 2006) or cuticular waxes composition (Szafranek & Synak, 2006) of potato leaf tissues have been more recently conducted. However, the fully composition of potato leaves has not been entirely elucidated. Additionally, the increasing interest from the pharmaceutical and food companies has given rise to several studies aimed to investigate the metabolite profiling of potato leaves in depth, emphasizing in bioactive compounds discovery. Among these bioactive compounds secondary metabolites represent an important group.

Secondary metabolites do not participate directly in plant growth and development but they play a major role in the adaptation of plants to their environment. Thus, plant-based foods contain numerous classes

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of secondary metabolites which may possess biological activity (Crozier, Jaganath, & Clifford, 2006). Potato has demonstrated to be a good source of secondary metabolites such as phenolic compounds. These phenolics have been closely related to the development and progression of several chronic pathological conditions including cancer, obesity or diabetes (Contreras Gámez, Rodríguez Pérez, García Salas, & Segura Carretero, 2014; Rodríguez-Pérez, Segura-Carretero, & del Mar Contreras, 2017). Within the potato by-products, potato peel from different potato varieties has been chemically characterized allowing identifying bioactive compounds such as chlorogenic or caffeic acids and derivatives, among others (Al-Weshahy & Rao, 2009; López-Cobo, Gómez-Caravaca, Cerretani, Segura-Carretero, & Fernández-Gutiérrez, 2014). Nevertheless, there are differences in the distribution of bioactive compounds e.g. phenolic compounds throughout the plant. In this regard, it is well-known that these compounds use to be most concentrated in the leaves than in the roots or peel at the same time that their concentration is higher in the peel than in the tuber (Akyol et al., 2016; Im et al., 2008).

To achieve a better understanding in the occurrence of the metabolite group in a given plant species, metabolomics emerged as a powerful tool in agriculture and food science. More specifically, metabolite profiling is focused on identifying and quantifying small metabolites (Fiehn, 2002). For that purpose, high performance liquid chromatography coupled to quadrupole-time of flight mass spectrometry (HPLC-ESI-QTOF-MS) is one of the most widely used techniques for complex naturally occurred molecules in plants separation and identification (Steinmann & Ganzera, 2011). In this regard, a non-targeted metabolite profiling was carried out in leaves of resistant and susceptible potato cultivars revealed the presence of secondary metabolites e.g. syringin, hydroxycoumarin, syringaresinol and derivatives (Pushpa, Yogendra, Gunnaiah, Kushalappa, & Murphy, 2014). Apart from that study, little literature regarding the characterization of secondary metabolites in potato leaves is available.

Taking into account the potential of the aforementioned cultivar and the growing interest in nutraceuticals, dietary supplements, cosmeceuticals and functional foods companies in discovering biologically active compounds from natural sources, potato leaves appear as a promising plant extract which deserves research attention. However, in order to exploit these properties, it is necessary a comprehensive knowledge of its composition which has not been fully investigated. Thus, the objective of this work was to analyze the chemical fingerprint of potato leaves extract using non-targeted HPLC–ESI-QTOF-MS approach.

2. Materials and methods

2.1. Chemical and reagents

All the reagents were purchased from Merck (Darmstadt, Germany). All the analytical standards were supplied by Sigma-Aldrich (Saint Louis, MO, USA).

2.2. Plant material and phenolic extraction

The samples were supplied by Pizzoli SpA in January 2018. Potato leaves (cv. Daisy) were collected in an organic experimental field located in Terrazzo (Verona, Italy, 45°10′26″N 11°23′55″E) in the same field. Potato leaves (2 kg) were collected from different potato plants representative of the entire field and they were dried at room temperature, grounded to a fine powder in a blender mixer (Ika-Werke M20; Staufen, Germany) and stored at −23 °C until the analysis. Phenolic compounds were collected by ultrasound assisted solid-liquid extraction according to the conditions previously established by Diaz de Cerio et al. (Díaz-de-Cerio, Gómez-Caravaca, Verardo, Fernández-Gutiérrez, & Segura-Carretero, 2016). Briefly, 0.5 g of air-dried and crushed potato leaves were extracted with 15 mL of ethanol/water 80/20 (*v*/v) (×3) using a sonicator during 10 min at room temperature. Then, samples were centrifuged for 15 min at 6000 rpm. The supernatants were pooled, evaporated and dissolved in 2 mL of methanol/water 1/1 (v/v). This solution was filtered through a 0.20-μm RC syringe filter and kept at −20 °C in amber vials until analysis.

2.3. Chromatographic separation

A liquid chromatography apparatus ACQUITY UPLC M-Class System from Waters (Waters Corp., Milford, MA, USA), including a degasser, a binary pump delivery system and an automatic liquid sampler, was used and coupled to mass spectrometer detector. The HPLC column was a fused-core Poroshell 120, SB-C18 (3.0×100 mm, 2.7 μm) from Agilent Technologies (Agilent Technologies, Palo Alto, CA, USA). Separation was carried according to the conditions established by Lopez-Cobo et al. (López-Cobo, Gómez-Caravaca, Švarc-Gajić, Segura-Carretero, & Fernández-Gutiérrez, 2015).

2.4. ESI-QTOF-MS conditions

The HPLC system was coupled to a micrOTOF-Q II mass spectrometer (Bruker Daltoniks, Bremen, Germany) equipped with an ESI interface (Bruker Daltoniks, Bremen, Germany) operating in negative ion mode using a capillary voltage of +4 kV. The other optimum values of the ESI–QTOF–MS parameters were drying gas temperature, 210 °C; drying gas flow, 8 L/min; and nebulizing gas pressure, 2 bar. Detection was carried out within a mass range of 50–1100 *m/z*. The MS/MS analyses were acquired by automatic fragmentation where the mass peaks where fragmented. Collision energy values for MS/MS experiments were adjusted as follows: m/z 100, 20 eV; m/z 500, 30 eV; m/z 1000, 35 eV. Nitrogen was used as drying, nebulizing and collision gas.

The accurate mass data of the molecular ions were processed using DataAnalysis 4.0 software (Bruker Daltoniks), which provided a list of possible elemental formulae via the SmartFormula Editor. The SmartFormula Editor uses a CHNO algorithm, which provides standard functionalities such as minimum/maximum elemental range, electron configuration and ring-plus double-bond equivalents, as well as a sophisticated comparison of the theoretical with the measured isotope pattern (Sigma Value) for increased confidence in the suggested molecular formula. During the development of the HPLC method, the instrument was calibrated externally with a 74,900–00-05 Cole Palmer syringe pump (Vernon Hills, Illinois, USA) directly connected to the interface and injected with a sodium acetate cluster solution containing 5 mM sodium hydroxide and 0.2% acetic acid in water:isopropanol (1:1, *v*/v). The calibration solution was injected at the beginning of each run and all the spectra were calibrated prior to compound identification. By using this method, an exact calibration curve based on numerous cluster masses, each differing by 82 Da ($NaC_2H_3O_2$) was obtained.

3. Results and discussion

3.1. Polar compounds identification

Peak identification was performed by generation of the candidate formula with a mass accuracy limit of 7 ppm. The characterization strategy was based on the accurate MS and MS/MS spectra of the compounds determined by QTOF mass analyzer. For the acquisition of chemical structure information and data from literature, the following databases were consulted: SciFinder Scholar (http://scifinder.cas.org),

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MassBank (http://massbank.jp), and METLIN Metabolite Database (http://metlin.scripps.edu). A total of 109 compounds were tentatively identified belonging to different chemical classes i.e. 33 phenolic acids and derivatives, 10 flavonoids and derivatives, 5 glycoalkaloids, 21 oxylipins, 5 jasmonates and other 35 polar and semipolar compounds belonging to different families such as organic acids, iridoids or amino acids, among others.

Table 1 shows retention time (RT), experimental *m/z* of negative molecular ions ($[M-H]^-$), molecular formula, mass error, main MS^2 fragments and the proposed identification for each compound. Compounds were numbered according to their elution order. Moreover, these compounds which have been identified for the first time in *Solanum tuberosum* plant are marked with an asterisk (*).

3.1.1. Phenolic acids and derivatives

Thirty three phenolic acids and derivatives have been tentatively identified in potato leaves. In this context, four quinic acid derivatives were found in potato leaves. Compounds 49 and 55 showed $[M-H]^-$ ion at *m/z* 367. Regarding compound 49, the fragment at m/z 134 corresponded to $[M\text{-}CH_3\text{-}CO_2\text{-}H]^-$ from ferulic acid, whereas the fragment at m/z 193 corresponded to ferulic acid. However, compound 55 showed different fragmentation pattern including the main ion fragment at *m/z* 191 (quinic acid) and other fragment at *m/z* 173 correspond the loss of one H_2O molecule. Hence, these structures were tentatively assigned to 3-feruloyl quinic acid and 5-feruloyl-quinic acid (Clifford, Johnston, Knight, & Kuhnert, 2003; Kuhnert, Jaiswal, Matei, Sovdat, & Deshpande, 2010; López-Cobo et al., 2014). Compound 53 (*m/z* 337) with molecular formula $C_{16}H_{18}O_8$ presented MS^2 fragments at *m/z* 191, 163, 119 and 127. On the basis of its fragmentation pattern and data from literature, it has been tentatively characterized as 5-p-coumaroyl quinic acid (Clifford et al., 2003).

Moreover, several gentisic acid derivatives glycosides have been tentatively characterized in the sample under study. Peaks 12, 18, 19 and 21 (*m/z* 315) were tentatively identified as isomers of gentisoyl glucoside. The fragments at *m/z* 153 matched with the gentisic moiety while fragment at m/z 108 corresponds to the loss of a carboxylic group. Furthermore, peaks 23 and 24 (*m/z* 447) have been previously described together with their fragments at m/z 153, 429 and 163 in potato tubers but not in potato leaves as gentisic acid pentosyl hexoside isomers (Shakya & Navarre, 2006). In agreement with the same author, peak 20 (m/z 153) was tentatively characterized as gentisic acid.

Additionally, compounds 13 and 32 (*m/z* 299) were tentatively identified for the first time in the Solanaceae family as p-hydroxybenzoic acid glucoside isomers. Their fragment yielded at m/z 137 matched with p-hydroxybenzoic acid after the loss of the glucose moiety (Rodríguez-Pérez, Quirantes-Piné, Fernández-Gutiérrez, & Segura-Carretero, 2013). Compound eluted at 5.09 min (peak 14) with molecular formula $C_6H_{10}O_5$, presented an ion fragment at *m/z* 117 ($[M\text{–}H\text{–}COO]^-$). This compound has been described for the first time in potato leaves and in the Solanaceae family as hydroxymethylglutaric acid. Likewise, compounds 24, 26 and 37 (m/z 343) were tentatively identified as homovanillic acid hexose isomers which have been described previously in the plant kingdom (García-Salas, Gómez-Caravaca, Morales-Soto, Segura-Carretero, & Fernández-Gutiérrez, 2014).

Six caffeoyl derivatives were tentatively characterized in the leaves of *Solanum tuberosum* L. Peak 22 which eluted at 6.93 min, presented fragments at *m/z* 179, 191 and 135 which have been described elsewhere (Rodríguez-Pérez, Quirantes-Piné, Amessis-Ouchemoukh, Khodir, Segura-Carretero, & Fernández-Gutierrez, 2013). This compound was tentatively assigned to caffeoylquinic acid conjugate. Moreover, compounds 35 and 38 (m/z 353) showed a strong ion at m/z 191 (MS^2) and a weak fragment at m/z 179 followed by a fragment at *m/z* 135 only in the case of compound 38. According with their fragmentation pattern (Clifford, M.N. et al. 2005), these compounds were tentatively characterized as 1-caffeoylquinic acid and 3-caffeoylquinic acid, respectively which have been early described in potato and potato by-products but not in its leaves (López-Cobo et al., 2014). Two isomers of N-caffeoylputrescine (peaks 45 and 66) were tentatively identified in potato leaves. The loss of $\text{–CO–NH–}(CH_2)_4\text{–}NH_2$ moiety resulted in a fragment of *m/z* 135 that was reported by Lopez-Cobo et al. (López-Cobo et al., 2014). On its behalf, compound 47 (*m/z* 295) presented a fragmentation pattern consisted on a main ion at m/z 133 which correspond to the malic acid moiety. Thus, this compound was tentatively identified for the first time in potato leaves as caffeoylmalic acid.

Peaks 30 and 39 with a molecular formula $C_{22}H_{28}O_{14}$ were tentatively characterized as chlorogenic acid glucopyranoside isomers. These compounds together with their fragmentation pattern which included fragments at *m/z* 179, 191, 135 and 173 have been earlier described in Colombian potato tubers and on other plants from the Solanaceae family (Narváez-Cuenca, Vincken, Zheng, & Gruppen, 2013; Wu, Meyer, Whitaker, Litt, & Kennelly, 2013).

The HPLC-ESI-QTOF-MS analysis revealed presence of five sinapic acid derivatives. Thus, compound 36 (*m/z* 385) was tentatively characterized as sinapic acid 4-O-glucoside. It showed ion fragments at m/z 223 and 163 correspond to the sinapic acid and the glucoside moieties, respectively. Compounds 58 and 61 showed a $[M-H]^-$ ion at *m/z* 449 and its MS/MS fragmentation pattern displayed ions at *m/z* 269 and 251 which have been described elsewhere as dihydrosinapoyl conjugate isomers (Narváez-Cuenca et al., 2013). Similarly, the precursor $[M-H]^-$ ion of compounds 63 and 64 was observed at *m/z* 405. In agreement with Narvaez-Cuenca et al., their fragmentation spectrum displayed product ions at m/z 181, 225, 179 and 161 (Narváez-Cuenca et al., 2013).

Moreover, compound 62 (m/z 279) with molecular formula $C_{13}H_{12}O_7$ was tentatively characterized as p-coumarylmalic acid, compound which was early reported in potato tubers (Narváez-Cuenca et al., 2013). Its fragmentation pattern is depicted in Fig. 1a. Likewise, compound 85 (*m/z* 305) and its ion fragment at m/z 263 have been reported in potato but not in potato leaves (Yogendra, Kushalappa, Sarmiento, Rodriguez, & Mosquera, 2015). Finally, two phenolic acids i.e. compounds 71 and 89 have been detected in potato leaves and in the Solanaceae family for the first time. Compound 71 showed a $[M-H]^-$ ion at *m/z* 237 and a main ion fragment at m/z 121 corresponded to benzoic acid. Hence, this compound was tentatively characterized as 3,4-diacetoxybenzoic acid. Compound 89 (*m/z* 311) eluted at RT 14.23 min and yielded an ion fragment at m/z 137 which can be due to the hydroxybenzoic acid moiety. Thus, this compound was tentatively assigned to 5-O-p-hydroxybenzoylquinic acid.

3.1.2. Flavonoids and derivatives

Ten flavonoids were tentatively identified in potato leaves. Despite most of them have been characterized in potato tuber (Navarre, Pillai, Shakya, & Holden, 2011), only one (peak 56) was previously described in potato leaves. This compound was tentatively characterized as rutin (Henriquez, Adam, & Daayf, 2012). Rutin together with other quercetin glycosides derivatives i.e. peaks 43, 48 and 50, presented their main fragments at *m/z* 300 and 301 which correspond to the quercetin core. Moreover, compound 43 and 50 showed a fragment at m/z 609 corresponding to the rutin moiety. Additionally, the ubiquitous flavonoid at RT 13.8 was tentatively characterized as quercetin which presented its typical fragments, according to the Metlin database, at m/z 151 and 121. Peak 65 (m/z 593) and 93 (m/z 285) with fragments at m/z 285 and 219, respectively were assigned to kaempferol rutinoside and kaempferol, respectively (Shakya & Navarre,

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Table 1
HPLC–ESI–QTOF–MS data of the compounds identified in *Solanum tuberosum* L. leaves.

Peak	RT	m/z experimental	Molecular formula	m/z calculated	error (ppm)	mSigma	Fragment	Proposed compound
Phenolic acid and derivatives								
12	4.64	315.0720	$C_{13}H_{16}O_9$	315.0722	0.5	12.6	108, 153, 152	Gentisoyl glucoside isomer 1
13	4.71	299.0775	$C_{13}H_{16}O_8$	299.0772	−0.9	41.7	137	p-Hydroxybenzoic acid glucoside isomer 1*
14	5.09	161.0453	$C_6H_{10}O_5$	161.0455	1.5	5.8	117	Hydroxymethylglutaric acid*
18	5.98	315.0730	$C_{13}H_{16}O_9$	315.0772	−2.6	6.7	108, 153, 152	Gentisoyl glucoside isomer 2
19	6.31	315.0772	$C_{13}H_{16}O_9$	315.0772	−0.2	7.3	108, 152, 153, 109	Gentisoyl glucoside isomer 3
20	6.40	153.0193	$C_7H_6O_4$	153.0193	0.0	4.7	109, 108	Gentisic acid
21	6.88	315.0772	$C_{13}H_{16}O_9$	315.0775	1.0	3.6	109, 153	Gentisoyl glucoside isomer 4
22	6.93	627.1930	$C_{28}H_{36}O_{16}$	627.1931	0.0	9.4	179, 191, 135, 435	Caffeoylquinic acid conjugate
23	7.07	447.1137	$C_{18}H_{24}O_{13}$	447.1144	1.6	3.0	153, 429, 163	Gentisic acid pentosyl hexoside isomer 1
24	7.22	447.1134	$C_{18}H_{24}O_{13}$	447.1144	2.3	4.0	153, 429, 163	Gentisic acid pentosyl hexoside isomer 2
26	7.35	343.1034	$C_{15}H_{20}O_9$	343.1035	0.2	30	181	Homovanillic acid hexose isomer 1*
27	7.49	343.1037	$C_{15}H_{20}O_9$	343.1035	0.2	9.5	181,137,121	Homovanillic acid hexose isomer 2*
30	7.94	515.1395	$C_{22}H_{28}O_{14}$	515.1406	2.3	14.5	179, 191	Chlorogenic acid, 4′-β-D-glucopyranoside isomer 1
32	8.16	299.0775	$C_{13}H_{16}O_8$	299.0772	−0.9	6.0	137, 138	p-Hydroxybenzoic acid glucoside isomer 2*
35	8.42	353.0877	$C_{16}H_{18}O_9$	353.0877	0.4	5.0	191, 192, 179	1-Caffeoylquinic acid
36	8.47	385.1149	$C_{17}H_{22}O_{10}$	385.1140	−2.4	37.5	223, 163	Sinapic acid 4-O-glucoside
37	8.52	343.1030	$C_{15}H_{20}O_9$	343.1035	1.4	6.2	181	Homovanillic acid hexose isomer 3*
38	8.64	353.0874	$C_{16}H_{18}O_9$	353.0877	1.2	11.9	191, 179, 135	3-Caffeoylquinic acid
39	8.76	515.1392	$C_{22}H_{28}O_{14}$	515.1406	2.7	31.5	191, 135, 179, 173	Chlorogenic acid, 4′-β-D-glucopyranoside isomer 2
45	9.41	249.1327	$C_{13}H_{18}N_2O_3$	249.1317	3.6	25.0	135	N-Caffeoylputrescine isomer 1
47	9.55	295.0463	$C_{13}H_{12}O_8$	295.0459	1.1	5.7	133, 179	Caffeoylmalic acid*
49	9.66	367.1030	$C_{17}H_{20}O_9$	367.1035	1.1	7.5	134, 193, 191	3-Feruloyl-quinic acid
53	9.96	337.0926	$C_{16}H_{18}O_8$	337.0929	1.0	12.8	191, 163, 119, 127	5-p-Coumaroyl quinic acid
55	10.18	367.1032	$C_{17}H_{20}O_9$	367.1035	0.7	7.9	191, 173	5-Feruloyl-quinic acid
58	10.47	449.2027	$C_{20}H_{34}O_{11}$	449.2028	0.8	8.5	269, 251	Dihydrosinapoyl conjugate isomer 1
61	10.68	449.2020	$C_{20}H_{34}O_{11}$	449.2028	1.9	1.4	269	Dihydrosinapoyl conjugate isomer 2
62	10.75	279.0513	$C_{13}H_{12}O_7$	279.0510	−1.0	4.4	117, 133, 146	p-Coumarylmalic acid
63	10.80	405.1757	$C_{18}H_{30}O_{10}$	405.1766	2.4	6.3	181, 225, 179, 161	Dihydrosinapoyl caffeoyl conjugate isomer 1
64	10.89	405.1765	$C_{18}H_{30}O_{10}$	405.1766	0.2	9.8	181, 225, 179, 161	Dihydrosinapoyl caffeoyl conjugate isomer 2
66	10.94	249.1325	$C_{13}H_{18}N_2O_3$	249.1317	3.2	22.1	135, 117	N-Caffeoylputrescine isomer 2
71	11.29	237.0408	$C_{11}H_{10}O_6$	237.0405	−1.3	6.0	121, 195	3,4-Diacetoxybenzoic acid*
85	12.79	305.1608	$C_{15}H_{22}N_4O_3$	305.1619	3.7	18.4	263	Feruloylagmatine
89	14.23	311.0769	$C_{14}H_{16}O_8$	311.0772	1.2	9.6	137	5-O-p-Hydroxybenzoylquinic acid*
Flavonoids and derivatives								
29	7.87	339.0711	$C_{15}H_{16}O_9$	339.0722	0.7	19.3	177	Aesculin
43	9.21	771.2126	$C_{37}H_{40}C_{18}$	771.2142	2.0	22.3	301,302,609	Quercetin-rut-glu
48	9.60	625.1411	$C_{27}H_{30}O_{17}$	625.1410	0.1	9.3	300, 301, 179, 445	Quercetin diglucoside
50	9.73	741.1890	$C_{32}H_{38}O_{20}$	741.1884	0.8	8.2	300,301,609,591,475	Quercetin-xyl-rut
56	10.28	609.1460	$C_{27}H_{30}O_{16}$	609.1461	0.1	4.7	300, 301	Rutin
60	10.57	593.2802	$C_{22}H_{20}O_{13}$	593.2815	2.1	30.6	285,593,329	Rhamnetin-glucuronide
65	10.90	593.1506	$C_{27}H_{30}O_{15}$	593.1512	1.0	1.4	285	Kaempferol-3-O-rutinoside
75	11.61	429.1756	$C_{20}H_{30}O_{10}$	429.1766	2.4	11.0	121, 101, 113, 137, 163, 179	2-Phenylethyl D-rutinoside*
88	13.8	301.0357	$C_{15}H_{10}O_7$	301.0354	−1.1	4.0	151, 121	Quercetin
93	15.36	285.0406	$C_{15}H_{10}O_6$	285.0405	−0.5	15.5	285, 219	Kaempferol
Glycoalkaloids and derivatives								
77	11.82	924.4974	$C_{47}H_{75}NO_{17}$	924.4962	−1.2	11.1	866, 702	Leptine II
78	11.87	908.5031	$C_{47}H_{75}NO_{16}$	908.5013	−2.0	7.2	848, 702	Leptine I
79	11.92	866.4939	$C_{45}H_{73}NO_{15}$	866.4907	−3.7	36.8	398, 704, 101, 119, 143, 161, 179, 559	α-Solanine

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Table 1 (*Continued*)

Peak	RT	m/z experimental	Molecular formula	m/z calculated	error (ppm)	mSigma	Fragment	Proposed compound
80	12.09	850.4979	$C_{45}H_{73}NO_{14}$	850.4958	−2.5	49.3	704, 101,119, 163, 143, 205, 179,161, 289, 558	α-chaconine isomer 1
82	12.21	850.4977	$C_{45}H_{73}NO_{14}$	850.4958	−2.2	43.3	704, 101,119, 163, 143, 205, 179,161, 289, 558	α-chaconine isomer 2
Oxylipins								
84	12.69	299.1869	$C_{16}H_{28}O_5$	299.1864	−1.7	1.0	183, 143, 155	1,14-Dimethyl 2-oxotetradecanedioate$_{*}$
86	13.01	343.2132	$C_{18}H_{32}O_6$	343.2126	−1.7	27.6	201, 171, 141, 127	Furannonanoic acid, tetrahydro- θ, 4- dihydroxy- 5- [(1E, 3R) - 3- hydroxy- 1- penten- 1- yl] - isomer 1$_{*}$
87	13.53	343.2139	$C_{18}H_{32}O_6$	343.2126	−3.7	10.1	201, 123, 171	Furannonanoic acid, tetrahydro- θ, 4- dihydroxy- 5- [(1E, 3R) - 3- hydroxy- 1- penten- 1- yl] - isomer 2$_{*}$
90	14.74	327.2179	$C_{18}H_{32}O_5$	327.2177	−0.6	18.0	171	Epoxyoctadecane- dioic acid isomer 1
91	14.85	327.2185	$C_{18}H_{32}O_5$	327.2177	−2.3	1.2	211, 171	Trihydroxyoctadecadienoic acid isomer 1
94	15.52	329.2334	$C_{18}H_{34}O_5$	329.2333	−0.1	22.2	211, 229, 171	Trihydroxyoctadecenoic acid$_{*}$
95	15.72	327.2183	$C_{18}H_{32}O_5$	327.2177	−1.9	29.1	211, 171, 229, 183	Trihydroxyoctadecadienoic acid isomer 2
96	15.89	327.2187	$C_{18}H_{32}O_5$	327.2177	−3.0	4.6	171, 137, 119	Epoxyoctadecane- dioic acid isomer 2
97	16.04	327.2184	$C_{18}H_{32}O_5$	327.2177	−2.2	20.0	171, 137, 197, 201	Epoxyoctadecane- dioic acid isomer 3
98	16.36	327.2178	$C_{18}H_{32}O_5$	327.2177	−0.4	46.6	171, 137, 197, 201	Epoxyoctadecane- dioic acid isomer 4
99	16.61	329.2343	$C_{18}H_{34}O_5$	329.2333	−3.0	31.9	171, 127, 139	9,12,13-Trihydroxy-trans-10-octadecenoic acid
100	17	307.1921	$C_{18}H_{28}O_4$	307.1915	−1.9	0.7	235, 211, 185, 121	Dihydrocapsiate$_{*}$
101	17.43	309.2082	$C_{18}H_{30}O_4$	309.2071	−3.5	47	181, 121, 209, 185, 291	11-Hydroperoxy-octadecatrienoic acid $_{*}$
102	17.72	311.2231	$C_{18}H_{32}O_4$	311.2228	−1.1	5.1	183, 137, 129	Hydroperoxy-octadecadienoic acid isomer 1$_{*}$
103	18.15	311.2230	$C_{18}H_{32}O_4$	311.2228	−0.6	18.8	183, 137, 129, 101, 139	Hydroperoxy-octadecadienoic acid isomer 2$_{*}$
104	18.39	293.2131	$C_{18}H_{30}O_3$	293.2122	−3.1	5.0	116, 158	Colneleic acid isomer 1
105	18.47	309.2088	$C_{18}H_{30}O_4$	309.2071	−5.4	19.6	291	Linolenic acid 13-hydroperoxide
106	18.55	323.2241	$C_{19}H_{32}O_4$	323.2228	−4.1	16.9	171, 188, 308	12, 15- Octadecadienoic acid, 9- hydroxy- 10- oxo- , methyl ester
107	18.65	291.1880	$C_{18}H_{30}O_3$	291.1866	−4.9	4.5	116	Colnelenic acid isomer 2
108	18.71	323.2246	$C_{19}H_{32}O_4$	323.2228	−5.6	5.1	121, 137, 139	Octadecatrienoic acid, 13-hydroperoxy-, methyl ester, (E,Z,Z)- isomer 1
109	18.71	323.2243	$C_{19}H_{32}O_4$	323.2228	−4.8	9.6	121, 137	Octadecatrienoic acid, 13-hydroperoxy-, methyl ester, (E,Z,Z)- isomer 2
Jasmonates								
25	7.29	401.1811	$C_{19}H_{30}O_9$	401.1817	1.6	8.9	179, 207	Methyl (1*R*,2*S*)-2-[(2Z)-5-(β-D-glucopyranosyloxy)-2-penten-1-yl]-3-oxocyclopentaneacetate isomer 1
40	8.91	387.1654	$C_{18}H_{28}O_9$	387.1661	1.6	5.8	163, 207, 225	Tuberonic acid glucoside isomer 1
41	9.13	387.1656	$C_{18}H_{28}O_9$	387.1661	1.2	9.5	163, 207	Tuberonic acid glucoside isomer 2
57	10.38	401.1806	$C_{19}H_{30}O_9$	401.1817	2.8	20.0	179, 207, 233	Methyl (1*R*,2*S*)-2-[(2Z)-5-(β-D-glucopyranosyloxy)-2-penten-1-yl]-3-oxocyclopentaneacetate isomer 2
92	14.97	323.1867	$C_{18}H_{28}O_5$	323.1864	−0.9	16.3	205, 121, 137, 155, 211	Cyclopentaneacetic acid, 3- oxo- 2- [(2Z) - 5- [(tetrahydro- 2H- pyran- 2- yl) oxy] - 2- pentenyl- 3, 4, 4, 5, 5- d5] - , methyl ester, (1R, 2R) - rel-
Other polar compounds								
1	1.33	133.0145	$C_4H_6O_5$	133.0142	−2.1	3.6	115, 103	Malic acid isomer 1
2	1.41	191.0203	$C_6H_8O_7$	191.0197	−2.7	9.5	111	Citric acid isomer 1
3	1.64	133.0144	$C_4H_6O_5$	133.0142	−1.4	2.2	115, 103	Malic acid isomer 2
4	1.74	191.0202	$C_6H_8O_7$	191.0197	−2.3	3.6	111, 133	Citric acid isomer 2
5	1.91	128.0358	$C_5H_7NO_3$	128.0353	−4.1	10.6	113	Pyroglutamic acid
6	2.03	175.0260	$C_6H_8O_6$	175.0248	−6.8	34.1	115, 169	Ascorbic acid
7	2.20	243.0629	$C_9H_{12}N_2O_6$	243.0623	−2.5	60.4	110, 152	Uridine$_{*}$
8	2.41	130.0873	$C_6H_{13}NO_2$	130.0874	0.1	12.9	130, 115, 103	Leucine or isoleucine
9	2.71	292.1403	$C_{12}H_{23}NO_7$	292.1402	−0.5	7.2	130	Fructoseleucine$_{*}$
10	3.90	191.0565	$C_7H_{12}O_6$	191.0561	−2.0	3.2	101, 115, 129, 111	Quinic acid isomer 1
11	4.09	191.0559	$C_7H_{12}O_6$	191.0561	−3.9	27.6	101, 115, 129	Quinic acid isomer 2

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Table 1 (*Continued*)

Peak	RT	m/z experimental	Molecular formula	m/z calculated	error (ppm)	mSigma	Fragment	Proposed compound
15	5.23	164.0717	$C_9H_{11}NO_2$	164.0717	0.2	3.6	147, 103	Phenilalanine isomer 1
16	5.48	164.0718	$C_9H_{11}NO_2$	164.0717	−0.7	1.7	147, 103	Phenilalanine isomer 2
17	5.70	326.1240	$C_{15}H_{21}NO_7$	326.1245	1.7	1.4	164, 147, 103	Fructose-phenylalanine$_*$
28	7.69	415.1596	$C_{19}H_{28}O_{10}$	415.1610	3.2	12.6	311, 191, 149	Phenethyl- β- primeveroside$_*$
31	8.02	443.1905	$C_{21}H_{32}O_{10}$	443.1923	3.9	6.6	281, 161, 101, 113, 119	Dihydrophaseic acid 4'-O-β-D-glucopyranoside
33	8.26	465.2325	$C_{21}H_{38}O_{11}$	465.2341	3.5	7.5	405	Cymal 3$_*$
34	8.32	293.1239	$C_{12}H_{22}O_8$	293.1242	0.8	4.2	131, 293	Glucopyranoside, 4-carboxy-1-methylbutyl$_*$
42	9.16	445.2070	$C_{21}H_{34}O_{10}$	445.2079	2.1	19.6	223, 153, 385	Sacranoside A$_*$
44	9.31	385.1856	$C_{19}H_{30}O_8$	385.1868	3.0	18.5	223	Roseoside A$_*$
46	9.46	241.1199	$C_{11}H_{18}N_2O_4$	241.1194	−2.1	5.0	141,197	5-Oxo-L-prolyl-L-isoleucine$_*$
51	9.83	371.0978	$C_{16}H_{20}O_{10}$	371.0984	1.6	3.6	249	Deacetylasperuloside$_*$
52	9.91	247.0830	$C_{10}H_{16}O_7$	247.0823	−2.6	1.0	191	Diethyl citrate
54	10.02	311.1140	$C_{15}H_{20}O_7$	311.1136	−1.4	3.5	223, 167	Triandrin isomer 1$_*$
59	10.50	311.1137	$C_{15}H_{20}O_7$	311.1136	0.1	6.1	223, 167	Triandrin isomer 2$_*$
67	11.00	289.0832	$C_{14}H_{14}N_2O_5$	289.0830	−0.7	12.9	245	Indole-3-acetylasparaginic acid$_*$
68	11.07	579.2096	$C_{28}H_{36}O_{13}$	579.2083	−2.2	13.2	181, 417, 101	Syringaresinol O-β-D-glucopyranoside
69	11.09	429.2102	$C_{21}H_{34}O_9$	429.2130	6.4	9.7	179, 193, 163, 387, 120	Dendroside F
70	11.17	325.1298	$C_{16}H_{22}O_7$	325.1287	−1.6	6.9	179	Eugenyl glucoside isomer 1$_*$
72	11.40	605.2455	$C_{27}H_{42}O_{15}$	605.2451	−0.7	2.7	427, 179	Penstebioside
73	11.47	431.2275	$C_{21}H_{36}O_9$	431.2287	2.7	13.4	371, 145, 181, 209, 149	Cyclohexanecarboxylic acid, 3-[[(2E)-3-[4-(β-D-glucopyranosyloxy)-3-methoxyphenyl]-1-oxo-2-propenyl]oxy]-1,4,5-trihydroxy-, (1*S*,3*R*,4*R*,5*R*)-
74	11.56	325.1287	$C_{16}H_{22}O_7$	325.1287	1.8	16.8	163, 179	Eugenyl glucoside isomer 2$_*$
76	11.69	347.1348	$C_{15}H_{24}O_9$	347.1348	−0.2	5.3	–	Ajugol
81	12.14	431.1918	$C_{20}H_{32}O_{10}$	431.1923	1.1	4.0	101, 114, 130, 273, 357	β- D- Glucopyranoside, hexyl, 2, 3, 4, 6- tetraacetate
83	12.43	857.4195	$C_{42}H_{66}O_{18}$	857.4176	−2.1	10.5	323, 357, 339, 375, 487, 535, 697	Thevetin B$_*$

$_*$ Described for the first time in *Solanum tuberosum* plant.

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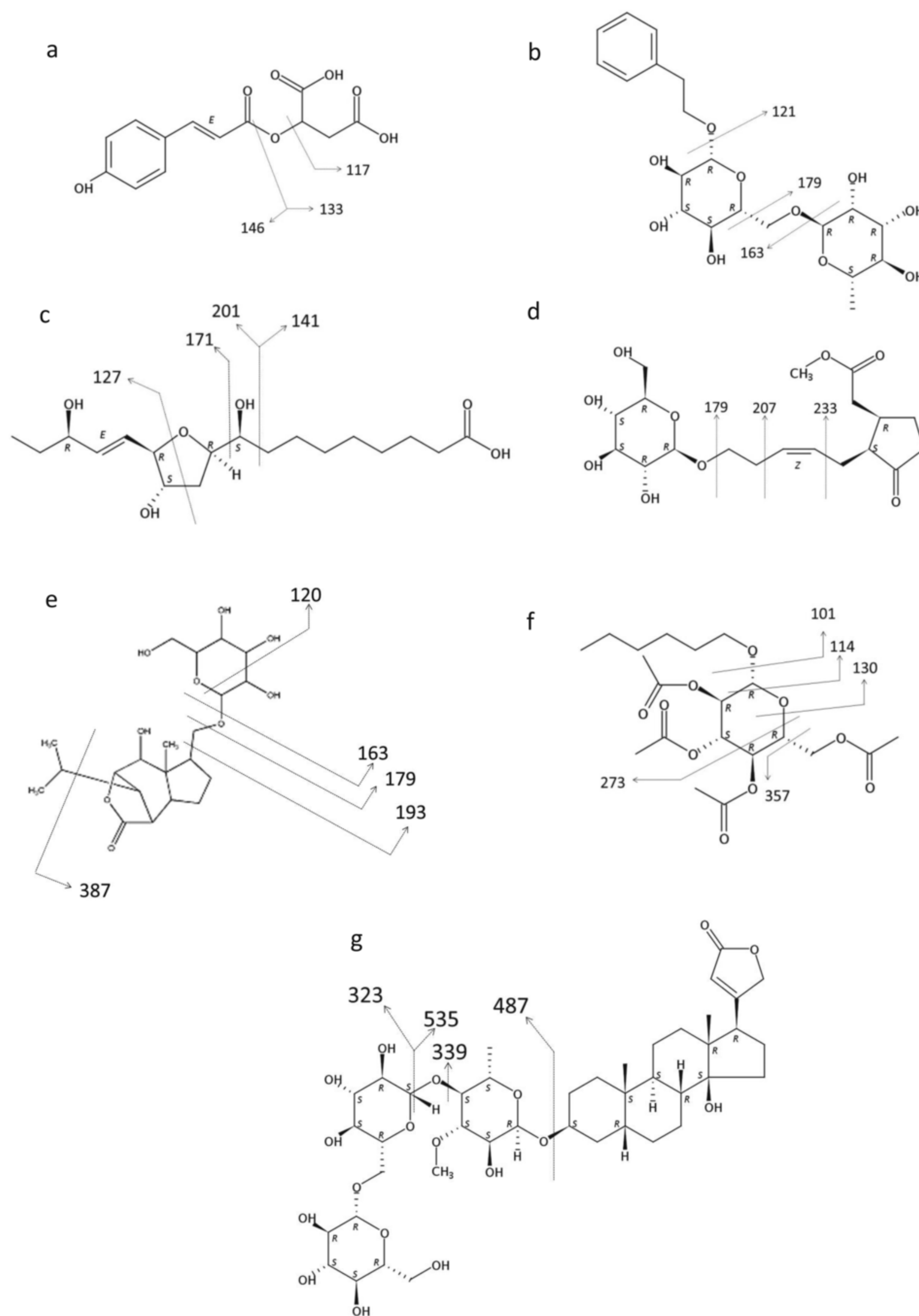

Fig. 1. Fragmentation pattern for (a) p-coumaroylmalic acid; (b) 2-phenylethyl-D-rutinoside; (c) furannonanoic acid, tetrahydro-θ,4-dihydroxy-5-[(1E,3R)-3-hydroxy-1-penten-1-yl]- isomer; (d) (1*R*,2*S*)-2-[(2Z)-5-(β-D-glucopyranosyloxy)-2-penten-1-yl]-3-oxocyclopentaneacetate; (e) dendroside F; (f) β-D-glucopyranoside, hexyl, 2,3,4,6-tetraacetate and (g) thevetin B.

2006). Compound 29 (*m/z* 339) with molecular formula $C_{15}H_{16}O_9$, has been found in potato and together with its main fragment at *m/z* 177 have been early described elsewhere (Fernandes, Griffiths, Bain, & Fernandes, 1996). It was tentatively characterized as aesculin. Peak 60, the molecular ion at RT 10.57 (*m/z* 593) with fragments at m/z 283 and 329, was previously identified in different potato genotypes as rhamnetin glucuronide (Navarre et al., 2011). Finally, peak at m/z 429 with molecular formula $C_{20}H_{30}O_{10}$ was characterized as 2-phenylethyl-D-rutinoside on the basis of its fragmentation pattern which included main fragments at *m/z* 121, 163 and 179 and that is depicted in Fig.

1b. This is the first time that this compound has been described in potato leaves and in the Solanaceae family.

3.1.3. Glycoalkaloids

Glycoalkaloids and leptine from potato leaves may be involved in protecting the plant against phytopathogens (M. Friedman, 2006). The higher concentrations of glycoalkaloids can be found in potato sprouts and flowers, while the content in potato leaves ranged from 230 to 1450 mg/kg fresh weight (Omayio, Abong, & Okoth, 2016). Friedman affirmed that most of the Solanum species in the potato germplasm collection are low-foliar glycoalkaloid species (M. Friedman, 2006). Contrarily, leptines are more present in the potato leaves (M. Friedman, 2006). In this regards, compounds 77 (*m/z* 924) and 78 (m/z 908) were tentatively characterized as leptine II and leptine I in agreement with previous analytical studies which also reported ion fragments at m/z 866 and 702 and m/z 848 and 702, respectively (Shakya & Navarre, 2008). The most representative glycoalkaloids from potato are α-solanine and α-chaconine. In this regard, α-solanine (peak 79) and two isomers of α-chaconine (peaks 80 and 82) have been tentatively characterized in the potato leaves under study. Their fragmentation pattern, including main ions at *m/z* 398 and at 704, respectively, has been fully described previously (Shakya & Navarre, 2008). Despite glycoalkaloids have reported to be toxic for humans, there are an increasing number of studies that have reported their anticarcinogenic effect (M. Friedman, 2015). Thus, their potential use as bioactive compounds should not be discarded.

3.1.4. Oxylipins

Tandem mass spectrometry allowed characterizing 21 oxylipins and derivatives. Oxylipins, which constitute a family of oxygenated derivatives of fatty acids, play an important role in plant defense against pathogens and in response to stress conditions as well as they act as signaling molecules between plants (Fauconnier, Welti, Blée, & Marlier, 2003). Early research demonstrated the presence of these compounds in potato leaves (Hamberg, 2000). Among the 21 oxylipins detected in the leaves of potato under study, eight have been tentatively characterized for the first time in the Solanaceae family. These new oxylipins included compounds 84 (*m/z* 299), 86 and 87 (m/z 343) which have been tentatively identified as 1,14-Dimethyl 2-oxotetradecanedioate and furannonanoic acid, tetrahydro-θ,4-dihydroxy-5-[(1E,3R)-3-hydroxy-1-penten-1-yl]- isomers, respectively. The fragmentation pattern of compound 84 showed fragments ion at *m/z* 183, 143 and 155 due to the C6\C7 bond cleavage followed by the loss of 2 methylene groups while the fragment 155 correspond to the remained molecule. The fragmentation pattern of compounds 86 and 87 is depicted in Fig. 1c. Compound 94 showed [M − H]$^-$ ion at *m/z* 329 with a main MS/MS fragments at m/z 211 due to the C15\C16 bond cleavage. Thus, this compound was tentatively characterized as trihydroxyoctadecenoic acid. Compound 100 (*m/z* 307) presented a fragmentation pattern consisted on several ion fragments at m/z 235, 211, 185 and 121. This compound has been tentatively assigned to dihydrocapsiate which, together with the fragmentation pattern, have been previously described in other plants (Abu-Reidah, Ali-Shtayeh, Jamous, Arráez-Román, & Segura-Carretero, 2015). Likewise, 11-hydroperoxy-octadecatrienoic acid (peak 101) and two isomers of hydroperoxy-octadecatrienoic acid (peaks 102 and 103) have been earlier described in the plant kingdom matching the fragmentation pattern obtained by HPLC-ESI-MS analysis (Jiménez-Sánchez, Lozano-Sánchez, Rodríguez-Pérez, Segura-Carretero, & Fernández-Gutiérrez, 2016).

On the other hand, compounds 90, 96, 97 and 98 (*m/z* 327) with molecular formula $C_{18}H_{32}O_5$ have been previously described in potato tuber but not in potato leaves as epoxyoctadecane-dioic acid isomers (Järvinen, Rauhala, Holopainen, & Kallio, 2011). Similarly, other two well-known oxylipins (peaks 91 and 95) were tentatively identified in potato leaves on the basis of their fragmentation pattern as trihydroxyoctadecadienoic acid isomers. On its behalf, compound 99 (*m/z* 329) was tentatively characterized as 9,12,13-trihydroxy-trans-10-octadecenoic acid. It has been reported that potato tuber contain a unique lipoxygenase pathway to form 9-hydroperoxy-10,12-octadecadienoic acid from linoleic acid which includes the formation of 9,12,13-trihydroxy-trans-10-octadecenoic acid (Kimura & Yokota, 2004). Compound 105 (*m/z* 309) yielded a fragment ion at *m/z* 291 corresponding to the loss of a hydroxyl group. Thus, it has been tentatively assigned to linolenic acid 13-hydroperoxide. Additionally, compounds 104 (*m/z* 293) and 107 (m/z 291) were tentatively characterized as colneleic and colnelenic acids, respectively. They showed a fragment ion at m/z 116 due to C6\C7 bond cleavage while colnelenic acid showed an additional fragment at *m/z* 158 $[C_3H_4O]^-$. They, both, are formed through the abovementioned lipoxygenase pathway and they have been previously described in potato leaves (Fauconnier et al., 2003).

Similarly, compound 106 which eluted at 18.55 min has been tentatively identified as 12,15-octadecadienoic acid, 9-hydroxy-10-oxo-, methyl ester (Hamberg, 2000). Its main fragments yielded at *m/z* 188, 171 and 308 correspond to the loss of one molecule of water, the C8\C9 bond cleavage and the loss of a methyl group, respectively. Lastly, two isomers of octadecatrienoic acid, hydroperoxy-, methyl ester (*m/z* 323) were tentatively characterized in potato leaves (peaks 108 and 109). Their main fragments at *m/z* 121 and 137 were assigned to the C9\C10 bond cleavage followed by dehydration, respectively.

3.1.5. Jasmonates

As the same that occurs with phenolic compounds and glycoalkaloids, other secondary metabolites such as derivatives of jasmonic acid e.g. peaks 25, 40, 41, 57 and 91 have demonstrated to be central signals coordinating plant responses to stress (Larrieu et al., 2015). In this regard, two isomers of methyl 2-[(2Z)-5-(β-D-glucopyranosyloxy)-2-penten-1-yl]-3-oxocyclopentaneacetate (peaks 25 and 57) have been tentatively characterized on the basis of their fragmentation pattern which presented three main fragments at *m/z* 179, 207 and 233 (See Fig. 1d). These jasmonates have been previously characterized in potato leaves (Šimko et al., 1996). Furthermore, peaks 40 and 41 (*m/z* 387) were tentatively identified as tuberonic acid glucoside isomers. Their MS^2 ions at *m/z* 225, 207 and 163 were consistent with the loss of glucose moiety followed by successive dehydration and decarboxylation, respectively. These compounds have been early described in potato leaves (Yoshihara et al., 1989). Finally, peak 92 (*m/z* 323) was tentatively characterized as cyclopentaneacetic acid, 3-oxo-2-[(2Z)-5-[(tetrahydro-2H-pyran-2-yl)oxy]-2-pentenyl-3,4,4,5,5-d5]-, methyl ester, (1*R*,2*R*)-rel- in agreement with Matsuura et al. who characterized this compound in potato tubers but not in the leaves (Matsuura, Ohmori, Kobayashi, Sakurai, & Yoshihara, 2000).

3.1.6. Other polar compounds

Among this category, 8 organic acids have been identified. Peaks 1 and 3 (*m/z* 133) with molecular formula $C_4H_6O_5$ showed a main fragment at m/z 105 corresponding to the molecule dehydration. These compounds were tentatively characterized as malic acid isomers and were previously described in potato tuber (Defernez et al., 2004). Similarly, peaks 2 and 4 (*m/z* 191) with a fragment yielded at m/z 111 correspond to $[M\text{-}H\text{-}CO_2\text{-}2H_2O]^-$, were tentatively characterized as citric acid isomers, while peak 52 (m/z 247) was tentatively identified as diethyl citrate. This compound presented a fragment at *m/z* 191 belonging from the citric acid. Peak at RT 2.03 (m/z 175) presented two main fragments, one at m/z 115 due to the loss of $[M - C_2H_4O_2]^-$ and other one at m/z 169 due to the loss of an hydroxyl group. According to its fragmentation pattern, it was tentatively identified as ascorbic acid

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which has been previously reported in potato leaves (Tedone, Hancock, Alberino, Haupt, & Viola, 2004). Additionally, 2 isomers of quinic acid (peaks 10 and 11) were tentatively characterized. The presence of quinic acid and its fragments at *m/z* 101, 115, 129 and 111 has been reported in potato flesh and peel (López-Cobo et al., 2014).

Furthermore, 7 compounds belonging to the family of amino acids and derivatives and one nucleoside were detected. In this regard, peak 5 (*m/z* 128) presented a main fragment at m/z 113 which matched with that described in Metlin database and identified as pyroglutamic acid. Peak 8 (m/z 130) was not fully fragmented but it presented a characteristic fragment at *m/z* 115 due to the loss of a methyl group which allow it being tentatively characterized as leucine or isoleucine. On its behalf, peak 9 (m/z 292) with molecular formula $C_{12}H_{23}NO_7$ was tentatively identified as fructose leucine on the basis of its fragmentation pattern consistent with the cleavage of the hexoside bond which produced a fragment at m/z 130, as previously reported by Rodríguez-Pérez et al. (Rodríguez-Pérez, Quirantes-Piné, Fernández-Gutiérrez et al., 2013). This is the first time that this amino acid derivative is described in *Solanum tuberosum*. Likewise, compound 17 (*m/z* 326) presented fragments at m/z 164 and 147 due to the cleavage of the glycosidic bond followed by a loss of a hydroxyl group, respectively. It was tentatively identified for the first time in the Solanaceae family as fructose-phenylalanine. Two isomers of the amino acid phenylalanine (peaks 15 and 16) were additionally characterized. That amino acid has been previously detected in potato tuber (Shakya & Navarre, 2006). Their fragments at *m/z* 147 and 103 were described elsewhere (Rodríguez-Pérez, Mendiola, Quirantes-Piné, Ibáñez, & Segura-Carretero, 2016). The tripeptide characterized as 5-oxo-L-prolyl-L-isoleucine (peak 46) presented two fragments at *m/z* 141 and 197 which were consistent with data from literature (Frerot & Chen, 2013). This has been the first time that this compound has been detected in the Solanaceae family. Peak 7 (*m/z* 243) yielded its main fragment at m/z 110 consistent with the uracil group. It has tentatively been determined as uridine for the first time in potato leaves. Peak 67 was also tentatively identified for the first time in potato leaves. It eluted at 11 min and presented an *m/z* 289 with a fragment yielded at m/z 245 corresponding to the loss of the carboxylic acid. Thus, it was tentatively characterized as indole-3-acetylasparaginic acid, a phytohormone which has been previously described in tomato (*Solanum lycopersicum*) plant (Van Meulebroek, Bussche, Steppe, & Vanhaecke, 2012).

Peak 28 (*m/z* 415) with molecular formula $C_{19}H_{28}O_{10}$ presented fragments at m/z 311, 191 and 149. This compound was identified for the first time in potato leaves and it was tentatively characterized as phenethyl primeveroside in agreement with previous analytical research (Fernández-Arroyo, Barrajón-Catalán, Micol, Segura-Carretero, & Fernández-Gutiérrez, 2010; Rodríguez-Pérez, Quirantes-Piné, Fernández-Gutiérrez, & Segura-Carretero, 2013). On its behalf, compound 33 (*m/z* 465) presented a fragment at m/z 405 due to the break of the glucose ring producing a [M-H-60] fragment as previously reported in other plants (Rodríguez-Pérez et al., 2013). It was tentatively characterized as cymal 3. Peak 31 with molecular formula $C_{21}H_{32}O_{10}$, was tentatively characterized as dihydrophaseic acid glucopyranoside on the basis of its fragmentation pattern which encompassed fragments at *m/z* 281, 161, 101, 113, 119 (Mekky et al., 2015) and data from literature (Pushpa et al., 2014). Peak 34 (*m/z* 293) yielded a fragment at m/z 131 corresponding with the carboxy methylbutyl group. It was identified as glucopyranoside, carboxy-methylbutyl. Furthermore, compounds eluted at RT 9.16 (m/z 445) and RT 9.31 (m/z 385) were tentatively identified for the first time in potato leaves as sacranoside A and roseoside A, respectively. Sacranoside A presented ions at *m/z* 223 and 385 resulting from the loss of glucose and the loss of [2(CH_2O)] from arabinosyl group, respectively (Rodríguez-Pérez, Quirantes-Piné, Amessis-Ouchemoukh, et al., 2013). Roseoside A presented a main fragment at *m/z* 223 corresponding to the loss of the glucose moiety. Similarly, peaks 54 and 59 (m/z 311) were described for the first time in the Solanaceae family. These cinnamylglycosides were tentatively characterized as isomers of the compound triandrin. Its fragmentation pattern consisting on fragments at *m/z* 223 and 167 that have previously been described in the plant kingdom (Kammerer, Kahlich, Biegert, Gleiter, & Heide, 2005).

Additionally, 3 compounds (peak 51, 72 and 76) were identified as iridoids derivatives for the first time in potato leaves. In this regard, compound 51 which presented a main fragment at m/z 249 was designed as deacetylasperuloside (Amessis-Ouchemoukh et al., 2014). According to Gómez-Caravaca et al. peak 72 with molecular formula $C_{27}H_{42}O_{15}$ was tentatively identified as penstebioside (Gómez-Caravaca, Segura-Carretero, Fernández-Gutiérrez, & Caboni, 2011). Finally, the iridoid correspond to peak 76 (m/z 347) was tentatively identified as ajugol based on its exact mass and data from literature (Elusiyan, Ani, Adewunmi, & Olugbade, 2011).

The lignan syringaresinol glucopyranoside (peak 68), which was previously reported in potato tuber (Pushpa et al., 2014), was tentatively characterized in potato leaves. It eluted at retention time 11.07 min with m/z 579. Likewise, peak 69 (m/z 429) presented fragments at m/z 179, 193, 163, 120 and 387 which have been previously reported in potato (Yogendra et al., 2015). It was tentatively identified as dendroside F and its fragmentation pattern is shown in Fig. 1e. Other compound previously reported in columbian potato tubers was peak 73 (m/z 431) which has been tentatively characterized as cyclohexanecarboxylic acid, 3-[[(2E)-3-[4-(β-D-glucopyranosyloxy)-3-methoxyphenyl]-1-oxo-2-propenyl]oxy]-1,4,5-trihydroxy-, (1*S*,3*R*,4*R*,5*R*)- (Narváez-Cuenca et al., 2013).

Finally, other 4 polar and semipolar compounds were tentatively characterized for the first time in potato leaves and in the Solanaceae family. In this regard, peaks 70 and 74 (m/z 325) were tentatively identified as eugenyl glucoside isomers. Their presented fragments at m/z 179 and 163 due to the loss of the glycoside moiety followed by a loss of hydroxyl group, respectively. Peak 81 (m/z 431) yielded fragments at m/z 101, 114, 130, 273, 357. Due to its fragmentation pattern (Fig. 1f), this compound was tentatively identified as β-D-glucopyranoside, hexyl, 2,3,4,6-tetraacetate. Peak 83 eluted at retention time 12.43 min and presented the following molecular formula $C_{42}H_{66}O_{18}$. On its behalf, peak 83 (m/z 857) was tentatively identified as thevetin B (Fig. 1g), a cardiac glycoside found in other plants which could be involved in allowing the selective control of human tumors (Tian et al., 2015).

3.2. Quantification of compounds from *Solanum tuberosum* L. leaves

Five standard calibration graphs for quantifying the main compounds found in potato leaves extract were prepared using the following available commercial standards: quinic acid, benzoic acid, vanillic acid, vanillin, rutin, ferulic acid. All calibration curves presented good linearity between different concentrations. The calibration showed a strong correlation between peak areas and analyte concentrations, and regression coefficients were near 0.999 in all cases.

Quinic acid isomers (peaks 10 and 11) were tentatively quantified using the quinic acid calibration curve, and benzoic acid derivatives (peaks 13, 32, 70 and 88) were tentatively quantified using the benzoic acid calibration curve; gentisic acid and vanillic acid derivatives, protocatechuic acid, sinapic acid glucoside and syringaresinol glucopyranoside were quantified using the vanillic acid calibration curve; flavonoids (peaks 43, 48, 50, 56, 60, 61, 74, 87 and 92) were quantified using the rutin calibration curve while ferulic acid calibration curve was used for the tentatively quantification of ferulic acid derivatives (peaks 49, 55 and 84), chlorogenic acid derivatives (peaks 30 and

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39), caffeic acid derivatives (peaks 22, 35, 38, 45, 47, 63, 34 and 65) and cumaric acid derivatives (peaks 35 and 62). Furthermore, phenethyl primeveroside was tentatively quantified using the vanillin calibration curve.

The quantitative results are presented in Table 2. Total bioactive compounds content was 6.2 mg/g of leaf d.w.; this amount is in the same order of magnitude of that reported by Payyavula and coworkers (Payyavula et al., 2015). Among phenolic compounds, it is possible to observe that phenolic acid and derivatives were presented in higher concentrations than flavonoids in potato leaves. In this regard, the leaves under study showed that compounds with the highest concentrations were quinic acid derivatives followed by benzoic acid derivatives.

Quinic acid derivatives accounted for 45.6% (equivalent to 2.8 mg/g potato leaf d.w.) of total compounds. Zhang, Zhang, Zhao, and Zhao-Wilson (2012) (Zhang et al., 2012) suggested that quinic acid is a reasonable antiaging candidate; in fact, they evaluated its antioxidant activity in vitro and in vivo underlyining as this acid is able to downregulate the ROS levels and to upregulate the sod-3 and hsp-16.2 that are involved in the life span and stress-resistance regulation.

Table 2
Bioactive compounds in *Solanum tuberosum* L. leaves extract expressed in mg/100 g of leaf d.w. ($n = 3$).

Peak	Compounds	Leaves (mg/100 g)
10	Quinic acid isomer 1	206.04 ± 0.56
11	Quinic acid isomer 2	66.80 ± 0.07
12	Gentisoyl glucoside isomer 1	2.71 ± 1.14
13	p-Hydroxybenzoic acid glucoside isomer 1	22.86 ± 1.26
18	Gentisoyl glucoside isomer 2	39.88 ± 0.03
19	Gentisoyl glucoside isomer 3	3.74 ± 0.03
20	Protocatechuic acid	3.41 ± 0.35
21	Gentisoyl glucoside isomer 4	8.37 ± 0.60
22	Caffeoylquinic acid conjugate	1.37 ± 0.01
23	Gentisic acid pentosyl hexoside isomer 1	19.67 ± 0.13
24	Gentisic acid pentosyl hexoside isomer 2	7.78 ± 0.16
27	Homovanillic acid hexose isomer 2	0.53 ± 0.03
28	Phenethyl-β-primeveroside	5.76 ± 0.01
30	Chlorogenic acid, 4′-β-D-glucopyranoside isomer 1	0.648 ± 0.002
32	p-Hydroxybenzoic acid glucoside isomer 2	86.38 ± 0.28
35	1-Caffeoylquinic acid	2.17 ± 0.02
36	Sinapic acid 4-O-glucoside	3.31 ± 0.36
37	Homovanillic acid hexose isomer 3	6.48 ± 0.07
38	3-Caffeoylquinic acid	1.10 ± 0.04
39	Chlorogenic acid, 4′-β-D-glucopyranoside isomer 2	0.049 ± 0.001
43	Quercetin-rut-glu	0.33 ± 0.01
45	N-Caffeoylputrescine isomer 1	0.178 ± 0.002
47	Caffeoylmalic acid	0.645 ± 0.001
48	Quercetin diglucoside	0.106 ± 0.001
49	3-Feruloyl-quinic acid	2.06 ± 0.01
50	Quercetin-xyl-rut	0.052 ± 0.002
53	5-p-Coumaroyl quinic acid	0.86 ± 0.03
55	5-Feruloyl-quinic acid	0.52 ± 0.02
56	Rutin	0.62 ± 0.01
58	Dihydrosinapoyl conjugate isomer 1	8.78 ± 0.49
60	Rhamnetin-glucuronide	0.070 ± 0.001
61	Dihydrosinapoyl conjugate isomer 2	3.64 ± 0.12
62	p-Coumarylmalic acid	0.507 ± 0.004
63	Dihydrosinapoyl caffeoyl conjugate isomer 1	0.43 ± 0.01
64	Dihydrosinapoyl caffeoyl conjugate isomer 2	6.20 ± 0.28
65	Kaempferol-3-O-rutinoside	0.020 ± 0.002
66	N-Caffeoylputrescine isomer 2	0.125 ± 0.003
71	3,4-Diacetoxybenzoic acid	37.75 ± 0.49
75	2-Phenylethyl D-rutinoside	0.11 ± 0.01
85	Feruloylagmatine	0.204 ± 0.001
88	Quercetin	0.059 ± 0.003
89	5-O-p-Hydroxybenzoylquinic acid	65.75 ± 0.37
	Total	**618.05 ± 6.99**

Pero's group worked on the efficacy of quinic acid from cat's claw extracts and other food supplements. They reported as quinic acid had DNA repair, immune and antiinflamatory enhancing properties (Pero & Lund, 2009; Sheng et al., 2005). Moreover, the data reported by the same authors (Pero, Lund, & Leanderson, 2009) supported the hypotesis that quinic acid supplementation increase the tryptophan synthesis via the gastrointestinal tract microflora.

The two isomers of p-hydroxybenzoic acid glucoside (peaks 13 and 32), 5-O-p-hydroxybenzoylquinic acid (peak 88), 3,4-diacetoxybenzoic acid (peak 70) were found at concentration of 22.86 ± 1.26, 86.38 ± 0.28, 65.75 ± 0.37 and 37.75 ± 0.49 mg/100 g of leaves, respectively. Additionally, considerable concentrations of two gentisic acid derivatives (peaks 18 and 23) i.e. 39.88 ± 0.03 and 19.67 ± 0.13 mg/100 g of leaves, respectively were found in potato leaves. However, Hyon Woon et al. reported 14.8, 13.3 and 1.2 mg/100 g of chlorogenic acid and its isomers, and caffeic acid, respectively accounting a total of 29.3 mg/100 g of fresh leaf extract (Im et al., 2008). Contrarily, our results showed a total of 0.7 and 5.59 mg/100 g of chlorogenic acid and caffeic acid derivatives, respectively.

Comparing to potato peel by-products (Lopez-Cobo et al., 2013), potato leaves studied in this work showed similar content of phenolic compounds; however, they reported amounts of cholorogenic acid (the main phenolic compound of potato peels) enormously lower than potato peels (about two order of magnitude). However, it should be noteworthy that the concentration will depend on other external factors i.e. variety, climatic or agronomic conditions (Akyol et al., 2016) that together to the scarce previous literature regarding potato leaves composition makes difficult to compare with other research.

4. Conclusions

Potato is one of the most important field crops of the world and potato leaves represent a waste that could be used as source of bioactive compounds for functional foods or cosmeceutical industry. However, literature data on the metabolites of potato leaves are scarce. To the authors' best knowledge, the current study is the first report on the metabolite profile of potato leaves. Because of that, HPLC-ESI-QTOF-MS platform was successfully used to tentantatively identify 108 polar metabolites. Different families such as organic acids, aminoacids, phenolic compounds, iridoids, oxylipins and other polar compounds were described. Among phenolic compounds, potato leaves showed high amount of quinic acid derivatives corresponding to 45% of total phenolic compounds. These preliminary data suggested that potato leaves could be used as source of bioactive compounds; however, the prospect of using these wastes for food or cosmetical purposes should be further investigated.

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Matsuura et al., 2000

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