

Article

# Phytochemical Profiling of *Coryphantha macromeris* (Cactaceae) Growing in Greenhouse Conditions Using Ultra-High-Performance Liquid Chromatography–Tandem Mass Spectrometry

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**Abstract:** Chromatographic separation combined with mass spectrometry is a powerful tool for the characterization of plant metabolites because of its high sensitivity and selectivity. In this work, the phytochemical profile of aerial and radicular parts of *Coryphantha macromeris* (Engelm.) Britton & Rose growing under greenhouse conditions was qualitatively investigated for the first time by means of modern ultra-high-performance liquid chromatography–tandem mass spectrometry (UHPLC-PDA-HESI-Orbitrap-MS/MS). The UHPLC-PDA-HESI-Orbitrap-MS/MS analysis indicated a high complexity in phenolic metabolites. In our investigation, 69 compounds were detected and 60 of them were identified. Among detected compounds, several phenolic acids, phenolic glycosides, and organic acids were found. Within this diversity, 26 metabolites were exclusively detected in the aerial part, and 19 in the roots. Twenty-four metabolites occurred in both plant parts. According to the relative abundance of peaks in the chromatogram, ferulic and piscidic acids and their derivatives may correspond to one of the main phenolic compounds of *C. macromeris*. Our results contribute to the phytochemical knowledge regarding *C. macromeris* and its potential applications in the pharmaceutical and cosmetic industries. Besides, some metabolites and their fragmentation patterns are reported here for the first time for cacti species.

**Keywords:** Cactaceae; phenolic compounds; secondary metabolites; UHPLC; succulent plants; fragmentation pattern; active compounds

## 1. Introduction

The family Cactaceae is one of the most threatened within the plant kingdom [1], and is the most important plant family of the arid and semiarid regions of America [2], comprising around 1600 species [3]. Cacti are succulent plants which have been used for their functional properties and industrial utility [4–6]. Different cacti species obtained by cultivated or wild-collected methods have been used as food sources and fodder, for ornamental purposes, and for medicinal purposes (due to their antioxidant [7], antimutagenic [8], and bactericidal [9] properties), and have been cataloged as a source of bioactive compounds including alkaloids [10,11] and phenolics [12,13].

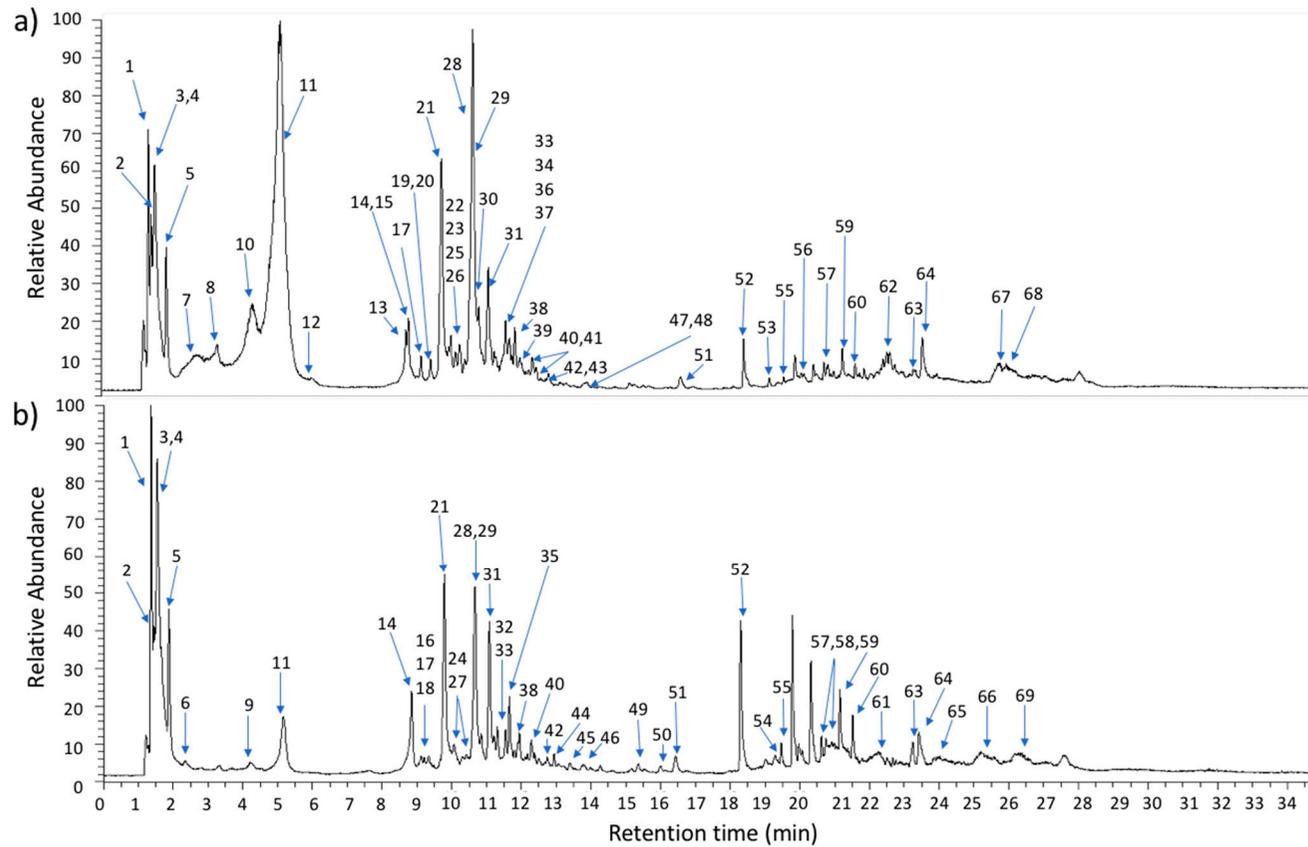
Plants contain different classes of metabolites found in different concentrations and of a wide structural diversity. Their phytochemical profiles and functional properties may vary according to: a) the solvent and extraction processes [14,15], b) the stage of growth [16], c) storage conditions [17], and d) the specific section of the plant [18,19]. This complexity makes it difficult to identify plant metabolites through a single analytical method or under a defined separation system [20]. Several techniques have been proposed to achieve the elucidation of the plant metabolome, including the coupling of mass spectrometry with different separation techniques [21,22]. The knowledge of natural product chemistry is important since identified metabolites may serve as the basis for the discovery or design of novel compounds with biological activities [23] and as chemotaxonomic markers for plant classification [24].

The genus *Coryphantha* is highly endemic, distributed in the arid and semiarid regions located between the Sierra Madre Oriental and the Sierra Madre Occidental in northern Mexico, expanding to the southern regions of Arizona, Texas, and New Mexico, USA [25]. Currently, natural populations of *Coryphantha* species are reduced due to overexploitation and destruction of habitats. *Coryphantha* spp. are slow growing plants and the environmental conditions of semiarid regions make their germination, growth, and reproduction difficult; for this reason, biotechnological approaches have been proposed for the *in vitro* propagation of *Coryphantha* spp. and other cacti species [26,27]. *Coryphantha macromeris* (Engelm.) Britton & Rose is a globose cactus traditionally known as “Dona Ana”, “long mamma cory-cactus”, “big needle cactus”, and “biznaga partida-partida”; it is mainly distributed in northern Mexico and southern United States. In Mexico, *C. macromeris* is used in folk medicine for healing stomach disorders; nevertheless, hallucinogenic properties have been proposed, due to the presence of alkaloids such as macromerine [28] and other  $\beta$ -phenethylamine derivatives [29]. More recently, Kikuchi, et al. [30] evaluated the chemical constituents of a psychotropic herbal product and, using DNA sequence analysis, suggested that *C. macromeris* could be one of its components, as the *rpl16* intron sequence of the herbal product showed 99% of similarity with that of *C. macromeris*. Information regarding the phytochemical composition and bioactive compounds in *C. macromeris* is scarce. Thus, the aim of this study was to identify, using UHPLC coupled with tandem mass spectrometry, the main secondary metabolites present in shoots and roots of *Coryphantha macromeris* growing under greenhouse conditions in order to contribute to the phytochemical knowledge of this species and its potential applications.

## 2. Results and Discussion

Methanolic extracts prepared with aerial and radicular parts of *C. macromeris* cultivated under greenhouse conditions were analyzed by ultra-high-performance liquid chromatography–tandem mass spectrometry and a photodiode array detector (UHPLC-PDA-HESI-Orbitrap-MS/MS). This technique has been used for the characterization of metabolites in complex mixtures [31], and the chromatographic conditions used in this work have shown efficiency for the separation and identification of different secondary metabolites [32–34]. For *C. macromeris* extracts, UHPLC conditions allowed a good separation of many sample components.

The phytochemical characterization of *C. macromeris* was achieved by comparing the obtained information by UHPLC-PDA-HESI-Orbitrap-MS/MS with spectroscopic evidences existing in the literature or by structure searching and studying the fragmentation pattern of molecules. Additionally, retention time and UV ( $\lambda_{\max}$ ) spectra were used for peak characterization. As far as we know, metabolite profiling of *C. macromeris* is reported for the first time in this work. Elution profile (Figure 1) and mass spectra obtained in negative ion mode indicated a highly complex phenolic composition. Peak characteristics (i.e., retention time, theoretical and measured mass, UV ( $\lambda_{\max}$ ), and fragmentation pattern) and tentative identification of each compound are summarized in Table 1. All detected compounds exhibited an accuracy smaller than 5 ppm. Under the proposed UHPLC-PDA-HESI-Orbitrap-MS/MS method, 69 compounds were separated, and 60 of them were tentatively identified in *C. macromeris* greenhouse plants (Table 1). Within this complexity, 26 compounds occurred in the aerial part, 19 in occurred in the roots, and 24 occurred in both plant parts, suggesting a translocation mechanism from actively photosynthetic tissues to metabolite consuming/storage areas.



**Figure 1.** Ultra-high-performance liquid chromatography (UHPLC) chromatogram of *Coryphantha macromeris* methanolic extracts prepared with aerial (a) and radicular (b) parts. Peak numbers refer to the metabolites indicated in Table 1; repeated numbers in (a) or (b) indicate that the metabolite is found in both plant parts.

**Table 1.** Metabolites identified in aerial and radicular parts of *Coryphantha macromeris* by ultra-high-performance liquid chromatography–tandem mass spectrometry (UHPLC-PDA-HESI-Orbitrap-MS/MS) data using heated electrospray ionization source (HESI) in negative ion mode.

Peak	Retention Time (min)	UVMax ( $\lambda_{\max}$ )	Tentative Identification	Elemental Composition [M-H] <sup>-</sup>	Theoretical Mass (m/z)	Measured Mass (m/z)	Accuracy (ppm)	MSn Ions	Plant Part
1	1.37	220, 272	Vaccihin A	C <sub>18</sub> H <sub>17</sub> O <sub>9</sub> <sup>-</sup>	377.08781	377.08600	4.80	361.09076 ([M-H-OH] <sup>-</sup> ) 347.07724 ([M-H-OCH <sub>3</sub> ] <sup>-</sup> ) 319.07990 ([M-H-C <sub>2</sub> H <sub>3</sub> O <sub>2</sub> ] <sup>-</sup> ) 289.06958 ([M-H-C <sub>2</sub> H <sub>3</sub> O <sub>2</sub> -OCH <sub>3</sub> ] <sup>-</sup> ) 125.02375 ([M-H-C <sub>8</sub> H <sub>9</sub> O <sub>4</sub> -C <sub>3</sub> H <sub>5</sub> O <sub>2</sub> ] <sup>-</sup> )	Root/shoot
2	1.45	220, 272	Dihydroxy methoxy butanoic acid	C <sub>5</sub> H <sub>9</sub> O <sub>5</sub> <sup>-</sup>	149.04555	149.04498	3.82	135.02925 ([M-H-CH <sub>3</sub> ] <sup>-</sup> ) 131.03433 ([M-H-OH] <sup>-</sup> ) 119.03425 ([M-H-CH <sub>3</sub> -OH] <sup>-</sup> ) 103.03932 ([M-H-OCH <sub>3</sub> -OH] <sup>-</sup> )	Root/shoot
3	1.52	220, 274	2-Hydroxy-succinic acid (malic acid)	C <sub>4</sub> H <sub>5</sub> O <sub>5</sub> <sup>-</sup>	133.01390	133.01363	2.03	115.00297 ([M-H-OH] <sup>-</sup> )	Root/shoot
4	1.55	224, 277	Iso citric acid	C <sub>6</sub> H <sub>7</sub> O <sub>7</sub> <sup>-</sup>	191.01973	191.01938	1.83	111.00790 ([M-H-CO <sub>2</sub> -2OH] <sup>-</sup> )	Root/shoot
5	1.87	277	Iso citric acid isomer	C <sub>6</sub> H <sub>7</sub> O <sub>7</sub> <sup>-</sup>	191.01973	191.01938	1.83	111.00790 ([M-H-CO <sub>2</sub> -2OH] <sup>-</sup> )	Root/shoot
6	2.35	220, 277	3,5-Dihydroxy-4-methylxolan-2-yl methoxy-6-hydroxymethyl oxane-3,4,5-triol	C <sub>12</sub> H <sub>21</sub> O <sub>9</sub> <sup>-</sup>	309.11911	309.11935	0.78	293.12424 ([M-H-OH] <sup>-</sup> ) 279.10870 ([M-H-OH-CH <sub>3</sub> ] <sup>-</sup> ) 147.06578 ([M-H-C <sub>6</sub> H <sub>11</sub> O <sub>5</sub> ] <sup>-</sup> ) 131.07106 ([M-H-C <sub>6</sub> H <sub>11</sub> O <sub>5</sub> -OH] <sup>-</sup> )	Root
7	2.74	224, 277	Piscidic acid isomer	C <sub>11</sub> H <sub>11</sub> O <sub>7</sub> <sup>-</sup>	255.05103	255.05098	0.20	193.05013 ([M-H-CHO <sub>2</sub> -OH] <sup>-</sup> ) 165.05521 ([M-H-C <sub>2</sub> H <sub>2</sub> O <sub>3</sub> -OH] <sup>-</sup> ) 135.04442 ([M-H-C <sub>2</sub> H <sub>2</sub> O <sub>3</sub> -CHO <sub>2</sub> ] <sup>-</sup> ) 119.04952 ([M-H-C <sub>2</sub> H <sub>2</sub> O <sub>3</sub> -CH <sub>2</sub> -OH] <sup>-</sup> ) 107.04927 ([M-H-C <sub>4</sub> H <sub>4</sub> O <sub>3</sub> ] <sup>-</sup> )	Shoot
8	3.34	228, 277	Piscidic acid isomer	C <sub>11</sub> H <sub>11</sub> O <sub>7</sub> <sup>-</sup>	255.05103	255.05098	0.20	193.05013 ([M-H-CHO <sub>2</sub> -OH] <sup>-</sup> ) 165.05521 ([M-H-C <sub>2</sub> H <sub>2</sub> O <sub>3</sub> -OH] <sup>-</sup> ) 135.04442 ([M-H-C <sub>2</sub> H <sub>2</sub> O <sub>3</sub> -CHO <sub>2</sub> ] <sup>-</sup> ) 119.04952 ([M-H-C <sub>2</sub> H <sub>2</sub> O <sub>3</sub> -CH <sub>2</sub> -OH] <sup>-</sup> ) 107.04927 ([M-H-C <sub>4</sub> H <sub>4</sub> O <sub>3</sub> ] <sup>-</sup> )	Shoot
9	4.22	197, 223, 278	Protocatechuic acid hesoxide	C <sub>13</sub> H <sub>15</sub> O <sub>9</sub> <sup>-</sup>	315.07230	315.07239	0.29	255.05104 ([M-H-C <sub>2</sub> H <sub>5</sub> O <sub>2</sub> ] <sup>-</sup> ) 211.06094 ([M-H-C <sub>2</sub> H <sub>5</sub> O <sub>2</sub> -CHO <sub>2</sub> ] <sup>-</sup> ) 153.01878 ([M-H-C <sub>6</sub> H <sub>11</sub> O <sub>5</sub> ] <sup>-</sup> ) 137.02385 ([M-H-C <sub>6</sub> H <sub>11</sub> O <sub>5</sub> -OH] <sup>-</sup> ) 121.02895 ([M-H-C <sub>6</sub> H <sub>11</sub> O <sub>5</sub> -2OH] <sup>-</sup> ) 109.02863 ([M-H-C <sub>6</sub> H <sub>11</sub> O <sub>5</sub> -CHO <sub>2</sub> ] <sup>-</sup> )	Root
10	4.34	223, 276	Piscidic acid isomer	C <sub>11</sub> H <sub>11</sub> O <sub>7</sub> <sup>-</sup>	255.05103	255.05098	0.20	193.05013 ([M-H-CHO <sub>2</sub> -OH] <sup>-</sup> ) 165.05521 ([M-H-C <sub>2</sub> H <sub>2</sub> O <sub>3</sub> -OH] <sup>-</sup> )	Shoot

Table 1. Cont.

Peak	Retention Time (min)	UVM <sub>max</sub> ( $\lambda_{\text{max}}$ )	Tentative Identification	Elemental Composition [M-H] <sup>-</sup>	Theoretical Mass (m/z)	Measured Mass (m/z)	Accuracy (ppm)	MSn Ions	Plant Part
								135.04442 ([M-H-C <sub>2</sub> H <sub>2</sub> O <sub>3</sub> -CHO <sub>2</sub> ] <sup>-</sup> ) 119.04952 ([M-H-C <sub>2</sub> H <sub>2</sub> O <sub>3</sub> -CH <sub>2</sub> -OH] <sup>-</sup> ) 107.04927 ([M-H-C <sub>4</sub> H <sub>4</sub> O <sub>3</sub> ] <sup>-</sup> )	
11	5.13	222, 275	Piscidic acid isomer	C <sub>11</sub> H <sub>11</sub> O <sub>7</sub> <sup>-</sup>	255.05103	255.05095	0.31	193.05013 ([M-H-CHO <sub>2</sub> -OH] <sup>-</sup> ) 165.05521 ([M-H-C <sub>2</sub> H <sub>2</sub> O <sub>3</sub> -OH] <sup>-</sup> ) 135.04442 ([M-H-C <sub>2</sub> H <sub>2</sub> O <sub>3</sub> -CHO <sub>2</sub> ] <sup>-</sup> ) 119.04952 ([M-H-C <sub>2</sub> H <sub>2</sub> O <sub>3</sub> -CH <sub>2</sub> -OH] <sup>-</sup> ) 107.04927 ([M-H-C <sub>4</sub> H <sub>4</sub> O <sub>3</sub> ] <sup>-</sup> )	Root/shoot
12	6.02	222, 275	Piscidic acid isomer	C <sub>11</sub> H <sub>11</sub> O <sub>7</sub> <sup>-</sup>	255.05103	255.05101	0.08	193.05013 ([M-H-CHO <sub>2</sub> -OH] <sup>-</sup> ) 165.05521 ([M-H-C <sub>2</sub> H <sub>2</sub> O <sub>3</sub> -OH] <sup>-</sup> ) 135.04442 ([M-H-C <sub>2</sub> H <sub>2</sub> O <sub>3</sub> -CHO <sub>2</sub> ] <sup>-</sup> ) 119.04952 ([M-H-C <sub>2</sub> H <sub>2</sub> O <sub>3</sub> -CH <sub>2</sub> -OH] <sup>-</sup> ) 107.04927 ([M-H-C <sub>4</sub> H <sub>4</sub> O <sub>3</sub> ] <sup>-</sup> )	Shoot
13	8.74	222, 277	Lucuminic acid	C <sub>19</sub> H <sub>25</sub> O <sub>12</sub> <sup>-</sup>	445.13515	445.13531	0.36	163.03947 ([M-H-C <sub>10</sub> H <sub>19</sub> O <sub>8</sub> -OH] <sup>-</sup> ) 119.04939 ([M-H-C <sub>11</sub> H <sub>19</sub> O <sub>10</sub> -OH] <sup>-</sup> ) 107.04942 ([M-H-C <sub>11</sub> H <sub>19</sub> O <sub>9</sub> -CHO <sub>2</sub> ] <sup>-</sup> )	Shoot
14	8.85	223, 276	Hyrtioerectine C	C <sub>11</sub> H <sub>12</sub> NO <sub>4</sub> <sup>-</sup>	222.07718	222.07703	0.68	206.08206 ([M-H-OH] <sup>-</sup> ) 198.07718 ([M-H-C <sub>2</sub> H <sub>3</sub> ] <sup>-</sup> ) 180.06580 ([M-H-C <sub>2</sub> H <sub>3</sub> -OH] <sup>-</sup> ) 178.08685 ([M-H-CHO <sub>2</sub> ] <sup>-</sup> )	Root/shoot
15	8.93	227, 283	Piscidic acid isomer	C <sub>11</sub> H <sub>11</sub> O <sub>7</sub> <sup>-</sup>	255.05103	255.05104	0.04	193.05013 ([M-H-CHO <sub>2</sub> -OH] <sup>-</sup> ) 165.05521 ([M-H-C <sub>2</sub> H <sub>2</sub> O <sub>3</sub> -OH] <sup>-</sup> ) 135.04442 ([M-H-C <sub>2</sub> H <sub>2</sub> O <sub>3</sub> -CHO <sub>2</sub> ] <sup>-</sup> ) 119.04952 ([M-H-C <sub>2</sub> H <sub>2</sub> O <sub>3</sub> -CH <sub>2</sub> -OH] <sup>-</sup> ) 107.04927 ([M-H-C <sub>4</sub> H <sub>4</sub> O <sub>3</sub> ] <sup>-</sup> )	Shoot
16	9.12	255, 207	Protocatechuic aldehyde	C <sub>7</sub> H <sub>5</sub> O <sub>3</sub> <sup>-</sup>	137.02442	137.02386	4.09	121.02882 ([M-H-OH] <sup>-</sup> ) 109.02884 ([M-H-COH] <sup>-</sup> )	Root
17	9.19	230, 286	Piscidic acid derivative	C <sub>21</sub> H <sub>27</sub> O <sub>13</sub> <sup>-</sup>	-	487.14600	-	255.05110 ([piscidic acid] <sup>-</sup> ) 193.05078 ([piscidic acid-CHO <sub>2</sub> -OH] <sup>-</sup> ) 165.05516 ([piscidic acid-C <sub>2</sub> H <sub>2</sub> O <sub>3</sub> -OH] <sup>-</sup> ) 135.04453 ([piscidic acid-C <sub>2</sub> H <sub>2</sub> O <sub>3</sub> -CHO <sub>2</sub> ] <sup>-</sup> ) 107.04935 ([piscidic acid-C <sub>4</sub> H <sub>4</sub> O <sub>3</sub> ] <sup>-</sup> )	Root/shoot
18	9.41	223, 278	Piscidic acid derivative	C <sub>20</sub> H <sub>27</sub> O <sub>13</sub> <sup>-</sup>	-	475.14606	-	255.05112 ([piscidic acid] <sup>-</sup> ) 193.05037 ([piscidic acid-CHO <sub>2</sub> -OH] <sup>-</sup> ) 165.05513 ([piscidic acid-C <sub>2</sub> H <sub>2</sub> O <sub>3</sub> -OH] <sup>-</sup> ) 135.04453 ([piscidic acid-C <sub>2</sub> H <sub>2</sub> O <sub>3</sub> -CHO <sub>2</sub> ] <sup>-</sup> ) 107.04923 ([piscidic acid-C <sub>4</sub> H <sub>4</sub> O <sub>3</sub> ] <sup>-</sup> )	Root

Table 1. Cont.

Peak	Retention Time (min)	UVMax ( $\lambda_{\max}$ )	Tentative Identification	Elemental Composition [M-H] <sup>-</sup>	Theoretical Mass (m/z)	Measured Mass (m/z)	Accuracy (ppm)	MSn Ions	Plant Part
19	9.45	231, 295	Sinapic acid derivative	C <sub>22</sub> H <sub>29</sub> O <sub>14</sub> <sup>-</sup>	-	517.15649	-	223.06104 ([sinapic acid] <sup>-</sup> ) 208.03767 ([sinapic acid-CH <sub>3</sub> ] <sup>-</sup> ) 179.07083 ([sinapic acid-CHO <sub>2</sub> ] <sup>-</sup> ) 164.04738 ([sinapic acid-CHO <sub>2</sub> -OH] <sup>-</sup> )	Shoot
20	9.50	231, 295	Sinapic acid	C <sub>11</sub> H <sub>11</sub> O <sub>5</sub> <sup>-</sup>	223.06070	223.06102	1.43	208.03757 ([M-2H-CH <sub>3</sub> ] <sup>-</sup> ) 179.07094 ([M-H-CHO <sub>2</sub> ] <sup>-</sup> ) 164.04730 ([M-2H-CHO <sub>2</sub> -OH] <sup>-</sup> )	Shoot
21	9.77	224, 276	Syringic acid acetate	C <sub>11</sub> H <sub>11</sub> O <sub>6</sub> <sup>-</sup>	239.05611	239.05594	0.71	197.04517 ([syringic acid] <sup>-</sup> ) 195.06580 ([M-H-CHO <sub>2</sub> ] <sup>-</sup> ) 179.03439 ([M-H-2CH <sub>3</sub> O] <sup>-</sup> ) 149.06023 ([M-H-2CH <sub>3</sub> O-OH] <sup>-</sup> ) 135.04456 ([M-H-CHO <sub>2</sub> -2CH <sub>3</sub> O] <sup>-</sup> ) 107.04944 ([M-H-CHO <sub>2</sub> -CH <sub>3</sub> O-C <sub>2</sub> H <sub>3</sub> O <sub>2</sub> ] <sup>-</sup> )	Root/shoot
22	9.97	231, 286	Piscidic acid derivative	C <sub>21</sub> H <sub>27</sub> O <sub>13</sub> <sup>-</sup>	-	487.14603	-	255.05101 ([piscidic acid] <sup>-</sup> ) 193.05025 ([piscidic acid-CHO <sub>2</sub> -OH] <sup>-</sup> ) 165.05528 ([piscidic acid-C <sub>2</sub> H <sub>2</sub> O <sub>3</sub> -OH] <sup>-</sup> ) 135.04456 ([piscidic acid-C <sub>2</sub> H <sub>2</sub> O <sub>3</sub> -CHO <sub>2</sub> ] <sup>-</sup> ) 107.04945 ([piscidic acid-C <sub>4</sub> H <sub>4</sub> O <sub>3</sub> ] <sup>-</sup> )	Shoot
23	10.04	233, 283	Syringic acid acetate derivative	C <sub>19</sub> H <sub>31</sub> O <sub>8</sub> <sup>-</sup>	-	387.20276	-	239.05594 ([syringic acid acetate] <sup>-</sup> ) 197.04517 ([syringic acid] <sup>-</sup> ) 195.06580 ([syringic acid acetate-CHO <sub>2</sub> ] <sup>-</sup> ) 179.03439 ([syringic acid acetate-2CH <sub>3</sub> O] <sup>-</sup> ) 149.06023 ([syringic acid acetate-2CH <sub>3</sub> O-OH] <sup>-</sup> ) 135.04456 ([syringic acid acetate-CHO <sub>2</sub> -2CH <sub>3</sub> O] <sup>-</sup> ) 107.04944 ([syringic acid acetate-CHO <sub>2</sub> -CH <sub>3</sub> O-C <sub>2</sub> H <sub>3</sub> O <sub>2</sub> ] <sup>-</sup> )	Shoot
24	10.08	231, 283	Caffeic acid	C <sub>9</sub> H <sub>7</sub> O <sub>4</sub> <sup>-</sup>	179.03498	179.03477	1.17	163.03950 ([M-H-OH] <sup>-</sup> ) 135.04510 ([M-H-CHO <sub>2</sub> ] <sup>-</sup> ) 109.02870 ([M-H-C <sub>3</sub> H <sub>3</sub> O <sub>2</sub> ] <sup>-</sup> )	Root
25	10.17	231, 286	Sinapic acid hexoside	C <sub>17</sub> H <sub>21</sub> O <sub>10</sub> <sup>-</sup>	385.11402	385.11438	0.93	223.06099 ([M-H-C <sub>6</sub> H <sub>11</sub> O <sub>5</sub> ] <sup>-</sup> ) 208.03757 ([sinapic acid-CH <sub>3</sub> ] <sup>-</sup> ) 179.07095 ([sinapic acid-CHO <sub>2</sub> ] <sup>-</sup> ) 164.04745 ([sinapic acid-CHO <sub>2</sub> -OH] <sup>-</sup> )	Shoot
26	10.27	234, 283	Propanedioic acid, [5-[[2-[(6-deoxy- $\alpha$ -L-galactopyranosyl)oxy]cyclohexyl]oxy]-Pentyl]	C <sub>20</sub> H <sub>33</sub> O <sub>10</sub> <sup>-</sup>	433.20792	433.20825	0.76	417.21347 ([M-H-OH] <sup>-</sup> ) 387.20309 ([M-H-CHO <sub>2</sub> ] <sup>-</sup> )	Shoot

Table 1. Cont.

Peak	Retention Time (min)	UVM <sub>max</sub> (λ <sub>max</sub> )	Tentative Identification	Elemental Composition [M-H] <sup>-</sup>	Theoretical Mass (m/z)	Measured Mass (m/z)	Accuracy (ppm)	MSn Ions	Plant Part
								287.15030 ([M-H-C <sub>6</sub> H <sub>11</sub> O <sub>4</sub> ] <sup>-</sup> ) 245.13950 ([M-H-C <sub>8</sub> H <sub>13</sub> O <sub>5</sub> ] <sup>-</sup> ) 131.07069 ([M-H-C <sub>14</sub> H <sub>23</sub> O <sub>6</sub> ] <sup>-</sup> )	
27	10.31	237, 283	Cyclohexanecarboxylic acid, 3-[(6-deoxy-3-O-methyl-D-galactopyranosyl)oxy]-1,4,5-trihydroxy	C <sub>14</sub> H <sub>22</sub> O <sub>10</sub> <sup>-</sup>	351.12967	351.13010	1.22	303.14487 ([M-H-3OH] <sup>-</sup> ) 287.14999 ([M-H-4OH] <sup>-</sup> ) 273.13449 ([M-H-3OH-CH <sub>3</sub> O] <sup>-</sup> )	Root
28	10.63	235, 326	Ferulic acid	C <sub>10</sub> H <sub>9</sub> O <sub>4</sub> <sup>-</sup>	193.05063	193.05032	1.61	179.03455 ([M-H-CH <sub>3</sub> ] <sup>-</sup> ) 149.06050 ([M-H-CHO <sub>2</sub> ] <sup>-</sup> ) 163.03963 ([M-H-CH <sub>3</sub> -OH] <sup>-</sup> ) 147.04456 ([M-H-CH <sub>3</sub> -2OH] <sup>-</sup> )	Root/shoot
29	10.69	235, 327	Ferulic acid derivative (fertaric acid)	C <sub>14</sub> H <sub>13</sub> O <sub>9</sub> <sup>-</sup>	325.05651	325.05664	0.40	193.05032 ([ferulic acid] <sup>-</sup> ) 179.03453 ([ferulic acid-CH <sub>3</sub> ] <sup>-</sup> ) 163.03954 ([ferulic acid-CH <sub>3</sub> -OH] <sup>-</sup> )	Root/shoot
30	10.84	237, 291	7,8,11-Trihydroxyguai-4-en-3-one 8-O-β-D-glucopyranoside	C <sub>21</sub> H <sub>33</sub> O <sub>9</sub> <sup>-</sup>	429.21250	429.21335	1.98	267.16003 ([M-H-C <sub>6</sub> H <sub>11</sub> O <sub>5</sub> ] <sup>-</sup> ) 249.14989 ([M-H-C <sub>6</sub> H <sub>11</sub> O <sub>5</sub> -OH] <sup>-</sup> )	Shoot
31	11.09	235, 286	Cinnamic acid derivative	C <sub>8</sub> H <sub>14</sub> O <sub>6</sub> <sup>-</sup>	-	206.08205	-	147.04449 ([cinnamic acid] <sup>-</sup> ) 103.05447 ([cinnamic acid-CHO <sub>2</sub> ] <sup>-</sup> )	Root/shoot
32	11.22	227, 283	2-Propenoic acid, 2-methyl-, 4-[2-(2,4-dioxo-1,5-dioxaspiro[5.5]undec-3-yl)ethenyl]-6-(2,4-dioxo-1,5-dioxaspiro[5.3]undec-3-ylidene)-4-hexenyl ester	C <sub>30</sub> H <sub>34</sub> O <sub>10</sub> <sup>-</sup>	554.21629	554.21448	3.27	193.05049 ([M-H-C <sub>20</sub> H <sub>25</sub> O <sub>6</sub> ] <sup>-</sup> )	Root
33	11.54	239, 289, 323	Ferulic acid isomer	C <sub>10</sub> H <sub>9</sub> O <sub>4</sub> <sup>-</sup>	193.05063	193.05048	0.78	179.03458 ([M-H-CH <sub>3</sub> ] <sup>-</sup> ) 149.06030 ([M-H-CHO <sub>2</sub> ] <sup>-</sup> ) 163.03954 ([M-H-CH <sub>3</sub> -OH] <sup>-</sup> )	Root/shoot
34	11.61	238, 292, 323	Ferulic acid isomer	C <sub>10</sub> H <sub>9</sub> O <sub>4</sub> <sup>-</sup>	193.05063	193.05038	1.29	179.03441 ([M-H-CH <sub>3</sub> ] <sup>-</sup> ) 149.06026 ([M-H-CHO <sub>2</sub> ] <sup>-</sup> ) 163.03937 ([M-H-CH <sub>3</sub> -OH] <sup>-</sup> ) 147.04457 ([M-H-CH <sub>3</sub> -2OH] <sup>-</sup> )	Shoot
35	11.66	226, 282	Ferulic acid derivative I	C <sub>24</sub> H <sub>24</sub> O <sub>5</sub> <sup>-</sup>	-	392.16193	-	193.05038 ([ferulic acid] <sup>-</sup> ) 149.06030 ([ferulic acid-CHO <sub>2</sub> ] <sup>-</sup> ) 163.03954 ([ferulic acid-CH <sub>3</sub> -OH] <sup>-</sup> )	Root
36	11.71	236, 286	Ferulic acid isomer	C <sub>10</sub> H <sub>9</sub> O <sub>4</sub> <sup>-</sup>	193.05063	193.05038	1.29	179.03452 ([M-H-CH <sub>3</sub> ] <sup>-</sup> ) 149.06024 ([M-H-CHO <sub>2</sub> ] <sup>-</sup> ) 163.03937 ([M-H-CH <sub>3</sub> -OH] <sup>-</sup> ) 147.04440 ([M-H-CH <sub>3</sub> -2OH] <sup>-</sup> )	Shoot

Table 1. Cont.

Peak	Retention Time (min)	UVMax ( $\lambda_{\max}$ )	Tentative Identification	Elemental Composition [M-H] <sup>-</sup>	Theoretical Mass (m/z)	Measured Mass (m/z)	Accuracy (ppm)	MSn Ions	Plant Part
37	11.79	235, 286, 380	2-Isoferulic piscidic acid-1-methyl ester	C <sub>22</sub> H <sub>21</sub> O <sub>10</sub> <sup>-</sup>	445.11400	445.11438	0.85	255.05092 ([piscidic acid] <sup>-</sup> ) 193.050380 ([ferulic acid] <sup>-</sup> ) 165.05516 ([piscidic acid-C <sub>2</sub> H <sub>2</sub> O <sub>3</sub> -OH] <sup>-</sup> ) 135.04440 ([piscidic acid-C <sub>2</sub> H <sub>2</sub> O <sub>3</sub> -CHO <sub>2</sub> ] <sup>-</sup> ) 107.04936 ([piscidic acid-C <sub>4</sub> H <sub>4</sub> O <sub>3</sub> ] <sup>-</sup> )	Shoot
38	11.86	240, 296, 381	Ferulic acid derivative II	C <sub>20</sub> H <sub>29</sub> O <sub>10</sub> <sup>-</sup>	-	429.17707	-	193.05029 ([ferulic acid] <sup>-</sup> ) 179.03450 ([ferulic acid-CH <sub>3</sub> ] <sup>-</sup> ) 163.03937 ([ferulic acid-CH <sub>3</sub> -OH] <sup>-</sup> ) 147.04440 ([ferulic acid-CH <sub>3</sub> -2OH] <sup>-</sup> )	Root/shoot
39	12.18	283, 368	Ferulic acid derivative III	C <sub>21</sub> H <sub>31</sub> O <sub>13</sub> <sup>-</sup>	-	491.17731	-	193.05026 ([ferulic acid] <sup>-</sup> ) 179.03456 ([ferulic acid-CH <sub>3</sub> ] <sup>-</sup> ) 163.03929 ([ferulic acid-CH <sub>3</sub> -OH] <sup>-</sup> ) 147.04446 ([ferulic acid-CH <sub>3</sub> -2OH] <sup>-</sup> )	Shoot
40	12.38	283	Azelaic acid	C <sub>9</sub> H <sub>15</sub> O <sub>4</sub> <sup>-</sup>	187.09758	187.09740	0.96	169.08130 ([M-H-OH] <sup>-</sup> ) 125.09650 ([M-H-CHO <sub>2</sub> -OH] <sup>-</sup> )	Root/shoot
41	12.47	284, 368	Ferulic acid derivative IV	C <sub>20</sub> H <sub>29</sub> O <sub>10</sub> <sup>-</sup>	-	429.17706	-	193.05023 ([ferulic acid] <sup>-</sup> ) 179.03427 ([ferulic acid-CH <sub>3</sub> ] <sup>-</sup> ) 163.03958 ([ferulic acid-CH <sub>3</sub> -OH] <sup>-</sup> ) 147.04450 ([ferulic acid-CH <sub>3</sub> -2OH] <sup>-</sup> )	Shoot
42	12.70	259	2-Phenylethyl β-D-glucopyranoside	C <sub>14</sub> H <sub>19</sub> O <sub>6</sub> <sup>-</sup>	283.11871	283.11893	0.78	267.12402 ([M-H-OH] <sup>-</sup> ) 251.12881 ([M-H-2OH] <sup>-</sup> ) 235.13390 ([M-H-3OH] <sup>-</sup> ) 121.06506 ([M-H-C <sub>6</sub> H <sub>11</sub> O <sub>5</sub> ] <sup>-</sup> )	Root/shoot
43	12.75	272, 368	Dalbergioidin	C <sub>15</sub> H <sub>11</sub> O <sub>6</sub> <sup>-</sup>	287.05611	287.05618	0.24	271.06094 ([M-H-OH] <sup>-</sup> ) 179.03467 ([M-H-C <sub>6</sub> H <sub>5</sub> O <sub>2</sub> ] <sup>-</sup> ) 165.05252 ([M-H-C <sub>6</sub> H <sub>5</sub> O <sub>3</sub> ] <sup>-</sup> ) 163.03951 ([M-H-C <sub>6</sub> H <sub>5</sub> O <sub>2</sub> -OH] <sup>-</sup> ) 147.04404 ([M-H-C <sub>6</sub> H <sub>5</sub> O <sub>2</sub> -2OH] <sup>-</sup> ) 125.02380 ([M-H-C <sub>9</sub> H <sub>9</sub> O <sub>3</sub> ] <sup>-</sup> ) 109.02868 ([M-H-C <sub>9</sub> H <sub>7</sub> O <sub>4</sub> ] <sup>-</sup> )	Shoot
44	12.95	260	4,8,12-trihydroxy-2,4-dodecadienoic acid,	C <sub>12</sub> H <sub>19</sub> O <sub>5</sub> <sup>-</sup>	243.1238	243.12383	0.12	199.1337 ([M-H-CHO <sub>2</sub> ] <sup>-</sup> ) 139.11221 ([M-H-CHO <sub>2</sub> -C <sub>2</sub> H <sub>3</sub> -2OH] <sup>-</sup> )	Root
45	13.40	283	Caffeic acid isomer	C <sub>9</sub> H <sub>7</sub> O <sub>4</sub> <sup>-</sup>	179.03498	179.03481	0.95	163.03954 ([M-H-OH] <sup>-</sup> ) 135.04454 ([M-H-CHO <sub>2</sub> ] <sup>-</sup> ) 109.02881 ([M-H-C <sub>3</sub> H <sub>3</sub> O <sub>2</sub> ] <sup>-</sup> )	Root
46	13.80	222, 284	β-D-Glucopyranoside, 1,1-dimethyl-5-methylenenonyl	C <sub>10</sub> H <sub>17</sub> O <sub>4</sub> <sup>-</sup>	345.22826	345.22849	0.67	327.21780 ([M-H-OH] <sup>-</sup> ) 315.21780 ([M-H-CH <sub>3</sub> O] <sup>-</sup> )	Root

Table 1. Cont.

Peak	Retention Time (min)	UVMax ( $\lambda_{\max}$ )	Tentative Identification	Elemental Composition [M-H] <sup>-</sup>	Theoretical Mass (m/z)	Measured Mass (m/z)	Accuracy (ppm)	MSn Ions	Plant Part
47	13.90	224, 284	Sebacic acid	C <sub>10</sub> H <sub>17</sub> O <sub>4</sub> <sup>-</sup>	201.11323	201.11293	1.49	185.11778 ([M-H-OH] <sup>-</sup> ) 157.12276 ([M-H-CHO <sub>2</sub> ] <sup>-</sup> )	Shoot
48	13.93	223, 284	alpha-Ionol O-[arabinosyl-(1->6)-glucoside]	C <sub>24</sub> H <sub>39</sub> O <sub>10</sub> <sup>-</sup>	487.25487	487.25504	0.35	473.24008 ([M-H-CH <sub>3</sub> ] <sup>-</sup> ) 459.22311 ([M-H-2CH <sub>3</sub> ] <sup>-</sup> ) 355.21292 ([M-H-C <sub>5</sub> H <sub>9</sub> O <sub>4</sub> ] <sup>-</sup> ) 341.19687 ([M-H-C <sub>5</sub> H <sub>9</sub> O <sub>4</sub> -CH <sub>3</sub> ] <sup>-</sup> )	Shoot
49	15.35	283, 368,	Buteine	C <sub>15</sub> H <sub>11</sub> O <sub>5</sub> <sup>-</sup>	271.0612	271.06131	0.41	163.03952 ([M-H-C <sub>6</sub> H <sub>5</sub> O <sub>2</sub> ] <sup>-</sup> ) 137.02380 ([M-H-C <sub>8</sub> H <sub>7</sub> O <sub>2</sub> ] <sup>-</sup> ) 135.04443 ([M-H-C <sub>7</sub> H <sub>5</sub> O <sub>3</sub> ] <sup>-</sup> ) 121.02880 ([M-H-C <sub>8</sub> H <sub>7</sub> O <sub>2</sub> -OH] <sup>-</sup> ) 108.02104 ([M-H-C <sub>9</sub> H <sub>7</sub> O <sub>3</sub> ] <sup>-</sup> )	Root
50	15.98	283	D-xylofuranose tetradecyl glycoside	C <sub>22</sub> H <sub>41</sub> O <sub>9</sub> <sup>-</sup>	449.27561	449.27576	0.33	403.27036 ([M-H-CH <sub>3</sub> O-OH] <sup>-</sup> ) 316.22061 ([M-H-C <sub>5</sub> H <sub>9</sub> O <sub>4</sub> ] <sup>-</sup> ) 329.23349 ([M-H-C <sub>4</sub> H <sub>9</sub> -4OH] <sup>-</sup> ) 117.05499 ([M-H-C <sub>17</sub> H <sub>32</sub> O <sub>5</sub> -OH] <sup>-</sup> )	Root
51	16.42	283	Corchorifatty acid F isomer	C <sub>18</sub> H <sub>31</sub> O <sub>5</sub> <sup>-</sup>	327.21770	327.21799	0.89	309.20665 ([M-H-OH] <sup>-</sup> ) 291.19684 ([M-H-2OH] <sup>-</sup> ) 173.11787 ([M-H-C <sub>9</sub> H <sub>15</sub> O <sub>2</sub> ] <sup>-</sup> ) 157.12346 ([M-H-C <sub>9</sub> H <sub>15</sub> O <sub>2</sub> -OH] <sup>-</sup> ) 125.09643 ([M-H-C <sub>3</sub> H <sub>5</sub> O <sub>2</sub> -C <sub>7</sub> H <sub>13</sub> O <sub>2</sub> ] <sup>-</sup> )	Root/shoot
52	18.30	283, 368	Tianshic acid	C <sub>18</sub> H <sub>33</sub> O <sub>5</sub> <sup>-</sup>	329.23335	329.23361	0.79	165.12788 ([M-H-C <sub>7</sub> H <sub>15</sub> O-3OH] <sup>-</sup> ) 127.11205 ([M-H-C <sub>10</sub> H <sub>19</sub> O <sub>2</sub> -2OH] <sup>-</sup> )	Root/shoot
53	19.15	283	Dimethyl sebacate (sebacic acid derivative)	C <sub>12</sub> H <sub>21</sub> O <sub>4</sub> <sup>-</sup>	229.14453	229.144	0.39	201.11287 ([sebacic acid] <sup>-</sup> ) 215.12865 ([M-H-CH <sub>3</sub> ] <sup>-</sup> ) 211.13374 ([M-H-O] <sup>-</sup> ) 199.13379 ([M-H-CH <sub>3</sub> O] <sup>-</sup> ) 185.11778 ([M-H-CH <sub>3</sub> O-CH <sub>3</sub> ] <sup>-</sup> ) 157.12303 ([M-H-C <sub>2</sub> H <sub>3</sub> O <sub>2</sub> -CH <sub>3</sub> ] <sup>-</sup> )	Shoot
54	19.28	282, 368	Unknown	C <sub>13</sub> H <sub>27</sub> O <sub>8</sub> <sup>-</sup>	-	311.16888	-	-	Root
55	19.47	283, 368	Corchorifatty acid F isomer	C <sub>18</sub> H <sub>31</sub> O <sub>5</sub> <sup>-</sup>	327.21770	327.21802	0.98	309.20731 ([M-H-OH] <sup>-</sup> ) 291.19672 ([M-H-2OH] <sup>-</sup> ) 173.11792 ([M-H-C <sub>9</sub> H <sub>15</sub> O <sub>2</sub> ] <sup>-</sup> ) 125.09679 ([M-H-C <sub>3</sub> H <sub>5</sub> O <sub>2</sub> -C <sub>7</sub> H <sub>13</sub> O <sub>2</sub> ] <sup>-</sup> )	Root/shoot
56	20.06	283	Unknown	C <sub>13</sub> H <sub>27</sub> O <sub>8</sub> <sup>-</sup>	-	311.16888	-	-	Shoot

Table 1. Cont.

Peak	Retention Time (min)	UVMax ( $\lambda_{\max}$ )	Tentative Identification	Elemental Composition [M-H] <sup>-</sup>	Theoretical Mass (m/z)	Measured Mass (m/z)	Accuracy (ppm)	MSn Ions	Plant Part
57	20.63	283	Nordihydrocapsiate	C <sub>17</sub> H <sub>25</sub> O <sub>4</sub> <sup>-</sup>	293.17583	293.17612	0.99	277.18088 ([M-H-OH] <sup>-</sup> ) 263.16534 ([M-H-CH <sub>3</sub> O] <sup>-</sup> ) 247.16968 ([M-H-CH <sub>3</sub> O-OH] <sup>-</sup> ) 157.12309 ([M-H-C <sub>8</sub> H <sub>9</sub> O <sub>2</sub> ] <sup>-</sup> ) 153.05524 ([M-H-C <sub>9</sub> H <sub>17</sub> O] <sup>-</sup> ) 141.12810 ([M-H-C <sub>8</sub> H <sub>9</sub> O <sub>3</sub> ] <sup>-</sup> )	Root/shoot
58	20.92	274	Plastoquinone 3	C <sub>23</sub> H <sub>31</sub> O <sub>2</sub> <sup>-</sup>	339.23296	339.23322	0.77	203.10753 ([M-H-C <sub>9</sub> H <sub>15</sub> ] <sup>-</sup> ) 163.11229 ([M-H-C <sub>6</sub> H <sub>11</sub> -C <sub>5</sub> H <sub>7</sub> O] <sup>-</sup> ) 149.06009 ([M-H-C <sub>13</sub> H <sub>21</sub> ] <sup>-</sup> ) 135.04454 ([M-H-C <sub>14</sub> H <sub>23</sub> ] <sup>-</sup> )	Root
59	21.25	283	Decyl gallate (gallic acid derivative)	C <sub>17</sub> H <sub>25</sub> O <sub>5</sub> <sup>-</sup>	309.17075	309.17093	0.58	293.17935 ([M-H-OH] <sup>-</sup> ) 169.01381 ([gallic acid] <sup>-</sup> ) 153.01903 ([M-H-C <sub>10</sub> H <sub>21</sub> O] <sup>-</sup> ) 125.02367 ([M-H-C <sub>11</sub> H <sub>21</sub> O <sub>2</sub> ] <sup>-</sup> )	Root/shoot
60	21.61	283	Nordihydrocapsiate isomer	C <sub>17</sub> H <sub>25</sub> O <sub>4</sub> <sup>-</sup>	293.17583	293.17612	0.99	277.18080 ([M-H-OH] <sup>-</sup> ) 263.16535 ([M-H-CH <sub>3</sub> O] <sup>-</sup> ) 247.16990 ([M-H-CH <sub>3</sub> O-OH] <sup>-</sup> ) 157.12309 ([M-H-C <sub>8</sub> H <sub>9</sub> O <sub>2</sub> ] <sup>-</sup> ) 153.05524 ([M-H-C <sub>9</sub> H <sub>17</sub> O] <sup>-</sup> ) 141.12810 ([M-H-C <sub>8</sub> H <sub>9</sub> O <sub>3</sub> ] <sup>-</sup> )	Root/shoot
61	22.30	283	Unknown	C <sub>13</sub> H <sub>27</sub> O <sub>8</sub> <sup>-</sup>	-	311.16904	-	-	Root
62	22.53	283	Unknown	C <sub>24</sub> H <sub>45</sub> O <sub>11</sub> <sup>-</sup>	-	509.29691	-	-	Shoot
63	23.36	283, 337	13-Hydroxyoctadecadienoic acid	C <sub>18</sub> H <sub>31</sub> O <sub>3</sub> <sup>-</sup>	295.22787	295.22797	0.34	281.21204 ([M-H-CH <sub>3</sub> ] <sup>-</sup> ) 279.23334 ([M-H-OH] <sup>-</sup> ) 169.12331 ([M-H-C <sub>8</sub> H <sub>15</sub> O] <sup>-</sup> ) 153.12767 ([M-H-C <sub>8</sub> H <sub>15</sub> O-OH] <sup>-</sup> )	Root/shoot
64	23.54	283, 337	p-Hydroxynonanophenone	C <sub>15</sub> H <sub>21</sub> O <sub>2</sub> <sup>-</sup>	233.1547	233.15462	0.34	219.17544 ([M-H-O] <sup>-</sup> ) 167.14342 ([M-H-C <sub>4</sub> H <sub>5</sub> O] <sup>-</sup> ) 135.04446 ([M-H-C <sub>7</sub> H <sub>15</sub> ] <sup>-</sup> ) 121.02875 ([M-H-C <sub>7</sub> H <sub>15</sub> -CH <sub>3</sub> ] <sup>-</sup> )	Root/shoot
65	24.03	283	Unknown	C <sub>15</sub> H <sub>31</sub> O <sub>8</sub> <sup>-</sup>	-	339.20029	-	-	Root
66	25.20	283	Unknown	C <sub>14</sub> H <sub>29</sub> O <sub>8</sub> <sup>-</sup>	-	325.18463	-	-	Root
67	25.72	283, 337	Unknown	C <sub>14</sub> H <sub>29</sub> O <sub>8</sub> <sup>-</sup>	-	325.18457	-	-	Shoot
68	25.98	283, 337	Unknown	C <sub>14</sub> H <sub>29</sub> O <sub>8</sub> <sup>-</sup>	-	325.18454	-	-	Shoot
69	26.24	283	Unknown	C <sub>14</sub> H <sub>29</sub> O <sub>8</sub> <sup>-</sup>	-	325.18463	-	-	Root

Compounds 1–5 were detected in both parts of *C. macromeris*. Compound 1 was assigned as vaccihehin A (Figure 2a). This antioxidant metabolite was isolated for the first time in *Vaccinium ashei* (Ericaceae) by Ono, et al. [35] and this is the first time that is reported for cacti species. Compounds 2–5 were assigned as carboxylic acids: compounds 2 and 3 were proposed as dihydroxy methoxy butanoic acid and malic acid [36], respectively, and compounds 4 and 5 as isocitric acid isomers [13]. Citric acid occurs as one of the main hydrophilic constituents in *Opuntia* species (Cactaceae) [13,37], and its presence may be also related to the crassulacean acid metabolism of cacti species [12].

Among the detected compounds, 31 metabolites were phenolic acids (compounds 6–13, 15–25, 31, 32, 34, 36–42, 44, 48 and 62) and 16 of them occurred in the aerial part (see Table 1). In our investigation, compound 6 was assigned as 3,5-dihydroxy-4-methyloxolan-2-yl methoxy-6-hydroxymethyl oxane-3,4,5-triol, due to the presence of fragments ions at  $m/z$ : 293.12424, 279.10870, 147.06578, and 131.07106 (see Table 1); Vankudothu and Anwar [38] proposed, through molecular docking, that this metabolite showed high affinity for the ACC2 protein, suggesting an effect against type 2 diabetes. Thus, the elicitation and isolation of this compound may be a potential use for *C. macromeris*. Also, two protocatechuic acid derivatives (compounds 9 and 16) were detected: compound 9 was proposed as protocatechuic acid hexoside (see Figure 2b) and compound 16 as protocatechuic aldehyde since pseudomolecular ion at  $m/z$ : 137.02386 yielded fragments at  $m/z$ : 121.02882 and 109.02884 (see Table 1). It has been proposed that protocatechuic aldehyde influences the pharmacokinetic activity of medicinal herbal extracts prepared with *Salvia miltiorrhiza* (Lamiaceae) [39], suggesting that the presence of this compound in *C. macromeris* extract may enhance its functional properties. Protocatechuic acid has been found as an aglycone in other cacti species such as *Opuntia ficus-indica* [40] and *Myrtillocactus geometrizans* [17], and as one of the main constituents in *Opuntia humifusa* [18].

Additionally, compound 13 was only detected in the aerial part and was assigned as lucuminic acid, since the pseudomolecular ion yielded fragments at  $m/z$ : 163.03947, 119.04939 and 107.04942 (see Table 1). Lucuminic acid has been reported for *Calocarpum sapota* (Sapotaceae) by Takeda, et al. [41] and this is the first time that is reported for cacti species. In our investigation, sinapic acid (compound 20) and two of its derivatives (compounds 19 and 25) were also detected and characterized as reported previously [42]. Sinapic acid is synthesized from ferulic acid through enzymatic mechanisms [43] and it has been proposed to have anti-inflammatory activities [44].

In the same way, other phenolic metabolites such as two syringic acid derivatives (compounds 21 and 23), two caffeic acid isomers [45] (compounds 24 and 45), and cinnamic and gallic acid derivatives (compound 31 and 59, respectively) were also found (see Table 1). In addition, piscidic and ferulic acid and/or their derivatives were detected as the most recurrent phenolic acids in *C. macromeris* extracts: six isomers of piscidic acid (compounds 7, 8, 10, 11, 12, and 15) and four if its derivatives (compounds 17, 18, 22, and 37) were detected and assigned as reported previously [46,47]. Piscidic acid has been previously identified in juices prepared with *Opuntia ficus-indica* fruits [13] and according to the number of peaks detected and the relative abundance shown in the chromatogram, piscidic acid may be one of the main constituents of the *C. macromeris* aerial part (see Figure 1a, Table 1); further studies are required to confirm the structure of this metabolite and its total concentration in each part of the plant. On the other hand, compounds 28, 33, 34, and 36 were assigned as ferulic acid isomers [48], and compounds 29, 35, 38, 39, and 41 as ferulic acid derivatives, since they showed characteristic fragment ions of ferulic acid (see Table 1). Our results indicate that ferulic acid is present in both parts of the plant but with a higher relative abundance in the shoots (Figure 1a). Ferulic acid has been detected in different cacti species [18,37,49,50] and its antiproliferative effect in human colon carcinoma HT29 cell line [51] as well its therapeutic potential against cardiovascular and neurodegenerative disorders [52] has been proposed. Our results suggest that *C. macromeris* could represent a potential source for the isolation of this compound or its derivatives; further studies are required to isolate and characterize the structure of these compounds (isomers) and to know their concentration, elicitation, and production in biotechnological systems.

In addition to compounds 2–5, compounds 26, 27, 32, 40, 44, 47, 51–53, 55, and 63 were also assigned as carboxylic acids. The fragmentation pattern of these metabolites was mainly characterized by the loss of water (see Table 1). Among these metabolites, compounds 51 and 55 were detected in both parts of the plant and assigned as corchorifatty acid F isomers. This metabolite has been previously identified in leaves of *Corchorus olitorius* (Tiliaceae) by Yoshikawa, et al. [53] and in aerial parts of *Chaenomeles sinensis* (Rosaceae) [54]. It also confers activity against pathogenic fungus *Pyricularia oryzae* in resistant rice cultivars [55]. To our knowledge, this is the first time that is reported for cacti species. On the other hand, compound 40 was identified as azelaic acid, according to Liu, et al. [56]. This dicarboxylic acid has been used for the treatment of acne and skin disorders [57,58] and skin hyperpigmentation [59]. Compound 52 was assigned as tianshic acid due to the presence of fragments at  $m/z$ : 165.12788 and 127.11205 (see Table 1). The occurrence of this metabolite has been previously reported for *Sambucus williamsii* (Adoxaceae) by Yang, et al. [60] and no information exists for cacti species.

In the same way, other polar compounds were characterized in *C. macromeris* methanolic extracts. Compound 14 was assigned as hyrtioerectine C (alkaloid). Youssef [61] isolated this alkaloid and proposed its cytotoxic activity against HeLa cells. In our research group, studies are being carried out to elucidate the presence of other alkaloids in, and the potential applications of, *C. macromeris* extracts. Signals revealed for compound 30 indicated the presence of a glucopyranoside derivative [62] in the aerial part of *C. macromeris*. Similarly, compound 42 was tentatively identified as 2-phenylethyl  $\beta$ -D-glucopyranoside. This phenolic glycoside has been previously reported in *Pachysandra terminalis* (Buxaceae) [63] and in *Lactuca indica* (Asteraceae) [64]. To our knowledge, this is the first time that it is reported for cacti species. Compound 43 was tentatively identified as dalbergioidin (see Figure 2d); this antifungal isoflavone was reported in *Vigna angularis* (Fabaceae) as one of the mechanisms against *Phytophthora vignae* zoospores germination [65], suggesting that its presence in the *C. macromeris* aerial part may correspond to a constitutive adaptation mechanism since no pathogenic conditions were given to the plants; further studies are required to assess this hypothesis. Compounds 46, 48, and 50 were also assigned as metabolites of glycosidic nature (see Table 1). On the other hand, the pseudomolecular ion and fragmentation pattern of compound 49 indicated the presence of buteine (chalcone; see Figure 2e) in the radicular part of *C. macromeris*. Buteine exists in *Rhus verniciflua* (Anacardiaceae), a traditional herb used for cancer treatment [66], and its antioxidant activity [67] and potential as a chemotherapeutic agent [68] has been proposed. Compounds 57 and 60 were tentatively identified as nordihydrocapsiate isomers (see Figure 2f) and compound 58 as plastoquinone 3.

Finally, compounds 54, 56, 61, 62, and 65–69 were not identified since molecular information obtained did not match with theoretical information existing in the literature. Absorption spectrum of these compounds suggest that they may contain benzoic acid within its structure (UV  $\lambda_{\max}$ : 280 nm). Further studies are required for structural elucidation of these metabolites.

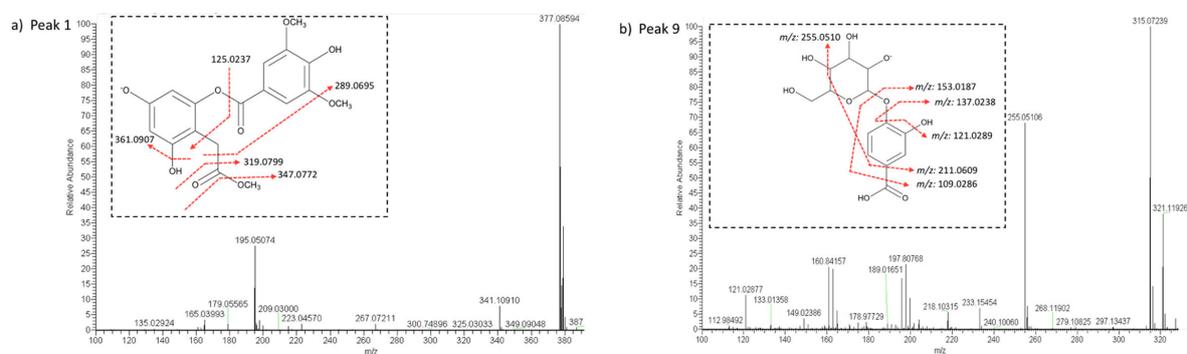
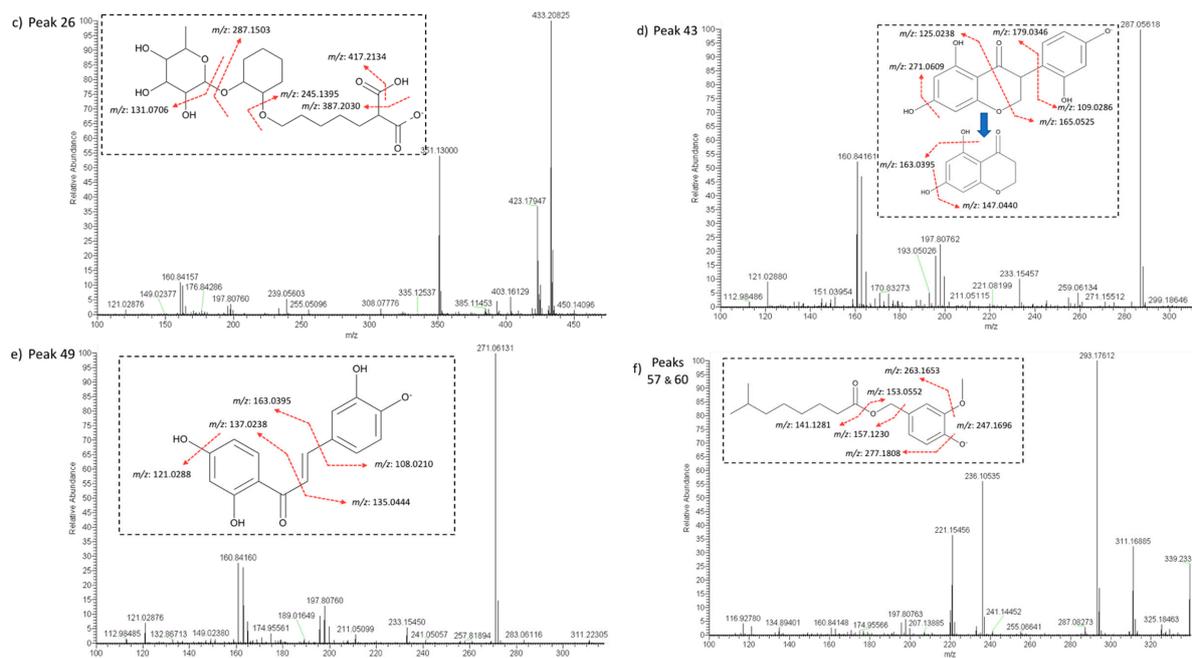


Figure 2. Cont.



**Figure 2.** Full scan of some metabolites identified for the first time in *C. macromeris*. Dotted inset represents the molecule and red dotted lines in each inset represent the proposed fragmentation pattern. Peak numbers in each figure, refer to the compounds indicated in Table 1.

### 3. Materials and Methods

#### 3.1. Plant Material

The plants of *Coryphantha macromeris* were obtained from the *in vitro* germplasm bank of the Autonomous University of Aguascalientes, México. *Coryphantha macromeris* was maintained on semisolid Murashige and Skoog medium [69] (3% sucrose, 8 g·L<sup>-1</sup> agar, and pH 5.7) and incubated at 25 °C with fluorescent light (40 μmol·m<sup>-2</sup>·s<sup>-1</sup>) and 16/8 (light/dark) photoperiod. Each plant was subcultured for three months during one year with the described conditions, and then *in vitro* plants were acclimated to greenhouse conditions as reported previously [26] and kept for one year until harvesting for phytochemical analysis. The plant material was botanically identified by Professor Miguel Alvarado Rodríguez. A voucher specimen was deposited at the herbarium of the Autonomous University of Aguascalientes (HUAA; Voucher No. 6386).

#### 3.2. Sample Preparation

For analysis, one-year-old plants growing under greenhouse conditions were collected and separated into aerial and radicular parts. Each part of the plant was sliced and dried in an oven (40 °C) during 1 week in dark conditions. Dried material was finally pulverized in a mortar and then extracted three times with methanol in an ultrasonic bath (30 min each time). The resultant extract was filtered and evaporated under reduced pressure at 40 °C and freeze-dried (Labconco Freeze Dryer; Labconco Corporation, Kansas City, MO, USA). Each freeze-dried sample was resuspended (2.5 mg·mL<sup>-1</sup>) in HPLC-MS-grade methanol and sonicated over 10 min. All samples were filtered (0.22 μm) and injected in an UHPLC system hyphenated with a mass spectrometer, as given below.

#### 3.3. UHPLC-PDA-HESI-Orbitrap-MS/MS Conditions

Phytochemical analysis was performed as reported previously [32–34], using a Dionex Ultimate 3000 UHPLC system (Thermo Fisher Scientific, Bremen, Germany) with a C18 column (ID: 150 × 4.6 mm, 5 μm; Restek Corporation, Bellefonte, PA, USA) and equipped with a Quaternary Series RS pump and a Dionex Ultimate 3000 Series TCC-3000RS column compartments with an

Ultimate 3000 Series WPS-3000RS autosampler (Thermo Fisher Scientific) and a rapid separations PDA detector. The detection wavelengths were 254, 280, 320, and 440 nm, and PDA was recorded from 200 to 800 nm for peak characterization. The separation was performed in a gradient elution mode composed by 1% formic aqueous solution (A) and acetonitrile (B). The flow rate was  $1.0 \text{ mL}\cdot\text{min}^{-1}$  and the injection volume  $10 \mu\text{L}$ . The gradient program [time (min), %B] was: (0.00, 5), (5.00, 5), (10.00, 30), (15.00, 30), (20.00, 70), (25.00, 70), (35.00, 5), and 12 min for column equilibration before each injection. The system was controlled by Chromeleon 7.2 Software (Thermo Fisher Scientific, Waltham, MA, USA and Dionex Softron GmbH division of Thermo Fisher Scientific) and hyphenated with a Thermo high resolution Q Exactive focus mass spectrometer (Thermo Fisher Scientific). The chromatographic system was coupled to the mass spectrometer with a heated electrospray ionization source II (HESI II). Nitrogen (purity > 99.999%) was employed as both the collision and damping gas. Nitrogen was obtained from a Genius NM32LA nitrogen generator (Peak Scientific, Billerica, MA, USA). Mass calibration for Orbitrap was performed once a week, in both negative and positive modes. Caffeine and *N*-butylamine (Sigma-Aldrich, Saint Louis, MO, USA) were the calibration standards for positive ions and buspirone hydrochloride, sodium dodecyl sulfate, and taurocholic acid sodium salt were used to calibrate the mass spectrometer. These compounds were dissolved in a mixture of acetic acid, acetonitrile, water, and methanol (Merck Darmstadt, Hesse, Germany) and infused using a Chemyx Fusion 100 syringe pump. XCalibur 2.3 software and Trace Finder 3.2 (Thermo Fisher Scientific, San Jose, CA, USA) were used for UHPLC control and data processing, respectively. Q Exactive 2.0 SP 2 (Thermo Fisher Scientific, Waltham, MA, USA) was used to control the mass spectrometer.

#### MS Parameters

The HESI parameters were optimized as follows: sheath gas flow rate 75 units; auxiliary gas flow rate 20 units; capillary temperature  $400 \text{ }^\circ\text{C}$ ; auxiliary gas heater temperature  $500 \text{ }^\circ\text{C}$ ; spray voltage 2500 V (for ESI-); and S lens RF level 30. Full scan data in negative mode was acquired at a resolving power of 70,000 full width half maximum (FWHM) at  $m/z$  200. For the compounds of interest, a scan range of  $m/z$  100–1000 was chosen; the automatic gain control (AGC) was set at  $3 \times 10^6$  and the injection time was set to 200 ms. Scan rate was set at  $2 \text{ scans s}^{-1}$ . External calibration was performed using a calibration solution in positive and negative modes before each sample series. In addition to the full scan acquisition method, for confirmation purposes, a targeted MS/MS analysis was performed using the mass inclusion list and expected retention times of the target analytes, with a 30 s time window, with the Orbitrap spectrometer operating both in positive and negative mode at 17,500 FWHM ( $m/z$  200). The AGC target was set to  $2 \times 10^5$ , with the maximum injection time of 20 ms. The precursor ions were filtered by the quadrupole operating at an isolation window of  $m/z$  2. The fore vacuum, high vacuum, and ultra-high vacuum were maintained at approximately 2 mbar, from 105 to below 1010 mbar, respectively. Collision energy (HCD cell) was operated at 30 eV. Detection was based on calculated exact mass and on retention time of target compounds presented in Table 1. The mass tolerance window was set to 5 ppm.

#### 4. Conclusions

The utilized procedures allowed the separation of 69 metabolites present in methanolic extracts of aerial and radicular parts of *C. macromeris*, and the identification of most of them. The aerial part showed higher diversity of metabolites compared with roots, and 24 metabolites occurred in both plant parts. Among detected compounds, ferulic and piscidic acid and their derivatives were the most recurrent phenolic metabolites in *C. macromeris*. In addition, different classes of compounds with reported functional properties were detected. To our knowledge, the phytochemical profile of aerial and root parts of *C. macromeris* is reported here for the first time by means of modern ultra-high-performance liquid chromatography–tandem mass spectrometry. Based on the detected compounds, *C. macromeris* may find potential applications in the pharmaceutical and cosmetic industries. The obtained information could be also useful as chemotaxonomic markers for *Coryphantha* species.

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