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Dracocephalum palmatum S. and Dracocephalum ruyschiana L. Originating from Yakutia: A High-Resolution Mass Spectrometric Approach for the Comprehensive Characterization of Phenolic Compounds

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Abstract: Dracocephalum palmatum S. and Dracocephalum ruyschiana L. contain a large number of target analytes, which are biologically active compounds. High performance liquid chromatography (HPLC) in combination with an ion trap (tandem mass spectrometry) was used to identify target analytes in extracts of D. palmatum S. and D. ruyschiana L. originating from Yakutia. The results of initial studies revealed the presence of 114 compounds, of which 92 were identified for the first time in the genus Dracocephalum. New identified metabolites belonged to 17 classes, including 16 phenolic acids and their conjugates, 18 flavones, 5 flavonols, 2 flavan-3-ols, 1 flavanone, 2 stilbenes, 10 anthocyanins, 1 condensed tannin, 2 lignans, 6 carotenoids, 3 oxylipins, 2 amino acids, 3 sceletum alkaloïds, 3 carboxylic acids, 8 fatty acids, 1 sterol, and 3 terpenes, along with 6 miscellaneous compounds. It was shown that extracts of D. palmatum are richer in the spectrum of polyphenolic compounds compared with extracts of D. ruyschiana, according to a study of the presence of these compounds in extracts, based on the results of mass spectrometric studies.

Keywords: Dracocephalum palmatum; Dracocephalum ruyschiana; ion trap; tandem mass spectrometry; polyphenolic compounds

1. Introduction

The genus Dracocephalum L. (family Lamiaceae) is represented on the territory of the Republic of Sakha (Yakutia) by five species—Dracocephalum jacutense Peschkova, D. nutans L., D. palmatum Stephan, D. ruyschiana L., and D. stellerianum Hilteb [1]. These are
perennial herbaceous plants, differing in both origin and habitat and belonging to the divisions of vegetation cover. The ranges of *Dracocephalum* are unequal, from extremely small (endemic *D. jacutense* Peschkova) to extensive Eurasian (*D. nutans* L., *D. ruyschiana* L.). The two species of *D. palmatuum* Stephan and *D. stellerianum* Hildebr are widespread in the Asian territory [2]. *Dracocephalum palmatuum* Steph. ex Willd. is found in the northeastern regions of Yakutia. It grows on dry stony, gravelly slopes, rocks, stony tundra, and mountain steppes. It is a perennial evergreen plant with creeping shoots and a very dense turf, which forms beneath [3]. *Dracocephalum palmatuum* forms continuous “carpet” populations on dry stony mountain slopes under the conditions of the Pole of Cold Oymyakon (N 63°13′32.0" E 142°53′56.2") (Figure 1).

![Figure 1](image)

**Figure 1.** *Dracocephalum palmatuum* S. in the Oymyakon area of Yakutia (photo taken by Okhlopkova, July 2019).

A total of 23 compounds (phenylpropanoids, coumarins, flavonoids, and triterpenes) were isolated from a crude alcoholic extract of the aerial parts of *Dracocephalum palmatuum* in studies by Olennikov et al. (2013) [4]. A research by Kim et al. (2020) aimed to evaluate the tumor suppressive effect of *D. palmatuum* extract in diffuse large B cell lymphoma (DLBCL) and its underlying mechanism. The effect of *D. palmatuum* extracts on several DLBCL cell lines significantly reduced cell viability and increased apoptosis and, at the same time, did not affect the survival of normal cells in vitro and in vivo. These studies indicate that the cytotoxic effect may be specific to cancer cells [5]. Lee et al. (2020) studied the anticancer potential of dried leaves of *D. palmatuum* Stephan using human prostate cancer PC-3 cells. The results showed that the use of *D. palmatuum* extract induces apoptosis and has intracellular ROS (reactive oxygen species)—independent antitumor effects on prostate cancer cells associated with increased expression of superoxide dismutase (SOD2) [6].

The habitat of *Dracocephalum ruyschiana* L. extends far to the north; its growth was noted in the Lena and Vilyui river basins, in grass, larch, birch, and mixed forests and meadow steppes. This species has erect stems 20–55 cm high, sparsely shortly pubescent at the nodes and in the upper part, with shortened vegetative shoots in the leaf axils. *Dracocephalum ruyschiana* forms continuous “carpet” populations in the Amga River valley in the conditions of Central Yakutia (N 60°31′09.0" E 131°26′26.7") (Figure 2). Kakasy et al. (2006) identified the composition of *D. ruyschiana* L. extracts using HPLC and GC–MS
with particular emphasis on their flavonoids, aliphatic, aromatic carboxylic acids, and sugars. GC–MS analysis identified and quantified as the main components monosaccharides, sugar alcohols, disaccharides, and trisaccharides, 33 components in total [7].

A review by Zeng et al. (2010) is devoted to the study of the chemical compositions of plants of the genus *Dracocephalum* L. Since the 1970s, 246 compounds, including terpenoids, steroids, flavonoids, alkaloids, lignans, phenols, and coumarins, have been identified from the genus *Dracocephalum*. As can be seen, terpenoids are the dominant constituents within the genus *Dracocephalum* [8].

![Figure 2. *Dracocephalum ruyschiana* L. in the Amga area of Yakutia (photo taken by Okhlopkova, July 2019).](image)

Five new flavone tetracygosides, 5 new benzyl alcohol glycosides, and 19 known compounds were isolated from the extract of the aerial parts of *D. ruyschiana*. *D. ruyschiana* L. (*Lamiaceae*) is a traditional medicinal plant in Mongolia [9].

In this work, we used an HPLC–MS/MS–ion trap to carry out a phytochemical study involving a detailed metabolomic and comparative analysis of *D. palmatum* and *D. ruyschiana* extracts. Aboveground, phytomass of *D. palmatum* was collected during expedition work on the territory of the Pole of Cold Oymyakon during the period of seed ripening (from 15 to 25 July 2019). Phytomass of *D. ruyschiana* was collected on the territory of the river Amga, Yakutia, in June 2019.

2. Results

Extracts of *D. palmatum* S. and *D. ruyschiana* L. were analyzed by an HPLC–MS/MS ion trap to better interpret the diversity of available phytochemicals. All of them have a rich bioactive composition. The structural identification of each compound was carried out on the basis of their accurate mass and MS/MS fragmentation by HPLC–ESI–ion trap–MS/MS. A total of 114 compounds were successfully characterized in extracts of *D. palmatum* and *D. ruyschiana* based on their accurate MS and fragment ions by searching online databases and the reported literature.
All the identified compounds along with molecular formulas, MS/MS data, and their comparative profile for two varieties of *Dracocephalum* are summarized in Table A1 (Appendix A). These are flavones: apigenin 8-C-pentoside-6-C-hexoside, nevadensin, apigenin 7-O-glucuronide, chrysin 6-C-glucoside chrysin glucuronide, and acacetin 7-O-glucoside; flavanols: dihydrokaempferol, dihydroquercetin, astragalin, kaempferol 3-O-rutinoside, and amelopsin; flavan-3-ols: catechin, gallocatechin, and flavanone fustin; phenolic acids: methylgallic acid, hydroxy methoxy dimethylbenzoic acid, ellagic acid, caffeoylshikimic acid, proline hydroxy acid, salvinolic acid G, and 3,4-O-dicaffeoylquinic acid; stilbenes: pinosylvin and resveratrol; anthocyanins: pelargonidin-3-O-glucoside, peonidin O-pentoside, cyanidin 3-(6″-malonylglucoside), and cyanidin 3-(acetyl)hexose; lignans: hinokinin and dimethyl-secoisolariciresinol; carotenoids: β-apo-12'carotenal, apo-carotenal, 5,8-epoxy-α-carotene, cryptoxanthin, and violaxanthin; and so forth.

3. Discussion

A total of 114 compounds were identified in extracts of *D. palmatum* and *D. ruyschiana*, and 92 compounds were identified for the first time in the genus *Dracocephalum*. New identified metabolites belonged to 17 classes, including 16 phenolic acids and their conjugates, 18 flavones, 5 flavonols, 2 flavan-3-ols, 1 flavanone, 2 stilbenes, 10 anthocyanins, 1 condensed tannin, 2 lignans, 6 carotenoids, 3 oxylipins, 2 amino acids, 3 scelletum alkaloids, 3 carboxylic acids, 8 fatty acids, 1 sterol, and 3 terpenes, along with 6 miscellaneous compounds. Metabolomic screening of polyphenols by *D. palmatum* and *D. ruyschiana* included flavones, flavonols, flavan-3-ols, flavanones, anthocyanins, condensed tannins, lignans, stilbenes, and phenolic acids.

3.1. Flavones

3.1.1. Trihydroxyflavones

The flavones apigenin (compound 2) and diosmetin (compound 7) have already been characterized as a component of Andean blueberry [10], *Lonicera japonicum* [11], Mexican lupine species [12], *Cirsium japonicum* [13], *Mentha* [14], and *Dracocephalum moldavica* [15].

The flavone apigenin was found in extracts of *D. palmatum* and *D. ruyschiana*. The flavone diosmetin was found in extracts of *D. palmatum*. The CID spectrum in positive ion modes of diosmetin from extracts of *D. palmatum* is shown in Figure 3.

![Figure 3](image_url)

**Figure 3.** CID spectrum of diosmetin from extracts of *D. palmatum*, m/z 301.

The [M + H]^+ ion produced one fragment ion at m/z 286 (Figure 3). The fragment ion with m/z 286 yields a daughter ion at m/z 258. It was identified in the bibliography in extracts of Andean blueberry [10], *Lonicera japonicum* [11], Mexican lupine species [12], *Cirsium japonicum* [13], *Mentha* [14], and *Dracocephalum moldavica* [15].
3.1.2. Tetrahydroxyflavones

The flavone luteolin (compound 5) has already been characterized as a component of *Eucalyptus* [16], and *Triticum aestivum* [17]. The flavone luteolin was found in extracts of *D. palmatum* and *D. ruyschiana*. The CID spectrum in positive ion modes of luteolin from extracts of *D. palmatum* is shown in Figure 4.

![Figure 4. CID spectrum of luteolin from extracts of *D. palmatum*, m/z 286.98](image)

The [M + H]+ ion produced two fragment ions at m/z 152 and m/z 237 (Figure 4). It was identified in the bibliography in extracts of *Eucalyptus* [16], and *Triticum aestivum* [17].

3.1.3. Dimethoxyflavones

The flavones negletein (compound 3) and acacetin (compound 4) have already been characterized as a component of *Wissadula periplocifolia* [18], and *Actinocarya tibetica* [19]. Flavone acacetin was found in extracts of *D. palmatum* and *D. ruyschiana*. The CID spectrum in positive ion modes of negletein from extracts of *D. palmatum* is shown in Figure 5.

![Figure 5. CID spectrum of negletein from extracts of *D. palmatum*, m/z 285.03](image)

The [M + H]+ ion produced one fragment ion at m/z 270 (Figure 5). The fragment ion with m/z 270 yields a daughter ion at m/z 241. The fragment ion with m/z 241 yields daughter ions at m/z 187. It was identified in the bibliography in extracts of *Wissadula periplocifolia* [18], and *Actinocarya tibetica* [19].

3.1.4. Trimethoxyflavone

The flavones salvigenin (compound 8) and nevadensin (compound 9) have already been characterized as components of *Ocimum* [20]. The trimethoxyflavones salvigenin and nevadensin were found in an extract of *D. palmatum*. 
3.1.5. Isoflavones

The isoflavones apigenin 7-O-β-D-(6″-O-malonyl)-glucoside (compound 23) and 2′-hydroxygenistein O-glucoside malonylated (compound 25) have already been characterized as a component of, Mexican lupine species [12], and Zostera marina [21]. Both isoflavones were found in extracts of *D. palmatum*.

3.1.6. Flavone Glucoside

The flavones apigenin 5-O-glucoside (compound 13), apigenin 7-O-glucoside (compound 14), acacetin 7-O-glucoside (compound 16), acacetin 8-O-glucoside (compound 17), luteolin 7-O-glucoside (compound 18), and diosmetin 7-O-β-glucoside (compound 21) have already been characterized as a component of rice [22], *Oxalis corniculata* [23], *Mentha" ruyschiana*. The flavones apigenin 7-O-glucoside (compound 14) and acacetin 7-O-glucoside (compound 16) were found in an extract of *D. palmatum* and *D. ruyschiana*.

The flavones apigenin 5-O-glucoside (compound 13), acacetin 8-C-glucoside (compound 17), and luteolin 7-O-glucoside (compound 18) were found in an extract of *D. palmatum*. The CID spectrum in positive ion modes of acacetin 7-O-glucoside from *D. palmatum* is shown in Figure 6.

![Figure 6. CID spectrum of acacetin 7-O-glucoside from *D. palmatum*, m/z 446.98.](image-url)

The [M + H]⁺ ion produced three fragment ions at m/z 285, m/z 430, and m/z 149 (Figure 6). The fragment ion with m/z 285 yields a daughter ion at m/z 269. The fragment ion with m/z 269 yields daughter ions at m/z 242. It was identified in the bibliography in extracts from *Bougainvillea* [27].

3.1.7. Flavone Glucuronide

The flavone chrysin glucuronide (compound 12) has already been characterized as a component of *F. pottsii* [28]. The flavone apigenin 7-O-glucuronide (compound 15) has already been characterized as a component of peppermint [29] and *Newbouldia laevis* [30]. The flavone luteolin 7-O-β-D-glucuronide (compound 20) has already been characterized as a component of *Mentha* [31], rat plasma [32], and *Thymus vulgaris* [33]. All flavone glucuronides were found in an extract of *D. ruyschiana*.

3.2. Flavonols

3.2.1. Trihydroxyflavones

The flavonols astragalin (compound 35) and kaempferol 3-O-rutinoside (compound 37) have already been characterized as a component of *Camellia kucha* [34], strawberry [35], and *Rhus cotia* [36]. Both flavonols were found in extracts of *D. palmatum*. The CID spectrum in negative ion modes of kaempferol 3-O-rutinoside from extracts of *D. palmatum* is shown in Figure 7.
Figure 7. CID spectrum of kaempferol 3-O-rutinoside from extracts of D. palmatum, m/z 593.21.

The [M – H]⁻ ion produced three fragment ions at m/z 285, m/z 534, and m/z 429 (Figure 7). The fragment ion with m/z 285 yields two daughter ions at m/z 241 and m/z 199. It was identified in the bibliography in extracts from Camellia kucha [34], strawberry [35], and Rhus coriaria [36].

3.2.2. Tetrahydroxyflavone

The flavonol kaempferol (compound 31) has already been characterized as a component of potato leaves [37], and rapeseed petals [38]. Flavonol kaempferol was found in extracts of D. palmatum and D. ruyschiana.

3.2.3. Hexahydroxyflavone

The hexahydroxyflavone ampelopsin (compound 34) has already been characterized as a component of Impatiens glandulifera Royle [39]. It was identified in extracts of D. palmatum. The CID spectrum in positive ion modes of ampelopsin from extracts of D. palmatum is shown in Figure 8.

Figure 8. CID spectrum of ampelopsin from extracts of D. palmatum, m/z 321.11.

The [M + H]⁺ ion produced one fragment ion at m/z 301 (Figure 8). The fragment ion with m/z 301 yields a daughter ion at m/z 284. The fragment ion with m/z 284 yields daughter ions at m/z 192. It was identified in the bibliography in extracts from Impatiens glandulifera Royle [39].

3.2.4. Dihydroflavonols

The dihydroflavonols dihydrokaempferol (compound 32) and dihydroquercetin (compound 33) have already been characterized as a component of strawberry [40] and Solanum tuberosum [41]. The flavonols dihydrokaempferol and dihydroquercetin were...
found in extracts of *D. palmatum*. The CID spectrum in negative ion modes of kaempferol 3-O-rutinoside from extracts of *D. palmatum* is shown in Figure 9.

![Image of Figure 9](image-url)

**Figure 9.** CID spectrum of dihydrokaempferol from extracts of *D. palmatum*, *m/z* 287.26.

The [M − H]⁺ ion produced two fragment ions at *m/z* 269 and *m/z* 151 (Figure 9). The fragment ion with *m/z* 269 yields two daughter ions at *m/z* 267 and *m/z* 183. This compound was identified in the bibliography in extracts from of strawberry [40] and *Solanum tuberosum* [41].

3.3. Condensed Tannin

The procyanidin A-type dimer (compound 78) has already been characterized as a component of *Vaccinium macrocarpon* [42] and *Vaccinium myrtillus* [43]. The CID spectrum in positive ion modes of procyanidin A-type dimer from *D. ruyschiana* is shown in Figure 10. The [M + H]⁺ ion produced four fragment ions at *m/z* 415, *m/z* 352, *m/z* 283, and *m/z* 164 (Figure 10). The fragment ion with *m/z* 415 yields three daughter ions at *m/z* 337, *m/z* 295, and *m/z* 193. This compound was identified in the bibliography in extracts from *Vaccinium macrocarpon* [42] and *Vaccinium myrtillus* [43].

![Image of Figure 10](image-url)

**Figure 10.** CID spectrum of procyanidin from extracts of *D. ruyschiana*, *m/z* 577.07.

The polyphenol composition distribution table is shown below (Table 1). The comparison table shows the presence of some flavonoids in both types of the genus *Dracocephalum* (apigenin, acacetin, luteolin, apigenin 7-O-glucoside, acacetin 7-O-glucoside, kaempferol, prunin, eriodictyol 7-O-glucoside, caffeic acid, caffeic acid-O-hexoside, dimethyl-secoisolaricresinol, petunidin, and pelargonidin 3-O-glucoside). Mass spectrometric studies have convincingly shown that the amount of polyphenolic compounds in the extracts of *D. palmatum* is greater than in the extracts of *D. ruyschiana*. The number of polyphenolic compounds identified as a result of the study in the extracts of *D. palmatum* is 57 compounds. In extracts of *D. ruyschiana*, 35 compounds.
Table 1. The flavonoid composition distribution of the genus *Dracocephalum* L. Blue square—presence in extracts of *D. ruyschiana*; magenta square—in extracts of *D. palmatum*.

| No. | Class of Compounds | Identified Compounds | Formula | *D. ruyschiana* | *D. palmatum* |
|-----|--------------------|----------------------|---------|-----------------|---------------|
| 1   | Flavone            | Apigeninidin         | C_{15}H_{10}O_{4} |                |               |
| 2   | Flavone            | Apigenin             | C_{15}H_{10}O_{5} |                |               |
| 3   | Flavone            | Negletein (5,6-dihydroxy-7-methoxyflavone) | C_{18}H_{12}O_{5} |                |               |
| 4   | Flavone            | Acacetin (linarigenin, buddeolflavonol) | C_{18}H_{12}O_{5} |                |               |
| 5   | Flavone            | Luteolin             | C_{18}H_{12}O_{6} |                |               |
| 6   | Flavone            | Apigenin-7, 4′-dimethyl ether | C_{17}H_{12}O_{5} |                |               |
| 7   | Flavone            | Diosmetin            | C_{18}H_{12}O_{6} |                |               |
| 8   | Flavone            | Salvigenin           | C_{18}H_{12}O_{6} |                |               |
| 9   | Flavone            | Nevadensin           | C_{18}H_{12}O_{7} |                |               |
| 10  | Flavone            | Apigenin 7-sulfate   | C_{18}H_{12}O_{5} |                |               |
| 11  | Flavone            | Chrysin 6-C-glucoside | C_{22}H_{10}O_{9} |                |               |
| 12  | Flavone            | Chrysin glucuronide  | C_{22}H_{10}O_{10} |                |               |
| 13  | Flavone            | Apigenin-5-O-glucoside | C_{22}H_{10}O_{10} |                |               |
| 14  | Flavone            | Apigenin-7-O-glucoside | C_{22}H_{10}O_{10} |                |               |
| 15  | Flavone            | Apigenin 7-O-glucuronide | C_{23}H_{10}O_{11} |                |               |
| 16  | Flavone            | Acacetin 7-O-glucoside | C_{23}H_{10}O_{10} |                |               |
| 17  | Flavone            | Acacetin 8-C-glucoside | C_{23}H_{10}O_{10} |                |               |
| 18  | Flavone            | Luteolin 7-O-glucoside (cyanoside, luteoloside) | C_{23}H_{10}O_{11} |                |               |
| 19  | Flavone            | Acacetin 7-O-beta-D-glucuronide | C_{23}H_{10}O_{11} |                |               |
| 20  | Flavone            | Luteolin-7-O-beta-glucuronide | C_{23}H_{10}O_{12} |                |               |
| 21  | Flavone            | Diosmetin-7-O-beta-glucoside | C_{22}H_{10}O_{11} |                |               |
| 22  | Flavone            | Luteolin O-acetyl-hexoside | C_{23}H_{10}O_{12} |                |               |
| 23  | Isoflavone         | Apigenin 7-O-beta-D-6‴-O-malonyl-glucoside | C_{23}H_{10}O_{13} |                |               |
| 24  | Flavone            | Acacetin 8-C-glucoside malonylated | C_{23}H_{10}O_{13} |                |               |
| 25  | Isoflavone         | 2′-Hydroxygenistein O-glucoside malonylated | C_{24}H_{10}O_{14} |                |               |
| 26  | Flavone            | Luteolin 7-O-beta-D-6‴-O-malonyl-glucoside | C_{23}H_{10}O_{14} |                |               |
| 27  | Flavone            | Acacetin C-glucoside methylmalonylated | C_{23}H_{10}O_{13} |                |               |
| 28  | Flavone            | Apigenin 8-C-hexoside-6-C-pentoside | C_{25}H_{10}O_{14} |                |               |
| 29  | Flavone            | Apigenin 8-C-pentoside-6-C-hexoside | C_{25}H_{10}O_{14} |                |               |
| 30  | Flavone            | Apigenin 6-C-[6‴-acetyl-2‴-O-deoxyhexosyl]-glucoside | C_{26}H_{10}O_{15} |                |               |
| 31  | Flavonol           | Kaempferol           | C_{13}H_{10}O_{6} |                |               |
| 32  | Flavonol           | Dihydrokaempferol (aromadendrin; katuranin) | C_{16}H_{10}O_{6} |                |               |
| 33  | Flavonol           | Dihydroquercetin (taxifolin, taxifoliol) | C_{18}H_{10}O_{7} |                |               |
| 34  | Flavonol           | Ampelopsin (dihydromyricetin, ampelophtin) | C_{18}H_{10}O_{8} |                |               |
| 35  | Flavonol           | Astragalalin (kaempferol 3-O-glucoside; kaempferol-3-beta-monoglucoside, astragaline) | C_{21}H_{10}O_{11} |                |               |
| 36  | Flavonol           | Kaempferol-3-O-glucuronide | C_{21}H_{10}O_{12} |                |               |
| 37  | Flavonol           | Kaempferol 3-O-rutinoside | C_{17}H_{10}O_{15} |                |               |
| 38  | Flavan-3-ol        | (epi)catechin        | C_{18}H_{10}O_{6} |                |               |
| 39  | Flavan-3-ol        | Galallocatechin [+(-)]galallocatechin | C_{18}H_{10}O_{7} |                |               |
| 40  | Flavanone          | Naringenin (naringetol, naringenin) | C_{18}H_{10}O_{5} |                |               |
| 41  | Flavanone          | Eriodictyol (3‴,4‴,5‴,7-tetrahydroxy-flavanone) | C_{18}H_{10}O_{6} |                |               |
| No. | Compounds            | Molecular Formula |
|-----|----------------------|-------------------|
| 42  | Flavanone            | C_{18}H_{12}O_{6} |
| 43  | Flavanone            | C_{24}H_{23}O_{14} |
| 44  | Flavanone            | C_{20}H_{19}O_{10} |
| 45  | Flavanone            | C_{22}H_{30}O_{6} |
| 46  | Hydroxycinnamic acid | C_{6}H_{8}O_{4}   |
| 47  | Phenolic acid        | C_{10}H_{6}O_{3}  |
| 48  | Phenolic acid        | C_{11}H_{12}O_{5} |
| 49  | Phenolic acid        | C_{15}H_{12}O_{6} |
| 50  | Phenolic acid        | C_{11}H_{13}O_{7} |
| 51  | Phenolic acid        | C_{15}H_{18}O_{9} |
| 52  | Phenolic acid        | C_{16}H_{14}O_{8} |
| 53  | Phenolic acid        | C_{18}H_{14}O_{8} |
| 54  | Gallate ester        | C_{13}H_{10}O_{8} |
| 55  | Phenolic acid        | C_{17}H_{10}O_{8} |
| 56  | Phenolic acid        | C_{16}H_{10}O_{8} |
| 57  | Phenolic acid        | C_{15}H_{12}O_{6} |
| 58  | Phenolic acid        | C_{13}H_{12}O_{4} |
| 59  | Phenolic acid        | C_{15}H_{18}O_{9} |
| 60  | Phenolic acid        | C_{16}H_{18}O_{9} |
| 61  | Phenolic acid        | C_{17}H_{18}O_{9} |
| 62  | Phenolic acid        | C_{18}H_{18}O_{9} |
| 63  | Phenolic acid        | C_{25}H_{24}O_{12} |
| 64  | Stilbene             | C_{14}H_{12}O_{2} |
| 65  | Stilbene             | C_{14}H_{12}O_{3} |
| 66  | Lignan               | C_{9}H_{8}O_{5}   |
| 67  | Lignan               | C_{15}H_{12}O_{6} |
| 68  | Anthocyanidin        | C_{14}H_{12}O_{2} |
| 69  | Anthocyanidin        | C_{18}H_{18}O_{9} |
| 70  | Anthocyanidin        | C_{22}H_{23}O_{11} |
| 71  | Anthocyanidin        | C_{20}H_{21}O_{10} |
| 72  | Anthocyanidin        | C_{22}H_{21}O_{10}+ |
| 73  | Anthocyanidin        | C_{22}H_{21}O_{10}+ |
| 74  | Anthocyanidin        | C_{22}H_{21}O_{10}+ |
| 75  | Anthocyanidin        | C_{22}H_{21}O_{10}+ |
| 76  | Anthocyanidin        | C_{22}H_{21}O_{10}+ |
| 77  | Anthocyanidin        | C_{22}H_{21}O_{10}+ |
| 78  | Condensed tannin      | C_{38}H_{28}O_{12} |

A total of 114 metabolome compounds were identified in the extracts of *D. palmatum* and *D. ruyshciana*, many of which are characteristic of the genus *Dracocephalum*. Of these, 92 components were identified for the first time in this plant species. These are flavones: apigenin 8-C-pentoside-6-C-hexoside, nevadensin, apigenin 7-O-glucuronide, negletein,
chrysin 6-C-glucoside, luteolin 7-O-β-glucuronide, chrysins glucuronide, and acacetin 7-O-glucoside; flavonols: dihydrokaempferol, dihydroquercetin, astragalin, kaempferol 3-O-rutinoside, and ampelopsin; flavan-3-ols: catechin, gallocatechin, and flavanone fustin; phenolic acids: 4-hydroxybenzoic acid, methylgallic acid, hydroxy methoxy dimethylbenzoic acid, ellagic acid, caffeoylshikimic acid, proliisomer acid, salvianolic acid G, and 3,4-O-dicaffeoylquinic acid; stilbene: pinosylvin and resveratrol; anthocyanins: pelargonidin-3-O-glucoside, peonidin 0-pentoside, cyanidin 3-(6''-malonylguloside), cyanidin 3-(acetyl)hexose, and condensed tannin procyanidin A-type dimer; lignans: hinokinin and dimethyl-secoisolariciresinol; stilbenes: resveratrol and pinosylvin; carotenoids: β-apo-12′carotenal, apocarotenal, 5,8-epoxy-α-carotene, cryptoxanthin, violaxanthin, and selenium; alkaloids: mesembrenol and 4′-O-desmethyl mesembranol; oxylipins: o xo-DHOD, THODE, and tetrahydroxyxanthen mangiferin; and so forth.

4. Materials and Methods

4.1. Materials

Aboveground, phytomass of D. palmatum S. was collected during expedition work on the territory of the Pole of Cold Oymyakon during the period of seed ripening (from 15 to 25 July 2019). Phytomass of D. ruychiana L. was collected on the territory of the river Amga, Yakutia, in June 2019. The identification of the species was carried out by E. G. Nikolin, PhD (IBPK SB RAS). All samples were morphologically authenticated according to the current standard of Pharmacopoeia of the Eurasian Economic Union [44]. Herbariums of plants are kept in the collection of the educational and scientific laboratory “Molecular Genetic and Cellular Technologies” of the Institute of Natural Sciences of Northeastern Federal University (Yakutsk, Republic of Sakha (Yakutia), Russian Federation).

4.2. Chemicals and Reagents

HPLC-grade acetonitrile was purchased from Fisher Scientific (Southborough, UK), and MS-grade formic acid was from Sigma-Aldrich (Steinheim, Germany). Ultrapure water was prepared from a Siemens Ultra Clear (Siemens Water Technologies, Munich, Germany), and all other chemicals were analytical grade.

4.3. Fractional Maceration

Fractional maceration technique was applied to obtain highly concentrated extracts [45]. From 500 g of the sample, 10 g of leaves was randomly selected for maceration. The total amount of the extractant (ethyl alcohol of reagent grade) was divided into three parts and consistently infused to the grains with the first, second, and third parts. A solid–solvent ratio was 1:20. The infusion of each part of the extractant lasted 7 days at room temperature.

4.4. Liquid Chromatography

HPLC was performed using Shimadzu LC-20 Prominence HPLC (Shimadzu, Kyoto, Japan), equipped with a UV sensor and C18 silica reverse phase column (4.6 × 150 mm, particle size: 2.7 μm) to perform the separation of multicomponent mixtures. The gradient elution with two mobile phases’ program (A, deionized water; B, acetonitrile with formic acid 0.1% v/v) was as follows: 0.01–5 min, 100% CH3CN; 5–45 min, 100–25% CH3CN; 45–55 min, 25–0% CH3CN; control washing, 55–60 min, 0% CH3CN. The entire HPLC analysis was performed with a UV–VIS detector, SPD-20A (Shimadzu, Kyoto, Japan), at a wavelength of 230 nm; the temperature was 50 °C, and the total flow rate was 0.25 mL/min. The injection volume was 10 μL. Additionally, liquid chromatography was combined with a mass spectrometric ion trap to identify compounds.
4.5. Mass Spectrometry

MS analysis was performed on an ion trap, amaZon SL (Bruker Daltonics, Bremen, Germany), equipped with an ESI source in negative and positive ion modes. The optimized parameters were obtained as follows: ionization source temperature: 70 °C, gas flow: 4 L/min, nebulizer gas (atomizer): 7.3 psi, capillary voltage: 4500 V, end plate bend voltage: 1500 V, fragmentary: 280 V, collision energy: 60 eV. A four-stage ion separation mode (MS/MS mode) was implemented. An ion trap was used in the scan range \( m/z \) 100–1,700 for MS and MS/MS. All experiments were repeated three times. A four-stage ion separation mode (MS/MS mode) was implemented.

5. Conclusions

The extracts of *D. palmatum* S. and *D. ruyschiana* L. contain a large number of polyphenolic complexes, which are biologically active compounds. For the most complete and safe extraction, the method of maceration with MeOH was used. To identify target analytes in extracts, HPLC was used in combination with an ion trap. The results of the preliminary study showed the presence of 114 compounds corresponding to the genus *Dracocephalum*, of which 92 were identified for the first time in the genus *Dracocephalum*.

The data obtained will help to intensify future research on the development and production of various medical products containing targeted extracts of *D. palmatum* S. and *D. ruyschiana* L. A wide variety of biologically active polyphenolic compounds open up rich opportunities for the creation of new drugs, as well as biologically active additives based on extracts from the genus *Dracocephalum*.

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## Appendix A

Table A1. Compounds identified from the extracts of *D. palmatum* S. and *D. ruyschiana* L. in positive and negative ionization modes by HPLC–ion trap–MS/MS.

| No | Variety of *Dracocephalum* | Class of Compounds | Identified Compounds | Formula | Mass       | Molecular Ion [M – H]– | Molecular Ion [M + H]+ | 2 Fragmentation MS/MS | 3 Fragmentation MS/MS | 4 Fragmentation MS/MS | References                       |
|----|---------------------------|---------------------|----------------------|---------|------------|------------------------|------------------------|----------------------|----------------------|----------------------|-----------------------------|
| 1  | D. ruyschiana             | Flavone             | Apigeninidin         | C₁₅H₁₁O₄| 255.2454   | 256                    | 168                    | 122                  |                      |                     | Triticum [46]                     |
| 2  | *D. palmatum, D. ruyschiana* | Flavone           | Apigenin (5,7-dihydroxy-2-(40hydroxypHENyl)-4H-chromen-4-one) | C₁₅H₁₆O₅| 270.2369   | 269                    | 225                    | 181                  | 117                  |                     | Dracocephalum palmatum [4], Andean blueberry [10], Lonicera japonicum [11], Mexican lupine species [12] |
| 3  | D. palmatum              | Flavone             | Negletein (5,6-dihydroxy-7-methoxy-flavone) | C₁₆H₁₂O₅| 284.2635   | 285                    | 271                    | 241                  | 187                  |                     | Actinocarya tibetica [19]                         |
| 4  | *D. palmatum, D. ruyschiana* | Flavone           | Acacetin (linarigenin, buddleoflavonol) | C₁₆H₁₂O₅| 284.2635   | 285                    | 268                    | 211; 143             |                     |                     | Dracocephalum palmatum [4], Mexican lupine species [12], Mentha [14], Dracocephalum moldavica [15], Wissadula periplocifolia [18] |
| 5  | *D. palmatum, D. ruyschiana* | Flavone           | Luteolin             | C₁₅H₁₀O₆| 286.2363   | 287                    | 286; 153               | 171                  | 153                  |                     | Dracocephalum palmatum [4], Eucalyptus [16], Lonicera japonicum [11] |
| 6  | D. palmatum              | Flavone             | Apigenin-7, 4′-dimethyl ether | C₁₇H₁₄O₅| 298.2901   | 299                    | 284                    | 256                  |                     |                     | Ocimum [20]                                 |
| 7  | D. palmatum              | Flavone             | Diosmetin (luteolin 4′-methyl ether, salinigricoflavonol) | C₁₆H₁₀O₆| 300.2629   | 301                    | 286                    | 258                  |                     |                     | Andean blueberry [10], Lonicera japonicum [11], Cirsium japonicum [13], Mentha [14], Dracocephalum moldavica [15] |
| 8  | D. palmatum              | Flavone             | Salvigenin           | C₁₈H₁₆O₆| 328.3160   | 329                    | 314; 240               | 154                  |                     |                     | Dracocephalum palmatum [4], Ocimum [20] |
|   | Species     | Type        | Compound Name                      | Molecular Formula | M.Wt | Act. Site 1 | Act. Site 2 | Act. Site 3 | Act. Site 4 | Act. Site 5 | Act. Site 6 | Act. Site 7 | Source                      |
|---|-------------|-------------|-----------------------------------|-------------------|------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-----------------------------|
| 9 | *D. palmatum* | Flavone     | Nevadensin                        | C_{18}H_{16}O_{7} | 344.3154 | 345         | 311         | 284         | 149         |             |             |               | Mentha [14], Ocimum [20]   |
| 10 | *D. ruyschiana* | Flavone     | Apigenin 7-sulfate                 | C_{18}H_{16}O_{5}S | 350.3001 | 349         | 269         | 223         |             |             |             |               |                         |
| 11 | *D. ruyschiana* | Flavone     | Chrysin 6-C-glucoside              | C_{21}H_{20}O_{9}S | 344.3154 | 417         | 51; 127     | 333; 267    | 165         |             |             |               | Passiflora incarnata [26]  |
| 12 | *D. ruyschiana* | Flavone     | Chrysin glucuronide                | C_{21}H_{18}O_{10} | 345       | 431         | 255         | 255; 153    | 171         |             |             |               | F. pottsii [28]            |
| 13 | *D. palmatum* | Flavone     | Apigenin-5-O-glucoside             | C_{21}H_{20}O_{10} | 432.3775 | 433         | 414; 274; 215; 145 | 371; 245; 147 | 327         |             |             |               | Rice [22]                  |
| 14 | *D. palmatum, D. ruyschiana* | Flavone     | Apigenin-7-O-glucoside (apigetrin, cosmosiin) | C_{21}H_{20}O_{10} | 432.3775 | 433         | 271         | 153         |             |             |             |               | Mao [4], Mentha [24], Mexican lupine species [12] |
| 15 | *D. ruyschiana* | Flavone     | Apigenin 7-O-glucuronide           | C_{21}H_{20}O_{11} | 345       | 447         | 271         | 153         | 271; 171    |             |             |               | Pear [25], Bougainvillea [27] |
| 16 | *D. palmatum, D. ruyschiana* | Flavone     | Acacetin 7-O-glucoside (tilianin)  | C_{22}H_{22}O_{10} | 446.4041 | 447         | 285; 149    | 270         | 242         |             |             |               | Dracocephalum palmatum [4], Bougainvillea [27] |
| 17 | *D. palmatum* | Flavone     | Acacetin 8-C-glucoside             | C_{22}H_{22}O_{10} | 446.4041 | 447         | 428; 344; 343; 230; 133 | 232         |             |             |             |               | Mexican lupine species [12] |
| 18 | *D. palmatum* | Flavone     | Luteolin 7-O-glucoside (cynaroside, luteoloside) | C_{21}H_{20}O_{11} | 448.3769 | 449         | 287; 199    | 153         |             |             |             |               | Lonicera japonicum [11], Pear [25], Passiflora incarnata [26] |
| 19 | *D. ruyschiana* | Flavone     | Acacetin 7-O-beta-D-glucuronide    | C_{22}H_{22}O_{11} | 460.3876 | 459         | 283; 343; 175 | 268         | 267         |             |             |               | Dracocephalum moldavica [15] |
| 20 | *D. ruyschiana* | Flavone     | Luteolin-7-O-beta-glucuronide      | C_{21}H_{20}O_{12} | 462.3604 | 463         | 287         | 268         | 245; 119    |             |             |               | Mentha [14], rat plasma [32], Neuboullia laevis [30] |
| 21 | *D. ruyschiana* | Flavone     | Diosmetin-7-O-beta-glucoside      | C_{22}H_{22}O_{11} | 462.4035 | 463         | 287         | 168         | 123         |             |             |               | Dracocephalum moldavica [15], Oxalis corniculata [23] |
| 22 | *D. palmatum* | Flavone     | Luteolin O-acetyl-hexoside        | C_{23}H_{22}O_{12} | 490.4136 | 489         | 285; 450    | 199         | 155         |             |             |               | Dracocephalum palmatum [4] |
| 23 | *D. palmatum* | Isoflavone  | Apigenin 7-O-beta-D-(6"-O-malonyl)-glucoside | C_{22}H_{22}O_{13} | 518.4237 | 519         | 502; 184    | 125         |             |             |             |               | Dracocephalum moldavica [14], Zostera marina [21] |
| No. | Species          | Class      | Compound Description                                      | Molecular Formula | Mass   | Parent Mass | IS 1 | IS 2 | IS 3 | IS 4 | Source(s)                     |
|-----|------------------|------------|-----------------------------------------------------------|-------------------|--------|-------------|------|------|------|------|-------------------------------|
| 24  | *D. palmatum*    | Flavone    | Acacetin 8-C-glucoside malonylated                         | C_{27}H_{24}O_{13} | 532.4503 | 533         | 497; 205 | 377; 335 |     | Mexican lupine species [12] |
| 25  | *D. palmatum*    | Isoflavone | 2'-Hydroxygenistein O-glucoside malonylated                | C_{26}H_{22}O_{14} | 534.4231 | 533         | 489     | 285; 326 | 284 | Mexican lupine species [12] |
| 26  | *D. palmatum*    | Flavone    | Luteolin 7-O-beta-D-(6" -O-malonyl)-glucoside             | C_{29}H_{24}O_{14} | 534.4231 | 535         | 436; 354; 287; 214 | 328; 238 |     | Dracocephalum moldavica [15], Zostera marina [21] |
| 27  | *D. palmatum*    | Flavone    | Acacetin C-glucoside methyldmalonylated                    | C_{26}H_{24}O_{14} | 546.4758 | 547         | 529; 496; 369 | 343 |     | Mexican lupine species [12] |
| 28  | *D. ruyschiana*  | Flavone    | Apigenin 8-C-hexoside-6-C-pentoside                       | C_{27}H_{24}O_{14} | 564.4921 | 565         | 547; 511; 427 | 529; 499 | 511 | Triticum aestivum L. [47,48], Bituminaria [49], Licania Rigid a [50] |
| 29  | *D. ruyschiana*  | Flavone    | Apigenin 8-C-pentoside-6-C-hexoside                       | C_{27}H_{24}O_{15} | 564.4921 | 565         | 547; 274 | 529; 474; 247 | 390 | Triticum aestivum L. [47,48], Bituminaria [49], Licania Rigid a [50] |
| 30  | *D. palmatum*    | Flavone    | Apigenin 6-C-[6" -acetyl-2" -O-deoxyhexosyl]glucoside     | C_{26}H_{24}O_{15} | 620.5554 | 621         | 561; 218 | 533 | 445; 222 | Passiflora incarnata [26] |
| 31  | *D. palmatum*,  | Flavonol   | Kaempferol (3,5,7-trihydroxy-2-(4-hydroxy-xyphenyl)-4H-chromen-4-one) | C_{15}H_{12}O_{6} | 286.2363 | 287         | 269; 202 | 233; 205 | 216 | Andean blueberry [10], Lonicer a japonicum [11], Rhus coriaria (Sumac) [36], potato leaves [37], rapeseed petals [38] |
|     | *D. ruyschiana*  |           |                                                           |                   |         |             |       |       |      |      | F. glaucescens [28], Camel lia kucha [34], Rhodiola rosea [51] |
| 32  | *D. palmatum*    | Flavonol   | Dihydrokaempferol (aromadendrin, katuranin)                | C_{15}H_{12}O_{6} | 288.2522 | 287         | 269; 151 | 267; 183 | 211 | Andean blueberry [10], Eucalyptus [16], Camellia kucha [34], strawberry [40] |
| 33  | *D. palmatum*    | Flavonol   | Dihydroquercetin (taxifolin, taxifolial)                   | C_{15}H_{12}O_{7} | 304.2516 | 305         | 287     | 286; 186 | 185 | Rhus coriaria [36], Impatiens glandulifera Royle [39] |
| 34  | *D. palmatum*    | Flavonol   | Ampelopsin (dihydmorycetin, am pe loptin)                 | C_{15}H_{12}O_{6} | 320.251  | 321         | 301     | 284     | 192 | Lonicer a japonicum [11], Mexican lupine species |
| 35  | *D. palmatum*    | Flavonol   | Astragalin (kaempferol 3-O-glucoside, kaempferol-3-beta-monoglucoside) | C_{27}H_{24}O_{15} | 448.3769 | 447         | 285; 327 | 241     | 199 | |
|   | Species          | Type     | Flavonoid                  | Molecular Formula | Molecular Weight |PubChem CID | Accurate Mass | Error (ppm) | Relative Error (%) |
|---|------------------|----------|---------------------------|-------------------|------------------|------------|--------------|-------------|-------------------|
| 36| *D. ruyschiana*  | Flavonol | Kaempferol-3-O-glucuronide| C_{21}H_{18}O_{12} | 462.3604         | 463        | 287          | 68; 169     | 241; 119          |
| 37| *D. palmatum*    | Flavonol | Kaempferol 3-O-rutinoside  | C_{22}H_{20}O_{15} | 594.5181         | 593        | 285          | 199; 199    | 199               |
| 38| *D. ruyschiana*  | Flavan-3-ol | (Epi)catechin   | C_{15}H_{14}O_{6}  | 290.2681          | 291        | 273; 117     | 255; 145    |                  |
| 39| *D. palmatum*    | Flavan-3-ol | Galloccatechin (+(-)-gallocatechin) | C_{15}H_{14}O_{7}  | 306.2675          | 307        | 289          | 259         |                  |
| 40| *D. palmatum*    | Flavanone | Naringenin (naringetol, naringenin) | C_{15}H_{12}O_{5}  | 272.5228          | 273        | 153; 256     | 125         |                  |
| 41| *D. palmatum*    | Flavanone | Eriodictyol (3',4',5,7-tetrahydroxy-flavanone) | C_{15}H_{12}O_{6}  | 288.2522          | 289        | 163; 271     | 145; 117    |                  |
| 42| *D. ruyschiana*  | Flavanone | Fustin (2,3-dihydrofistein) | C_{15}H_{12}O_{6}  | 288.2522          | 287        | 269; 141     | 267; 185    | 249               |
| Molecule | Plant/Species | Type | Molecular Formula | Molecular Weight | Plant/Species Reference |
|----------|---------------|------|-------------------|------------------|------------------------|
| **43** D. palmatum, D. ruyschiana | Flavanone | Prunin (naringenin-7-O-glucoside) | C_{21}H_{22}O_{10} | 434.3934 | 271; 151; 269; 151 | Dracocephalum palmatum [4], rapeseed petals [38], tomato [54] |
| **44** D. palmatum, D. ruyschiana | Flavanone | Eriodictyol-7-O-glucoside (pyrancanthoside, miscanthoside) | C_{21}H_{22}O_{11} | 450.3928 | 285; 151; 243; 151 | Dracocephalum palmatum [4], Impatiens glandulifera Royle [39], peppermint [29], Mentha [24] |
| **45** D. palmatum | Flavanone | Eriodictyol O-malonyl-hexoside | C_{21}H_{24}O_{14} | 536.4390 | 491; 287; 287; 151 | Dracocephalum palmatum [4] |
| **46** D. palmatum; D. ruyschiana | Hydroyxycinnamic acid | Caffeic acid | C_{9}H_{8}O_{4} | 180.1574 | 181 | 135 | 119 | Dracocephalum palmatum [4], Eucalyptus [16], Triticum [46], Salvia miltiorrhiza [55] |
| **47** D. palmatum | Phenolic acid | Methylgallic acid (methyl gallate) | C_{9}H_{6}O_{5} | 184.1461 | 183 | 139 | 137 | 119 | Eucalyptus [16], papaya [35], Rhus coriaria [36] |
| **48** D. ruyschiana | Phenolic acid | Hydroxy methoxy dimethylbenzoic acid | C_{10}H_{12}O_{4} | 196.1999 | 197 | 179 | 161 | 133 | F. herrerae, F. glaucescens [28] |
| **49** D. palmatum | Phenolic acid | Ethyl caffeate (ethyl 3,4-dihydroxyphenylacacetate) | C_{11}H_{12}O_{4} | 208.2106 | 207 | 179 | 135 | Lepechinia [56] |
| **50** D. palmatum | Hydroxybenzoic acid | 4-Hydroxybenzoic acid (PHBA, benzoic acid, p-hydroxybenzoic acid) | C_{6}H_{5}O_{3} | 138.1207 | 139 | 122 | Bougainvillea [27], Triticum [46], Bittuminaria [49], Vigna unguiculata [57], Eucalyptus globulus [58], |
| **51** D. ruyschiana | Hydroxybenzoic acid | Ellagic acid (benzoic acid, elagostic acid) | C_{4}H_{6}O_{5} | 302.1926 | 301 | 284 | 221 | 112 | Rhus coriaria [36], Eucalyptus [16], Eucalyptus globulus [58], Rubus occidentalis [59] |
| **52** D. palmatum | Hydroyxycinnamic acid | Sinapic acid (trans-sinapic acid) | C_{11}H_{10}O_{5} | 224.21 | 225 | 206 | 138 | Andean blueberry [10], rapeseed petals [38], Triticum [46], Cranberry [53], Cherimoya [60] |
| 53 | D. ruyschiana | Hydroxyquinic acid | 1-O-(4-coumaroyl)-glucose | C_{15}H_{18}O_{8} | 326.2986 | 325 | 145 | 117 | Cranberry [53], strawberry [40], Rubus occidentalis [59] |
| 54 | D. palmatum | Gallate ester | Beta-glucogallin (1-O-galloyl-beta-d-glucose, galloyl glucose) | C_{15}H_{18}O_{11} | 332.2601 | 333 | 314 | 271; 151 | 244; 159 | Strawberry [40, 61], carao tree seeds [62] |
| 55 | D. ruyschiana | Phenolic acid | Caffeoylshikimic acid (5-O-cafeoylshikimate) | C_{15}H_{18}O_{8} | 335.2855 | 335 | 179 | 135 | 133 | Andean blueberry [10], pear [25], passion fruits [35], Vaccinium myrtillus [43] |
| 56 | D. palmatum | Phenolic acid | Salvianolic acid G | C_{15}H_{12}O_{7} | 340.2837 | 341 | 296; 208 | 278; 208 | 235; 164 | Mentha [14], Salvia miltiorrhiza [55] |
| 57 | D. palmatum | Phenolic acid | 1-cafeoyl-beta-D-glucose (cafeic acid-3-O-beta-D-gluoside) | C_{15}H_{18}O_{8} | 342.298 | 341 | 178; 119 | 135 | Passiflora incarnata [26], strawberry [40], Cranberry [53] |
| 58 | D. palmatum, D. ruyschiana | Phenolic acid | Caffeic acid-O-hexoside (cafeoyl-O-hexoside) | C_{15}H_{18}O_{8} | 342.298 | 341 | 178; 113 | | pear [25], Cherimoya, papaya [35], Sasa vechii [63] |
| 59 | D. palmatum | Phenolic acid | Prolithospermic acid | C_{15}H_{18}O_{8} | 358.2990 | 359 | 341; 207 | 314; 267; 149 | Mentha [14], Salvia miltiorrhiza [55] |
| 60 | D. palmatum | Phenolic acid | Rosmarinic acid | C_{15}H_{18}O_{8} | 360.3148 | 359 | 161 | 133 | Dracocephalum palmatum [4], Mentha [14], Zostera marina [21], peppermint [29], Salvia miltiorrhiza [55], Lepechinia [56] |
| 61 | D. palmatum, D. ruyschiana | Phenolic acid | Caffeic acid derivative | C_{15}H_{18}O_{8}Na | 377.2985 | 377 | 341; 215 | 179 | Bougainvillea [27] |
| 62 | D. palmatum | Phenolic acid | Salvianic acid C | C_{15}H_{18}O_{8} | 378.3301 | 377 | 359; 315 | 289 | 229 | Salvia miltiorrhiza [55], Lepechinia [56] |
| 63 | D. ruyschiana | Phenolic acid | 3,4-O-dicafeoylquinic acid (iso-chlorogenic acid B) | C_{15}H_{18}O_{12} | 516.4509 | 517 | 397 | 337; 135 | Lonicera japonicum [11], Pear [25], Stevia rebaudiana [64] |
| No. | Species          | Type       | Name                                    | Molecular Formula | Molecular Weight | Mass/Intensity   | Reference                          |
|-----|------------------|------------|-----------------------------------------|-------------------|------------------|------------------|------------------------------------|
| 64  | *D. ruyschiana*  | Stilbene   | Pinosylvin (3,5-stilbenediol, trans-3,5-dihydroxystilbene) | C_{14}H_{12}O_{2} | 212.2439         | 213; 168; 126    | *Pinus sylvestris* [50], *Pinus resinosa* [65] |
| 65  | *D. ruyschiana*  | Stilbene   | Resveratrol (trans-resveratrol, 3,4',5-trihydroxystilbene, stilbentriol) | C_{14}H_{12}O_{3} | 228.2433         | 229; 142; 210; 114 | A. cordifolia, F. glaucescens [28], F. herrerae [28], Radix polygoni multiflori [52] |
| 66  | *D. palmatum*    | Lignan     | Hinokinin                               | C_{20}H_{18}O_{6} | 354.3533         | 355; 337; 189; 319; 226 | Triticum aestivum L. [46], Rhodiola rosea [51], lignans [66] |
| 67  | *D. palmatum, D. ruyschiana* | Lignan | Dimethyl-secoisolariciresinol | C_{22}H_{30}O_{6} | 390.4700         | 391; 373; 249; 121; 355; 225; 313; 226 | Lignans [66] |
| 68  | *D. palmatum, D. ruyschiana* | Anthocyanin | Petunidin                               | C_{16}H_{13}O_{7}+ | 317.2702         | 318; 166; 300; 121 | A. cordifolia, C. edulis [28] |
| 69  | *D. palmatum*    | Anthocyanin | Cyanidin O-pentoside                    | C_{18}H_{19}O_{10} | 419.3589         | 419; 287; 219; 201 | Andean blueberry [10], Gaultheria mucronata, Gaultheria antarctica [60], Myrtle [67] |
| 70  | *D. palmatum, D. ruyschiana* | Anthocyanin | Pelargonidin-3-O-glucoside (calystephin) | C_{18}H_{21}O_{10} | 433.3854         | 433; 271; 153; 225; 171 | strawberry [61], Triticum aestivum [68], Rubus ulmifolius [69] |
| 71  | *D. palmatum*    | Anthocyanin | Peonidin O-pentoside                    | C_{18}H_{21}O_{10} | 433.3854         | 433; 301; 215; 145; 229; 139 | Andean blueberry [10], Myrtle [67] |
| 72  | *D. palmatum*    | Anthocyanin | Cyanidin-3-O-glucoside (cyanidin 3-O-beta-D-glucoside, kuromarin) | C_{18}H_{21}O_{11}+ | 449.3848         | 449; 287; 153 | rice [22], Triticum [46,68], acerola [70] |
| 73  | *D. palmatum*    | Anthocyanin | Peonidin-3-O-glucoside                  | C_{21}H_{23}O_{11}+ | 463.4114         | 463; 301; 286; 258; 140 | Berberis ilicifolia, Berberis empetrifolia [60], Andean blueberry [10], strawberry [61], Triticum aestivum [68] |
| 74  | *D. palmatum*    | Anthocyanin | Cyanidin 3-(acetyl)hexose                | C_{23}H_{23}O_{12}+ | 491.4215         | 491; 287; 245; 153; 171 | Acerola [70] |
|   |   |   |   |   |   |   |   |   |   |   |
|---|---|---|---|---|---|---|---|---|---|---|
|   |   |   |   |   |   |   |   |   |   |   |
| 75 | *D. palmatum* | Anthocyanidin | Cyanidin 3-(6”-malonylglucoside) | C_{26}H_{23}O_{14} | 535.4310 | 535 | 287 | 285; 179 | 242; 153 | strawberry [40], strawberry [61], *Triticum aestivum* [68] |
| 76 | *D. palmatum* | Anthocyanidin | Cyanidin 3-O-coumaroyl hexoside | C_{26}H_{23}O_{13} | 595.533 | 595 | 287 | 153 |   | Grape vine varieties [71] |
| 77 | *D. palmatum* | Anthocyanidin | 7-O-Methyl-delphinidin-3-O-(2”galloyl)galactoside | C_{26}H_{28}O_{16} | 630.5071 | 631 | 317; 519 |   |   | *Rhus coriaria* [36] |
| 78 | *D. ruyschiana* | Condensed tannin | Procyanidin A-type dimer | C_{20}H_{16}O_{12} | 576.501 | 577 | 416; 352; 283; 164 | 337; 295; 193319; 225; 150 |   | pear [25], *Vaccinium myrtillus* [43] |
|   |   |   |   |   |   |   |   |   |   |   |
|   |   |   |   |   |   |   |   |   |   |   |
| 79 | *D. palmatum* | Amino acid | L-Leucine (S)-2-amino-methylpentanoic acid) | C_{6}H_{13}NO_{2} | 131.1729 | 132 | 130 |   |   |   |
| 80 | *D. palmatum* | Alpha-omega dicarboxylic acid | Hydroxymethyl glutaric acid | C_{6}H_{10}O_{5} | 162.1406 | 163 | 145 | 117 |   | Potato leaves [37] |
| 81 | *D. palmatum* | Cyclohexene carboxylic acid | Perillic acid | C_{10}H_{14}O_{2} | 166.217 | 167 | 149 | 121 |   | *Mentha* [14] |
| 82 | *D. palmatum*, *D. ruyschiana* | Amino acid | L-tryptophan (tryptophan; (S)-tryptophan) | C_{11}H_{12}N_{2}O_{2} | 204.2252 | 205 | 188 | 144 | 118 | *Passiflora incarnata* [26], *Camellia kucha* [34], *Vigna unguiculata* [57] |
| 83 | *D. palmatum* | Aminoalkylidine | 5-Methoxydimethyltryptamine | C_{15}H_{16}N_{2}O_{2} | 218.2948 | 219 | 201 | 159; 118 |   | *Camellia kucha* [34] |
| 84 | *D. palmatum* | Sesquiterpenoid | Epiglobulol ((-)globulol) | C_{15}H_{26}O | 222.3663 | 223 | 205; 153 | 133 |   | Olive leaves [72] |
| 85 | *D. palmatum* | Omega-5 fatty acid | Myristoleic acid (cis-9-tetradecanoic acid) | C_{14}H_{26}O_{2} | 226.3550 | 227 | 209 | 139 |   | *F. glaucescens* [28] |
| 86 | *D. palmatum* | Medium-chain fatty acid | Hydroxydodecanoic acid | C_{12}H_{22}O_{5} | 246.3001 | 247 | 229 | 216 |   | *F. glaucescens* [28] |
| No. | Species          | Compound                           | Formula       | Mass 1 | Mass 2 | Mass 3 | Mass 4 | Source                                      |
|-----|------------------|------------------------------------|---------------|--------|--------|--------|--------|---------------------------------------------|
| 87  | D. palmatum      | Omega-3 unsaturated fatty acid     |               |        |        |        |        | F. glaucescens [28]                         |
|     |                  | Hexadecatrienoic acid (hexadeca-2,4,6-trienoic acid) | C_{16}H_{26}O_{2} | 250.3764 | 251    | 233; 191 | 187   |                                             |
| 88  | D. ruyschiana    | Propionic acid                     | C_{3}H_{6}O_{2} | 74.1004 |        |        |        | Ginkgo biloba [73]                          |
|     |                  | Ketoprofen                         | C_{16}H_{14}O_{3} | 254.2806 | 253    | 210    | 180   |                                             |
| 89  | D. palmatum; D. ruyschiana | Ribonucleoside composite of adenine (purine) | C_{6}H_{13}N_{5}O_{4} | 267.2413 | 268    | 136; 258 |       | Lonicera japonica [11]                     |
|     |                  | Adenosine                          | C_{6}H_{13}N_{5}O_{4} | 267.2413 | 268    | 136; 258 |       |                                             |
| 90  | D. palmatum      | Sceletium alkaloid                 | C_{19}H_{23}NO_{3} | 289.3694 | 290    | 242    | 226   | A. cordifolia [28]                          |
| 91  | D. ruyschiana    | O-Methyl-dehydrojoubertamine       | C_{19}H_{23}NO_{3} | 289.3694 | 290    | 242    | 226   | A. cordifolia [28]                          |
| 92  | D. palmatum      | Omega-9 unsaturated fatty acid     | C_{18}H_{34}O_{2} | 282.4614 | 283    | 209; 114 |       | Sanguisorba officinalis [74], Pinus sylvestris [75] |
| 93  | D. palmatum      | 2-Hydroxy fatty acid               | C_{18}H_{34}O_{2} | 286.4501 | 285    | 265    | 186   | F. pottsii [28]                            |
| 94  | D. palmatum      | Alkaloid                           | C_{19}H_{18}O_{4} | 310.3438 | 311    | 283; 137 | 119   | Sceletium [76]                             |
| 95  | D. palmatum, D. ruyschiana | Diterpenoid | C_{19}H_{18}O_{4} | 310.3438 | 311    | 283; 137 | 119   | Salviae miltiorrhiza [77]                   |
|     |                  | Tanshinone IIB ((S)-6-(hydroxyxymethyl)-1,6-dimethyl-6,7,8,9-tetrahydrophenanthro[1,2-B]furan-10,11-dione) | C_{19}H_{18}O_{4} | 310.3438 | 311    | 283; 137 | 119   |                                             |
| 96  | D. palmatum      | Alpha-omega dicarboxylic acid      | C_{18}H_{32}O_{5} | 314.4602 | 315    | 297; 179 | 212   | F. glaucescens [28]                         |
|     |                  | Octadecanedioic acid (1,16-heptadecanedicarboxylic acid) | C_{18}H_{32}O_{5} | 314.4602 | 315    | 297; 179 | 212   |                                             |
| 97  | D. palmatum      | Unsaturated essential fatty acid   | C_{20}H_{36}O_{5} | 318.4504 | 319    | 300    | 282; 167 | 240  | Potato leaves [37]                         |
| 98  | D. ruyschiana    | Oxylinps                           | C_{18}H_{32}O_{5} | 328.4437 | 327    | 229    | 209   | Bituminaria [49], Phyllostachys nigra [63] |
| 99  | D. ruyschiana    | Oxylinps                           | C_{18}H_{32}O_{5} | 328.4437 | 327    | 229    | 209   | Potato leaves [37]                         |
|   |   | **100** D. *ruyschiana* | **Docosahexaenoic acid** | C_{22}H_{32}O_{2} | 328.4883 | 327 | 309; 201 | 291; 171 | 273 | Marine extracts [78] |
|---|---|---|---|---|---|---|---|---|---|---|
|   |   | **101** D. *palmatum, D. ruyschiana* | **13- Trihydroxy-octadecenoic acid** (THODE) | C_{18}H_{30}O_{3} | 330.4596 | 329 | 229; 311 | 211 | 167 | Bituminaria [49], Sasa veitchii [63], Brassica oleracea [79] |
|   |   | **102** D. *ruyschiana* | **Beta-apo-12'-carotenal** | C_{35}H_{56}O_{3} | 350.5369 | 351 | 259; 147 | 231; 145 | Carotenoids [80, 81] |
|   |   | **103** D. *palmatum* | **Sterol** | **Stigmasterol** (stigmasterin, beta-stigmasterol) | C_{29}H_{48}O | 412.6908 | 413 | 301 | 188 | A. cordifolia, F. pottsii [28], Olive leaves [72], *Hedyotis diffusa* [82] |
|   |   | **104** D. *ruyschiana* | **Carotenoid** | **Apocarotenal** ((all-E)-beta-apo-caroten-8'-al) | C_{30}H_{40}O | 416.6380 | 417 | 399; 200 | 351 | 267 | Carica papaya [83] |
|   |   | **105** D. *palmatum* | **Tetrahydroxyxanthene** | **Mangiferin** | C_{19}H_{18}O_{11} | 422.3396 | 423 | 387; 238 | 345 | [84, 85] |
|   |   | **106** D. *palmatum* | **Long-chain fatty acid** | **Nonacosanoic acid** | C_{29}H_{58}O_{2} | 438.7696 | 439 | 395; 353; 245 | 245 | C. edulis [28] |
|   |   | **107** D. *palmatum* | **Anabolic steroid, androgen, androgen ester** | **Vebonol** | C_{30}H_{44}O_{3} | 452.6686 | 453 | 435; 336; 226 | 336 | 209 | Rhus coriaria [36], *Hylocereus polyrhizus* [86] |
|   |   | **108** D. *ruyschiana* | **Triterpenic acid** | **Oleanolic acid** (oleanic acid, cario-phyllin, astrantiagenin C, virgaureagenin B) | C_{30}H_{48}O_{3} | 456.7003 | 457 | 410; 325 | 342; 164 | C. edulis [28], *Hedyotis diffusa* [82], *Folium Eriobotryae* [87], *Eleutherococcus* [88] |
|   |   | **109** D. *palmatum* | **Indole sesquiterpene alka-loid** | **Sespendole** | C_{33}H_{45}NO_{4} | 519.7147 | 520 | 184; 359 | 124 | Rhus coriaria [36], *Hylocereus polyrhizus* [86] |
|   |   | **110** D. *ruyschiana* | **Carotenoid** | **(Z)-lutein** | C_{20}H_{30}O | 550.8562 | 551 | 533 | Physalis peruviana [89], carotenoids [90] |
|   |   | **111** D. *palmatum* | **Carotenoid** | **5,8-epoxy-alpha-carotene** | C_{20}H_{30}O | 552.872 | 553 | 536; 412; 207 | 299; 261 | Physalis peruviana [89] |
|   |   | **112** D. *ruyschiana* | **Carotenoid** | **Cryptoxanthin (beta-cryptoxanthin)** | C_{20}H_{30}O | 552.872 | 553 | 535; 325; 223 | 517 | Carotenoids [81, 91], *Smilax aspera* [92] |
|   | Species       | Type                  | Compound            | Formula  | Mass   | M/Z   | M/Z   | M/Z   |   | Carotenoids [91] |
|---|---------------|-----------------------|---------------------|----------|--------|-------|-------|-------|---|-----------------|
|113| *D. ruyschiana* | Carotenoid Violaxanthin (zeaxanthin dieperoxide, all-trans-violaxanthin) | C_{40}H_{56}O_{4} | 600.8702 | 601    | 364; 582 | 346; 202; 142 | 114 | | |
|   |               | Macro cyclic glycolipid lactone | Resinoside A       | C_{31}H_{34}O_{13} | 614.5939 | 615   | 287; 203 | 162 | | *Eucalyptus genus* [93] |
References

1. Zakharova, V.I.; Kuznetsova, L.V. Abstract of the Flora of Yakutia: Vascular Plants; Nauka: Novosibirsk, Russia, 2012; p. 272 (In Russian).

2. Karavaev, M.N. Summary of the Flora of Yakutia; Publishing House of the USSR Academy of Sciences: Moscow, Russia, 1958; p. 189 p. (In Russian).

3. Danilova, N.S.; Borisova, S.Z.; Ivanova, N.S. Ornamental Plants of Yakutia: Atlas-Key; JSC “Fiton +”: Moscow, Russia, 2012; 248p. (In Russian).

4. Olennikov, D.N.; Chirikova, N.K.; Okhlopkova, Z.M.; Zulfugarov, I.S. Chemical Composition and Antioxidant Activity of Tánara Otó (Dracocephalum palmatum Stephan), a Medicinal Plant Used by the North-Yakutian Nomads. Molecules 2013, 18, 14105.

5. Kim, J.; Kim, J.N.; Park, 1.; Sivtseva, S.; Okhlopkova, Z.; Zulfugarov, I.S.; Kim, S.-W. Dracocephalum palmatum Stephan extract induces caspase and mitochondria dependent apoptosis via Myc induction in diffuse large B cell lymphoma. Oncol. Rep. 2020, 44, 2746–2756.

6. Lee, S.E.; Okhlopkova, Z.M.; Lim, C.; Cho, S.I. Dracocephalum palmatum Stephan extract induces apoptosis in human prostate cancer cells via the caspase-8-mediated extrinsic pathway. Chin. J. Nat. Med. 2020, 18, 793–800.

7. Kekasy, A.; Fuzfai, Z.; Kursinszki, L.; Molnar-Perl, I.; Lemberkovics, E. Analysis of non-volatile constituents in Dracocephalum species by HPLC and GC-MS. Chromatographia 2006, 63, S17–S22.

8. Zeng, Q.; Jin, H.Z.; Qin, J.J.; Fu, J.J.; Hu, X.J.; Liu, J.H.; Yan, L.; Chen, M.; Zhang, W.D. Chemical Constituents of Plants from the Genus Dracocephalum. Chem. Biodivers. 2010, 7, 1911–1929.

9. Selenge, E.; Murata, T.; Kobayashi, K.; Batkhun, J.; Yoshizaki, F. Flavone tetraglycosides and benzyl alcohol glycosides from the mongolian medicinal plant Dracocephalum ryschiana. J. Nat. Prod. 2013, 76, 186–193.

10. Aita, S.E.; Capirotti, A.L.; Cavaliere, C.; Cerrato, A.; Giannelli Moneta, B.; Montone, C.M.; Piovesana, S.; Lagana, A. Andean Blueberry of the Genus Disterigma: A High-Resolution Mass Spectrometric Approach for the Comprehensive Characterization of Phenolic Compounds. Separations 2021, 8, 58.

11. Cai, Z.; Wang, C.; Zou, L.; Liu, X.; Chen, J.; Tan, M.; Mei, Y.; Wei, L. Comparison of Multiple Bioactive Constituents in the Flower and the Caulus of Lonicera japonica Based on UFLC-QTRAP-MS/MS Combined with Multivariate Statistical Analysis. Molecules 2019, 24, 1936.

12. Wojakowska, A.; Piasecka, A.; Garcia-Lopez, P.M.; Zamora-Natera, F.; Krajewski, P.; Marczak, L.; Khakchlik, P.; Stobiecki, M. Structural analysis and profiling of phenolic secondary metabolites of Mexican lupine species using LC–MS techniques. Phytochemistry 2013, 92, 71–86.

13. Zhang, Z.; Jia, P.; Zhang, X.; Zhang, Q.; Yang, H.; Shi, H.; Zhang, L. LC-MS/MS determination and pharmacokinetic study of seven flavonoids in rat plasma after oral administration of Cirsium japonicum DC. extract. J. Ethnopharmacol. 2014, 158, 66–75.

14. Xu, L.L.; Xu, J.J.; Zhong, K.R.; Shang, Z.P.; Wang, F.; Wang, R.F.; Liu, B. Analysis of non-volatile chemical constituents of Mentha haplocalyx herba by ultra-high performance liquid chromatography–high resolution mass spectrometry. Molecules 2017, 22, 1756.

15. Martinez-Vazquez, M.; Estrada-Reyes, R.; Martinez-Laurrabauquio, A.; Lopez-Rubalcava, C.; Heinze, G. Neuropharmacological study of Dracocephalum moldavica L. (Lamiaceae) in mice: Sedative effect and chemical analysis of an aqueous extract. J. Ethnopharmacol. 2012, 141, 908–917.

16. Santos, S.A.O.; Freire, C.S.R.; Domingues, M.R.M.; Silvestre, A.J.D.; Neto, C.P. Characterization of Phenolic Components in Polar Extracts of Cynara cardunculus L. Bark by High-Performance Liquid Chromatography–Mass Spectrometry. Agrid. Food Chem. 2011, 59, 9386–9393.

17. Levandi, T.; Fussa, T.; Vahter, M.; Ingver, A.; Koppel, R. Principal component analysis of HPLC–MS/MS patterns of wheat (Triticum aestivum) varieties. Food Chem. 2014, 163, 86–92.

18. Teles, Y.C.E.; Rebello Horta, C.C.; de Fatima Agra, M.; Siheri, W.; Boyd, M.; Igoli, J.O.; Gray, A.I.; de Fatima Vanderlei de Souza, M. New Sulphated Flavonoids from Wissadula periplocifolia (L.) C. Presl (Malvaceae). Molecules 2015, 20, 20161–20172.

19. Singh, A.; Baijai, V.; Kumar, S.; Sharma, K.R.; Kumar, B. Profiling of Gallic and Ellagic Acid Derivatives in Different Plant Parts of Terminalia arjuna by HPLC-ESI-QTOF-MS/MS. Nat. Prod. Com. 2016, 11, 239–244.

20. Pandey, R.; Kumar, B. HPLC-QTOF–MS/MS-based rapid screening of phenolics and triterpenic acids in leaf extracts of Ocimum species and their interspecies variation. J. Liq. Chromatogr. Relat. Tech. 2016, 39, 225–238.

21. Enerstvedt, K.H.; Jordheim, M.; Andersen, O.M. Isolation and Identification of Flavonoids Found in Zostera marina Collected in Norwegian Coastal Waters. Am. J. Plant Sci. 2016, 7, 1163–1172.

22. Chen, W.; Gong, L.; Guo, Z.; Wang, W.; Zhang, H.; Liu, X.; Yu, S.; Xiong, L.; Luo, J. A novel integrated method for large-scale detection, identification, and quantification of widely targeted metabolites: Application in the study of rice metabolomics. Mol. Plant. 2013, 6, 1769–1780.

23. Pandey, B.P.; Pradhan, S.P.; Adhikari, K. LC-ESI-QTOF-MS for the Profiling of the Metabolites and in Vitro Enzymes Inhibition Activity of Bryophyllum pinnatum and Oxalis corniculata Collected from Ramechhap District of Nepal. Chem. Biodivers. 2020, 17, e2001555.

24. Li, X.; Tian, T. Phytochemical Characterization of Mentha spicata L. Under Differential Dried-Conditions and Associated Neoptoxicity Screening of Main Compound With Organ-on-a-Chip. Front. Pharmacol. 2018, 9, 1067.
25. Sun, L.; Tao, S.; Zhang, S. Characterization and Quantification of Polyphenols and Sterpenoids in Thinned Young Fruits of Ten Pear Varieties by UPLC-Q TRAP-MS/MS. *Molecules* 2019, 24, 159.

26. Ozarowski, M.; Piaecka, A.; Paszel-Jaworska, A.; Siqueira de A. Chaves, D.; Romanuik, A.; Rybczynska, M.; Gryszcynska, A.; Sawickowska, A.; Kachlicki, P.; Mikolajczak, P.L.; et al. Comparison of bioactive compounds content in leaf extracts of *Passiflora incarnata, P. caerulea* and *P. alata* and in vitro cytotoxic potential on leukemia cell lines. *Braz. J. Pharmacol.* 2018, 28, 179–191.

27. El-Sayed, M.A.; Abbass, F.A.; Refaat, S.; El-Shafae, A.M.; Fikry, E. UPLC-ESI-MS/MS Profile Of The Ethyl Acetate Fraction of Aerial Parts of Bougainvillea ‘Scarlett O’Hara’ Cultivated in Egypt. *Egypt. J. Chem.* 2021, 64, 22.

28. Hamed, A.R.; El-Hawary, S.S.; Ibrahim, R.M.; Abdelmohsen, U.R.; El-Halawany, A.M. Identification of Chemopreventive Components from *Halophytes* Belonging to Aizoaceae and Cactaceae Through LC/MS –Bioassay Guided Approach. *J. Chrom. Sci.* 2021, 59, 618–626.

29. Bodalska, A.; Kowalczyk, A.; Wlodarczyk, M.; Feska, I. Analysis of Polyphenolic Composition of a Herbal Medicinal Product—Peppermint Tincture. *Molecules* 2020, 25, 69.

30. Thomford, N.E.; Dzobo, K.; Chopera, D.; Wonkam, A.; Maroyi, A.; Blackhurst, D.; Dandara, C. In vitro reversible and time-dependent CYP450 inhibition profiles of medicinal herbal plant extracts *Neuwallia laevis* and *Cassia abbreviata*: Implications for herb-drug interactions. *Molecules* 2016, 21, 891.

31. Cirilini, M.; Mena, P.; Tassotti, M.; Herrlinger, K. A.; Nieman, K. M.; Dall’Asta, C.; Del Rio, D. Phenolic and volatile composition of a dry spearmint (*Mentha spicata* L.) extract. *Molecules* 2021, 26, 1007.

32. Shi, F.; Pan, H.; Lu, Y.; Ding, L. An HPLC-MS/MS method for the simultaneous determination of luteolin and its major metabolites in rat plasma and its application to a pharmacokinetic study. *J. Sep. Sci.* 2018, 41, 3830–3839.

33. Justesen, U. Negative atmospheric pressure chemical ionisation low-energy collision activation mass spectrometry for the characterisation of flavonoids in fresh herbs. *J. Chromatogr. A.* 2000, 92, 369–379.

34. Qin, D.; Wang, Q.; Li, H.; Jiang, X.; Fang, K.; Wang, Q.; Li, B.; Pan, C.; Wu, H. Identification of key metabolites based on non-targeted metabolomics and chemometrics analyses provides insights into bitterness in Kucha [Cameillia kucha (Chang et Wang) Chang]. *Food Res. Int.* 2020, 138, 109798.

35. Spinola, V.; Pinto, J.; Castilho, P.C. Identification and quantification of phenolic compounds of selected fruits from Madeira Island by HPLC-DAD-ESI-MSn and screening for their antioxidant activity. *Food Chem.* 2015, 173, 14–30.

36. Abu-Reidah, I.M.; Ali-Shtayeh, M. S.; Jamous, R. M.; Araas-Roman, D.; Segura-Carretero, A. HPLC-DAD-ESI-MS/MS screening of bioactive components from *Rhus coriaria* L. (sumac) fruits. *Food Chem.* 2015, 166, 179–191.

37. Rodríguez-Perez, C.; Gomez-Caravaca, A.M.; Guerra-Hernandez, E.; Cerretani, L.; Garcia-Villanova, B.; Verardo, V. Comprehensive metabolite profiling of *Solanum tuberosum* L. (potato) leaves T by HPLC-ESI-QTOF-MS. *Molecules* 2018, 112, 390–399.

38. Yin, N.-W.; Wang, S.-X.; Jia, L.-D.; Zhu, M.-C.; Yang, J.; Zhou, B.-J.; Yin, J.-M.; Lu, K.; Wang, R.; Li, J.-N.; et al. Identification and Characterization of Major Constituents in Different-Colored Rapeseed Petals by UPLC-HESI-MS/MS. *Agric. Food Chem.* 2019, 67, 11053–11065.

39. Viera, M.N.; Winterhalter, P.; Jerz, G. Flavonoids from the flowers of *Impatiens glandulifera* Royle isolated by high performance countercurrent chromatography. *Phytochem. Anal.* 2016, 27, 116–123.

40. Hanhineva, K.; Karenlampi, S.O.; Aharoni, A. Resent Advances in Strawberry Metabolomics. *Genes Genomes Genom.* 2011, 5, 65–75.

41. Oertel, A.; Matros, A.; Hartmann, A.; Arapitissa, P.; Dehmer, K.J.; Martens, S.; Mock, H.P. Metabolite profiling of red and blue potatoes revealed cultivar and tissue specific patterns for anthocyanins and other polyphenols. *Planta* 2017, 246, 281–297.

42. Rafsanjany, N.; Senker, J.; Brandt, S.; Dobrindt, U.; Hensel, A. In Vivo Consumption of Cranberry Exerts ex Vivo Antiadhesive Activity against FimH-Dominated Uropathogenic Escherichia coli: A Combined in Vivo, ex Vivo, and in Vitro Study of an Extract from *Vaccinium macrocarpon*. *J. Agric. Food Chem.* 2015, 63, 8804–8818.

43. Bujor, O.-C. Extraction, Identification and Antioxidant Activity of the Phenolic Secondary Metabolites Isolated from the Leaves, Stems and Fruits Of Two Shrubs of the *Eriaceae* Family. Ph.D. Thesis, Technical University of Iasi, Iasi, Romania, 2016.

44. Pharmacopoeia of the Eurasian Economic Union, Approved by Decision of the Board of Eurasian Economic Commission No. 100 Dated August 11, 2020. Available online: http://www.eurasiancommission.org/ru/act/txnreg/dept txnreg/LSMI/Documents/Фармакопея%20созюса%202011%202008.pdf (accessed on 7 February 2022)

45. Azmir, J.; Zaidul, I.S.M.; Rahman, M.M.; Sharif, K.; Mohamed, A.; Sahena, F.; Jahurul, M.; Ghafoor, K.; Norulaini, N.; Omar, A. Techniques for extraction of bioactive compounds from plant materials: A review. *J. Food Eng.* 2013, 117, 426–436.

46. Sharma, M.; Sandhir, R.; Singh, A.; Kumar, P.; Mishra, A.; Jachak, S.; Singh, S.P.; Singh, J.; Roy, J. Comparison analysis of phenolic compound characterization and their biosynthesis genes between two diverse bread wheat (*Triticum aestivum*) varieties differing for chapatti (unleavened flat bread) quality. *Front. Plant. Sci.* 2016, 7, 1870.

47. Geng, P.; Sun, J.; Zhang, M.; Li, X.; Harnil, J. M.; Chen, P. Comprehensive characterization of C-glycosyl flavones in wheat (*Triticum aestivum* L.) germ using UPLC-PDA-ESI/HRMS and mass defect filtering. *J. Mass Spectr.* 2016, 51, 914–930.

48. Stallmann, J.; Schweiger, R.; Pons, C. A.; Müller, C. Wheat growth, applied water use efficiency and flag leaf metabolome under continuous and pulsed deficit irrigation. *Sci. Rep.* 2020, 10, 1–13.

49. Llorente-Martinez, E.J.; Spinola, V.; Gouveia S.; Castilho, P.C. HPLC-ESI-MSn characterization of phenolic compounds, terpenoid saponins, and other minor compounds in *Bituminaria bituminosa*. *Ind. Crops Prod.* 2015, 69, 80–90.

50. De Freitas, M.A.; Silva Alves, A.I.; Andrade, J.C.; Leite-Andreade, M.C.; Lucas dos Santos, A.T.; de Oliveira, T.F.; dos Santos, F.; Silva Buenafina, M.D. Evaluation of the Antifungal Activity of the *Licania Riga* Leaf Ethanolic Extract against Biofilms Formed by *Candida* Sp. Isolates in Acrylic Resin Discs. *Antibiotics* 2019, 8, 250.
51. Zakharenko, A.M.; Razgonova, M.P.; Pikula, K.S.; Golokhvat, K.S. Simultaneous determination of 76 compounds of Rhodiola rosea extract using supercritical CO2-extraction and HPLC-ESI-MS/MS spectrometry. HINDAWI. Biochem. Res. Int. 2021, 2021, 9957490.

52. Zhu, Z.-W.; Li, J.; Gao, X.-M.; Amponsem, E.; Kang, L.-Y.; Hu, L.-M.; Zhang, B.-L.; Chang, Y.-X. Simultaneous determination of stilbenes, phenolic acids, flavonoids and anthraquinones in Radix polygoni multiflori by LC–MS/MS. J. Pharm. Biomed. Anal. 2012, 62, 162–166.

53. Wang, Y.; Vorsa, N.; Harrington, P.; Chen, P. Nontargeted Metabolomic Study on Variation of Phenolics in Different Cranberry Cultivars Using UPLC-IM-HRMS. Agric. Food Chem. 2018, 66, 12206–12216.

54. Vallverdu-Queralt, A.; Jauregui, O.; Medina-Román, A.; Lamuela-Raventos, R.M. Evaluation of a method to characterize the phenolic profile of organic and conventional tomatoes. J. Agric. Food Chem. 2012, 60, 3373–3380.

55. Jiang, R.-W.; Lau, K.-M.; Hon, P.-M.; Mak, T.C.W.; Woo, K.-S.; Fung, K.-P. Chemistry and Biological Activities of Caffeic Acid Derivatives from Salvia miltiorrhiza. Curr. Med. Chem. 2005, 12, 237–246.

56. Serrano, C.A.; Villena, G.K.; Rodriguez, E.F. Phytochemical profile and rosmarinic acid purification from two Peruvian Lepidium wild. species (Salviinae, Mentheae, Lamiaceae). Sci. Rep. 2021, 11, 7260.

57. Perchuk, I.; Shelenga, T.; Gurkina, M.; Miroshnichenko, E.; Burlyaeva, M. Composition of Primary and Secondary Metabolite Compounds in Seeds and Pods of Asparagus Bean (Vigna unguiculata (L.) Walp.) from China. Molecules 2020, 25, 3778.

58. Pan, M.; Lei, Q.; Zang, N.; Zhang, H. A Strategy Based on GC-MS/MS, UPLC-MS/MS and Virtual Molecular Docking for Analysis and Prediction of Bioactive Compounds in Eucalyptus Globules Leaves. Int. J. Mol. Sci. 2019, 20, 3875.

59. Paudel, L.; Wyzgoski, F.J.; Scheerens, J.C.; Chanon, A.M.; Reese, R.N.; Smiljanic, D.; Wesdemiotis, C.; Blakeslee, J.J.; Riedl, K.M.; Rinaldi, P.L. Nonanthocyanic secondary metabolites of black raspberry (Rubus occidentalis L.) fruits: Identification by HPLC-DAD, NMR, HPLC-ESI-MS, and ESI-MS/MS analyses. J. Agric. Food Chem. 2013, 61, 12032–12043.

60. Ruiz, A.; Hermosin-Gutiérrez, I.; Vergara, C.; von Baer, D.; Zapata, M.; Hitschfeld, A.; Obando, L.; Mardones, C. Anthocyanin profiles in south Patagonian wild berries by HPLC-DAD-ESI-MS/MS. Food Res. Int. 2013, 51, 706–713.

61. Sun, J.; Liu, X.; Yang, T.; Slovin, J.; Chen, P. Profiling polyphenols of two diploid strawberry (Fragaria vesca) inbred lines using UHPLC-HRMS®. Food Chem. 2014, 146, 289–298.

62. Marcia Fuentes, J.A.; Lopez-Salas, L.; Borras-Linares, I.; Navarro-Alarcon, M.; Segura-Carretero, A.; Lozano-Sanchez, J. Development of an Innovative Pressurized Liquid Extraction Procedure by Response Surface Methodology to Recover Bioactive Compounds from Carao Tree Seeds. Foods 2021, 10, 398.

63. Van Hoyweghen, L.; De Bosscher, K.; Haegeman, G.; Deforce, D.; Heyerick, A. In Vitro Inhibition of the Transcription Factor NF-κB and Cyclooxygenase by Bamboo Extracts. Phytother. Res. 2014, 28, 224–230.

64. Lee, S.Y.; Shaari, K. LC–MS metabolomics analysis of Stevia rebaudiana Bertoni leaves cultivated in Malaysia in relation to different developmental stages. Phytochem. Anal. 2021, 1–13. https://doi.org/10.1002/pca.3084

65. Simard, F.; Legault, J.; Lavoie, S.; Mshvidladze, V.; Fichette, A. Isolation and Identification of Cytotoxic Compounds from the Wood of Pinus resinosa. Phytother. Res. 2008, 22, 919–922.

66. Eklund, P.C.; Backman, M.J.; Kronberg, L.A.; Smeds, A.I.; Sjoholm, R.E. Identification of lignans by liquid chromatography-electrospray ionization ion-trap mass spectrometry. J. Mass Spectr. 2008, 43, 97–107.

67. D’Urso, G.; Sarais, G.; Lai, C.; Pizza, C.; Montoro, P. LC-MS based metabolomics study of different parts of myrtle berry from Sardinia (Italy). J. Berry Res. 2017, 7, 217–229.

68. Garg, M.; Chawla, M.; Chunduri, V.; Kumar, R.; Sharma, S.; Sharma, N.K.; Kaur, N.; Kumar, A.; Mundey, J.K.; Saini, M.K. Transfer of grain colors to elite wheat cultivars and their characterization. J. Cereal Sci. 2016, 71, 138–144.

69. Da Silva, L.P.; Pereira, E.; Pires, T.C.S.P.; Alves, M.J.; Pereira O.R.; Barros L.; Ferreira, I.C.F.R. Rhus alpinus Schott fruits: A detailed study of its nutritional, chemical and bioactive properties. Food Res. Int. 2019, 119, 34–43.

70. Vera de Rosso, V.; Hillebrand, S.; Cuevas Montilla, E.; Bobbio, F.O.; Winterhalter, P.; Mercadante, A.Z. Determination of anthocyanins from acerola (Malpighia emarginata DC.) and ac-ai (Euterpe oleracea Mart.) by HPLC–PDA–MS/MS. J. Food Compos. Anal. 2008, 21, 291–299.

71. Pantelic, M.M.; Dabic Zagorac, D.C.; Davidovic, C.M.; Todic, S.R.; Beslic, Z.S.; Gasic, U.M.; Tesic, Z.L.; Natic, M.M. Identification of phenolic compounds in berry skin, pulp, and seeds in 13 grapevine varieties grown in Serbia. Food. Chem. 2016, 211, 243–252.

72. Suarez Montenegro, Z.J.; Alvarez-Rivera, G.; Mendiola, J.A.; Ibanez, E.; Cifuentes, A. Extraction and Mass Spectrometric Characterization of Terpenes Recovered from Olive Leaves Using a New Adsorbent-Assisted Supercritical CO2 Process. Foods 2021, 10, 1301.

73. Xie, J.; Ding, C.; Ge, Q.; Zhou, Z.; Zhi, X. Simultaneous determination of ginkgolides A, B, C and bilobalide in plasma by LC–MS/MS and its application to the pharmacokinetic study of Ginkgo biloba extract in rats. J. Chromatogr. B 2008, 864, 87–94.

74. Kim, S.; Oh, S.; Noh, H.B.; Ji, S.; Lee, S.H.; Koo, J.M.; Choi, C.W.; Juhn, H.P. In Vitro Antioxidant and Anti-Propionibacterium acnes Activities of Cold Water, Hot Water, and Methanol Extracts, and Their Respective Ethyl Acetate Fractions, from Sanguisorba officinalis L. Roots. Molecules 2018, 23, 3001.

75. Ekeberg, D.; Flate, P.-O.; Eikenes, M.; Fongen, M.; Naess-Andresen, C.F. Qualitative and quantitative determination of extractives in heartwood of Scots pine (Pinus sylvestris L.) by gas chromatography. J. Chromatogr. A 2006, 1109, 267–272.

76. Patnala, S.; Kanfer, I. Medicinal use of Sceletium: Characterization of Phytochemical Components of Sceletium Plant Species using HPLC with UV and Electrospray Ionization-Tandem Mass Spectroscopy. J. Pharm. Pharm. Sci. 2015, 18, 414–423.
77. Yang, S.T.; Wu, X.; Rui, W.; Guo, J.; Feng, Y.F. UPLC-Q-TOF-MS analysis for identification of hydrophilic phenolics and lipo-philic diterpenoids from Radix Salviee Millotrhizae. Acta Chromatogr. 2015, 27, 711–728.

78. Thomas, M.C.; Dunn, S.R.; Altwater, J.; Dove, S.G.; Nette, G.W. Rapid Identification of Long-Chain Polyunsaturated Fatty Acids in a Marine Extract by HPLC-MS Using Data-Dependent Acquisition. Anal. Chem. 2012, 84, 5976–5983.

79. Park, S.K.; Ha, J.S.; Kim, J.M.; Kang, J.Y.; Lee, D.S.; Guo, T.J.; Lee, U.; Kim, D.-O.; Heo, H.J. Antiamnesic Effect of Broccoli (Brassica oleracea var. italicai) Leaves on Amyloid Beta (Aβ)1-42-Induced Learning and Memory Impairment. J. Agric. Food Chem. 2016, 64, 3353–3361.

80. Mercadante, A.Z.; Rodrigues, D.B.; Petry, F.C.; Barros Mariutti, L.R. Carotenoid esters in foods—A review and practical directions on analysis and occurrence. Food Res. Int. 2017, 99, 830–850.

81. Zoccali, M.; Giuffrida, D.; Salafia, F.; Giofre, S.V.; Mondello, L. Carotenoids and apocarotenoids determination in intact human blood samples by online supercritical fluid extraction-supercritical fluid chromatography-tandem mass spectrometry. J. Pharm. Biomed. Anal. 2018, 103, 40–47.

82. Chen, X.; Zhu, P.; Liu, B.; Wei, L.; Xu, Y. Simultaneous determination of fourteen compounds of Hedyotis diffusa Willd extract in rats by UHPLC-MS/MS method: Application to pharmacokinetics and tissue distribution study. J. Pharm. Biomed. Anal. 2018, 159, 490–512.

83. Lara-Abia, S.; Lobo-Rodrigo, G.; Welti-Chanes, J.; Pilar Cano, M. Carotenoid and Carotenoid Ester Profile and Their Deposition in Plastids in Fruits of New Papaya (Carica papaya L.) Varieties from the Canary Islands. Roots. Foods 2021, 10, 434.

84. Geodakyan, S.V.; Voskoboinikova, I.V.; Tjukavkina, N.A.; Sokolov, S.J. Experimental pharmacokinetics of biologically active plant phenolic compounds. I. Pharmacokinetics of mangiferin in the rat. Phytother. Res. 1992, 6, 332–334.

85. Han, D.; Chen, C.; Zhang, C.; Zhang, Y.; Tang, X. Determination of mangiferin in rat plasma by liquid–liquid extraction with UPLC–MS/MS. J. Pharm. Biomed. Anal. 2010, 51, 260–263.

86. Wu, Y.; Xu, J.; He, Y.; Shi, M.; Han, X.; Li, W.; Zhang, X.; Wen, X. Metabolic Profiling of Pitaya (Hylocereus polyrhizus) during Fruit Development and Maturation. Molecules 2019, 24, 1114.

87. Li, Z.-X.; Zhu, H.; Cai, X.-P.; He, D.-D.; Hua, J.-L.; Ju, J.-M.; Lv, H.; Ma, L.; Li, W.-L. Simultaneous determination of five triterpene acids in rat plasma by liquid chromatography–mass spectrometry and its application in pharmacokinetic study after oral administration of Falium Eriobotryae effective fraction. Biomed. Chromatogr. 2015, 29, 1791–1797.

88. Jin, L.; Schmiech, M.; El Gaafary, M.; Zhang, X.; Syrovets, T.; Simmet, T. A comparative study on root and bark extracts of Eleutherococcus senticosus and their effects on human macrophages. Phytotherapy 2020, 68, 153181.

89. Eitzel, L.; Pfeiffer, A.; Weber, F.; Schieber, A. Characterization of carotenoid profiles in goldenberry (Physalis peruviana L.) fruits at various ripening stages and in different plant tissues by HPLC-DAD-APCI-MSn. Food Chem. 2018, 245, 508–517.

90. Petry, F.C.; Mercadante, A.Z. Composition by LC-MS/MS of New Carotenoid Esters in Mango and Citrus. J. Agric. Food Chem. 2016, 64, 8207–8224.

91. Mi, J.; Jia, K.-P.; Wang, J.Y.; Al-Babili, S. A rapid LC-MS method for qualitative and quantitative profiling of plant apocarotenoids. Anal. Chim. Acta 2018, 1035, 87–95.

92. Delgado-Pelayo, R.; Homero-Mendez, D. Identification and Quantitative Analysis of Carotenoids and Their Esters from Sarsaparilla (Smilax aspera L.) Berries. J. Chromatogr. A 2012, 60, 8225–8232.

93. Heskes, A.M.; Goodger, J.Q.D.; Tsegay, S.; Quach, T.; Williams, S.J.; Woodrow, I.E. Localization of Oleuropeyol Glucose Esters and a Flavanone to Secretory Cavities of Myrtaceae. PLoS ONE 2012, 7, e40856.