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# Global metabolome profiles of *Lonicera caerulea L.* and *Lonicera caerulea ssp. kamtschatica* (Sevast.) Gladkova

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**Abstract:** *Lonicera caerulea,* commonly known as honeysuckle, is widespread on the Eurasian continent. Its berries are rich in bioactive compounds. However, limited studies have explored the metabolome composition of the berries of varieties and wild accessions in different subspecies of *L. caerulea.* Herein, the metabolomic compositions of four varieties of *L. caerulea* ssp. *caerulea* and one variety and five wild accessions of *L. caerulea* ssp. *kamtschatica* (Sevast.) Gladkova were investigated using high-performance liquid chromatography-electrospray ionization-tandem mass spectrometry (HPLC-ESI-MS) and ESI-MS/MS. As a result, 151 compounds were identified in the two *L. caerulea* subspecies. In total, 88 and 84 compounds were detected in *L. caerulea* and *L. caerulea* ssp. *kamtschatica*, respectively. Twenty-one compounds were common in both subspecies, whereas 67 and 63 compounds were specific to each subspecies, respectively. The honeysuckle berries were rich in polyphenols including flavonoids, flavanones, flavanols, flavan-3-ols, and anthocyanins. The metabolome of the *L. caerulea* berries had high compound diversity (39 compound classes) compared to that of *L. caerulea* ssp. *kamtschatica* (27 compound classes). Of the detected metabolites, 44 compounds were tentatively newly identified, consisting of 37 polyphenols and seven others. Prevalent anthocyanins in the two subspecies were different, such that the *L. caerulea* berries had delphinidins, pelargonidins, and peonidins, whereas the *L. caerulea* ssp. *kamtschatica* berries had cyanidins, delphinidins, and peonidins. These results provide new data on the metabolome composition of honeysuckle berries, which is important for the future exploration into the health benefits of honeysuckle berries.

**Key words:** Anthocyanins, flavonoids, honeysuckle berries, *Lonicera caerulea*, *Lonicera caerulea ssp. Kamtschatica*, metabolomics, polyphenols, tandem mass spectrometry

## 1. Introduction

Blue honeysuckle (*Lonicera caerulea* L.) and *Lonicera caerulea* ssp. *kamtschatika* are widespread on the Eurasian continent, mainly in its northern part and come from high mountainous or humid regions. This plant is used both as a food source and in traditional medicine in the Siberian part of Russia, and Asian countries including China and Japan (Mikulic-Petkovsek et al., 2012; Perova et al., 2023). Its berries are soft to hard, bluish to dark purple, with a length and width of 1–2 cm and 1 cm, respectively. The plants can withstand fairly low temperatures (–40 °C) (Senica et al., 2018a). More than 180 compounds have been reported in the fruits of honeysuckle. Honeysuckle berries contain more than 85% moisture, followed by fiber (~8%), crude protein (~2%), fats (>0.1%), and carbohydrates (~0.9%). They are rich in amino acids and their derivatives, vitamins, minerals, sugars (e.g., fructose, glucose, sucrose, saccharose, sorbitol, and others), phenolic acids, flavonoids, terpenoids, fatty acids, organic acids, and carotenoids (Senica et al., 2018b, Zhang et al., 2023). Based on the presence of a range of vitamins, several studies have referred to it as a "super fruit" compared to citrus fruits (Rupasinghe et al., 2018).

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Regular consumption of the berries have been associated with health benefits such as the prevention of chronic diseases (e.g., diabetes and cardiovascular diseases) (Sharma and Lee, 2021). Research has highlighted that the berries are rich in polyphenols, such as tannins, anthocyanins/anthocyanidins, and phenolic acids. These may provide mild protection in the prevention of various metabolic disorders, including lipid imbalance, thereby protecting against severe disorders associated with diseases such as nonalcoholic fatty liver disease (Gołba et al., 2020). Of the phenolic compounds, cyanidin-3-*O*-glucoside, the most abundant anthocyanin in nature, has been found to be predominant. An earlier study demonstrated that cyanidin-3-*O*-glucoside, isolated from blue honeysuckle, improved insulin biosynthesis, which then led to activation of the insulin signaling pathway. Moreover, it has also been implicated in reactive oxygen species (ROS) homeostasis by the activation of antioxidant processes (Park et al., 2017). Anthocyanins can improve metabolism by activating adenosine monophosphate-activated protein kinase (AMPK). Kim et al. (2010) showed that AMPK inactivates hepatic steatosis in animal models induced by a high-fat diet. Other than their beneficial health properties, these anthocyanins and flavonols contribute to the distinct blue color of the berries (Liu et al., 2023). The metabolomic composition of honeysuckle fruits also offers other health benefits. These include activities such as antiobesity, antiinflammatory, antidiabetic, antitumor, cardioprotective, protection from lung inflammation, and several other protective effects on the liver and thyroid (Gołba et al., 2020; Bieniek et al., 2021).

The phytochemical composition also offers several benefits to the plants themselves for growth and development and resistance to stresses (Li et al., 2022). Thus, the range of compounds present in honeysuckle plants can also be beneficial for the plants' interaction with the environment. For example, one study found that metabolites related to alkaloid biosynthesis, the tricarboxylic acid cycle, phenylpropanoid biosynthesis, and terpenoid biosynthesis were upregulated in salt-stressed plants compared to the control (Cai et al., 2020). Similarly, honeysuckle plants increase their phenolic acid contents under salt stress (Yan et al., 2017). These studies highlight that the understanding of the metabolome is important under natural and stress conditions for both the growth and development of plants, as well as health-related applications. However, as noted in our recent work, the metabolome composition of honeysuckle fruits can differ within varieties as well as under different growth conditions (Razgonova, et al., 2023a). Other researchers have also highlighted that honeysuckle berries collected from different locations differ in their primary and secondary metabolite contents (Senica et al., 2018a). Considering that honeysuckle is grown on a wide geographical range on the Eurasian continent, continued exploration of the metabolomic composition of different varieties grown under different conditions is needed. This information is useful for both the discovery of new compounds as well as to understand the impact of growing honeysuckle at different locations, so that appropriate strategies can be adapted to harvest the desired metabolomic contents for medicinal uses.

Herein, the metabolome composition of extracts from *L. caerulea* berries (four varieties) and *L. caerulea ssp. kamtschatica* berries (one variety and five wild accessions) were investigated using high-performance liquid chromatography-electrospray ionization-tandem mass spectrometry (HPLC-ESI-MS) and ESI-MS/MS analyses.

## 2. Materials and methods

### 2.1. Plant material

Six *L. caerulea ssp. kamtschatica* accessions and four *L. caerulea* varieties were studied. The *L. caerulea ssp. kamtschatica* varieties (wild accession No. 1, wild accession No. 2, wild accession No. 3, wild accession No. 4, wild accession No. 5, and the Elena variety) were collected and grown in Kamchatsky Scientific Research Institute, Kamchatka, Russia (N 43°6′34″, E 131°52′41″). Four *L. caerulea* varieties (Goluboe vereteno, Tomichka, Amfora, and Volhova) were collected and grown in N.I. Vavilov All-Russian Institute of Plant Genetic Resources, Primorsky Territory (N. 53°11′, E 158°23′). The plants were grown according to the agricultural practices recommended by the institute. Ripened berries were collected during the last week of July 2023 from three-year-old plants (Figure 1). Triplicate samples were collected for each accession/variety. For sampling, three healthy plants were selected, and berries were collected from all sides of each plant and considered as one replicate. Care was taken to collect healthy, disease- and insect-free berries. The samples were washed with distilled water and stored at –80 °C until processed. All the samples morphologically corresponded to the pharmacopoeial standards of the State Pharmacopoeia of the Russian Federation (Commission 2020).

### 2.2. Global metabolome analysis

Analytical grade reagents used were purchased for the analyses. HPLC grade acetonitrile and MS grade formic acid were procured from Fisher Scientific (Southborough, United Kingdom) and Sigma-Aldrich (Steinheim, Germany), respectively.

Berries (50 g) stored at –80 °C were used for the extraction via fractional maceration. The extraction was carried out according to the method described in our previous study (Razgonova, et al., 2023a). The LC and MS processing of the extracts, experimental conditions,

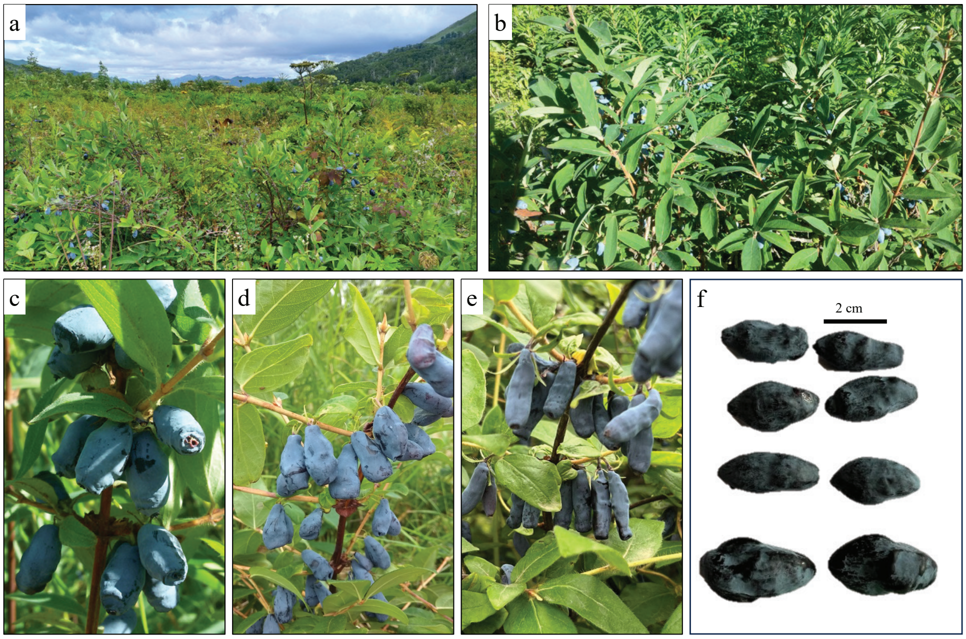


**Figure 1.** Representative figure of the *L. caerulea ssp. kamtschatica* samples used for the metabolome analysis. a–b) *L. caerulea ssp. kamtschatica* growing in the N.I. Vavilov All-Russian Institute of Plant Genetic Resources, Primorsky Territory. c) wild *L. caerulea spp. kamtschatica* No. 4, d) wild *L. caerulea spp. kamtschatica* No. 5, e) wild *L. caerulea spp. kamtschatica* Elena, and f) berries of *L. caerulea* (photos by E. Rusakova).

equipment, column, reagents, software, and detection were also performed as described in our previous study (Razgonova, et al., 2023a).

**2.3[1]. Data analysis**

The detected compounds were annotated according to a database built and maintained by Far Eastern Federal University, Russia. Moreover, the PubChem database was used for annotating the compounds[1]. Bar plots were prepared using Microsoft Excel 2019 (Microsoft Corp., Redmond, WA, USA). The Venn diagram was prepared using InteractiVenn (Heberle et al., 2015). Scatter plots were prepared in TBtools (Chen et al., 2020).

## 3. Results

### 3.1. Global metabolome profiles of *L. caerulea* and *L. caerulea spp. kamtschatica*

In order to achieve the highest resolution and signal in the shortest amount of run time, the HPLC conditions were optimized. For the purpose of separating the polyphenol chemicals, a variety of chromatographic parameters, including the gradient program, injection volume, flow rate, column temperature, and mobile phase composition, were investigated and optimized. The gradient program was evaluated at a flow rate of 0.25 mL/min with several mobile phase compositions (ethanol–water, ethanol–0.1% (v/v) formic acid aqueous solution, acetonitrile–water, and acetonitrile–0.1% (v/v) formic acid aqueous solution) (data not shown). The maximum number of peaks in the berry extracts of *L. caerulea* and *L. caerulea* ssp. kamtschatica within 60 min were resolved best using a mobile phase consisting of 0.1% (v/v) formic acid aqueous solution (A) and acetonitrile (B) at a flow rate of 0.25 mL/min and column temperature of 50 °C.

A total of 151 compounds were detected from the berry extracts of *L. caerulea* and *L. caerulea kamtschatica*: 101 chemical compounds from the polyphenol group and 44 others (Appendix 1). The polyphenols belonged to subclasses such as lignans, coumarins, stilbenes, flavan-3-ols, flavones, flavonols, phenolic acids, anthocyanidins, etc. Overall, the detected metabolites were annotated to 41 compound classes (Figure 2a). Of these, 88 and 84 compounds were detected in *L. caerulea* and *L. caerulea spp. kamtschatica,* respectively; 21 compounds were common in both subspecies (Figure 2b). The highest number of metabolites were flavonols (20), followed by flavone (18), anthocyanins (17), phenolic acids (11), flavan-3-ols (1), and hydroxycinnamic acid (8) (Figure 2a). These numbers indicate that the *L. caerulea* berries are rich in flavonoids. Moreover, the observation of a higher number of anthocyanins indicates their roles in the color formation of the berries.

[1]https://pubchem.ncbi.nlm.nih.gov/ [accessed on 29 July 2024].

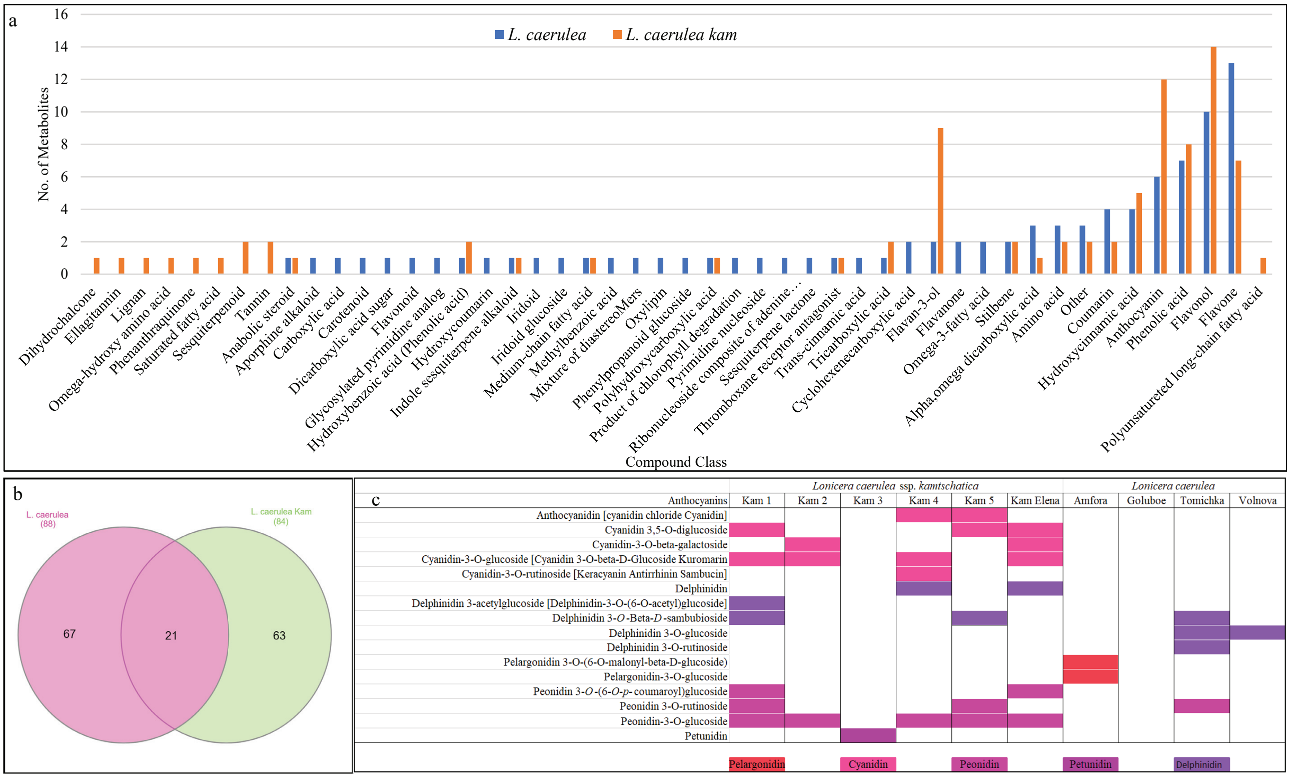


**Figure 2.** Statistics summary of the metabolite compounds detected in *L. caerulea* and *L. caerulea* spp. *kamtschatika.* a) Bar plot of the number of metabolites for each compound class. b) Venn diagram showing the number of common and specific metabolites. The Venn diagram was prepared using InteractiVenn (Heberle et al., 2015). c) Anthocyanins were detected in the extracts of the *L. caerulea* and *L. caerulea* spp. *kamtschatika* berries. Kam = *L. caerulea* spp. *kamtschatika.*

Of the detected compounds, 67 and 63 were specifically detected in both *L. caerulea* and *L. caerulea spp. kamtschatica,* respectively, whereas 21 were common in the two types of honeysuckle (Figure 2b). The detection of the 21 compounds in both indicated fair similarities between the two subspecies. This similarly was particularly characterized by the occurrence of polyphenols, including flavonols, flavones, phenolic acids, and others (Appendix 1).

Anthocyanins are major color forming pigments in honeysuckle berries (Guo et al., 2023). The extract analyses of the berries of both *L. caerulea* (four varieties) and *L. caerulea* ssp. *kamtschatica* (six accessions) by employing HPLC-ESI-MS and ESI-MS/MS resulted in the detection of 16 anthocyanins. A notable result was that the berry extracts of the four *L. caerulea* varieties contained delphinidin 3-*O*-glucoside, delphinidin 3-*O*-rutinoside, delphinidin 3-*O*-*b*-*D*-sambubioside, pelargonidin 3-*O*-(6-*O*-malonyl-*b*-*D*-glucoside), pelargonidin-3-*O*-glucoside, and peonidin 3-O-rutinoside. However, cyanidins were absent from the extracts of the *L. caerulea* berries, whereas those of the *L. caerulea* ssp. *kamtschatica* berries had cyanidins, delphinidins, and peonidins, but lacked pelargonidins (Figure 2c). These observations provided interesting insight into the color formation mechanism of both subspecies and indicated the need for further exploration of the key pathways at the metabolome and transcriptome levels.

### 3.2. Newly detected compounds in *L. caerulea* and *L. caerulea spp. kamtschatica*

Of the detected metabolites in the berries of the two *L. caerulea* subspecies, 37 polyphenols and seven other compounds were identified for the first time. These included flavones (2'-hydroxygenistein, diosmetin *O*-hexoside, chrysoeriol *O*-diglucoside), flavonols (myricetin, astragalin, kaempferol-3-*O*-glucoside, taxifolin-3-*O*-hexoside, kaempferol glycosyl-rhamnoside, kaempferol-3,7-di-*O*-glucoside), flavan-3-ols (*(epi)*-catechin *O*-hexoside, *(epi)*-gallocatechin-*(epi)*-catechin dimer, lignan syringaresinol, coumarin 4-methylesculetin), etc. Whereas the other newly detected compound classes in the berries were omega-hydroxy amino acid (hydroxy decenoic acid), saturated fatty acid (hydroxydodecenoic acid), sesquiterpenoid (atractylenolide II), polyunsaturated long-chain fatty acid (hexadecadienoic acid), and phenanthraquinone tanshinone V, etc.

Several of the newly and tentatively identified collision-induced dissociation (CID)-spectrums of the chemical compounds in the *L. caerulea spp. kamtschatika* berry extracts are presented in Figure 3. Among the newly identified metabolites, neochlorogenic acid was found in the *L. caerulea spp. kamtschatika* berry extracts (Figure 3a). The $[M-H]^-$ ion produced a fragment ion with *m/z* 191.22, which further produced a characteristic daughter ion with *m/z* 172.64. This fragment ion with *m/z* 172.64 further produced one daughter ion (*m/z* 126.80). The *L. caerulea spp. kamtschatika* extracts also contained phenanthraquinone tanshinone (Figure 3b) and the dihydrochalcone phloretin (Figure 3c). The $[M+H]^+$ ion produced one fragment ion with *m/z* 257.19 (Figure 3c), which produced a characteristic daughter ion (*m/z* 230.08). This fragment ion further produced one daughter ion with *m/z* 229.24. However, stilbene resveratrol was identified in both the *L. caerulea* and *L. caerulea spp. kamtschatica* berry extracts (Figure 3d-e). The $[M+H]^+$ ion produced one fragment ion with *m/z* 179.17 (Figure 3e). The fragment ion with *m/z* 179.17 produced one characteristic daughter ion with *m/z* 151.22.

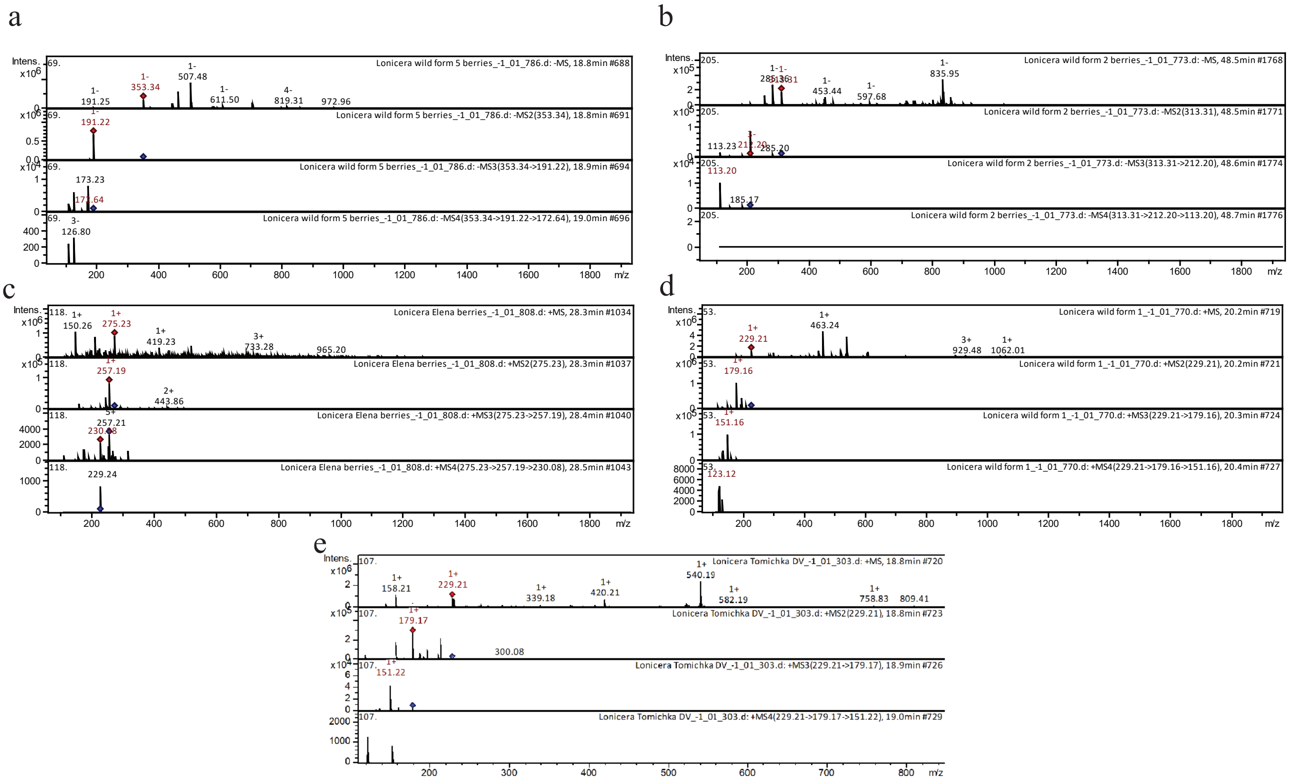


**Figure 3.** Collision-induced spectrum of the newly identified compounds from the extracts of the *L. caerulea* and *L. caerulea spp*. berries. *kamtschatica.* a) CID-spectrum of neochlorogenic acid from extracts of the *L. caerulea spp. kamtschatica* (wild form 5) berries, *m/z* 353.34. At the top is an MS scan in the range of 100–1700 m/z, at the bottom are fragmentation spectra (from top to bottom): MS2 of the protonated neochlorogenic acid ion (353.34 *m/z*, red diamond), MS3 of the fragment 353.34→191.22 *m/z* and MS4 of the fragment 353.34→191.22 →172.64 *m/z.* b) CID-spectrum of tanshinone from extracts from berries of *L. caerulea spp. kamtschatica* (wild form 2), *m/z* 313.31. At the top is an MS scan in the range of 100–1700 m/z, at the bottom are fragmentation spectra (from top to bottom): MS2 of the protonated tanshinone ion (313.31 *m/z*, red diamond), MS3 of the fragment 313.31→212.20 *m/z* and MS4 of the fragment 313.31→212.20→113.20 *m/z.* c) CID-spectrum of phloretin from extracts from berries of *L. caerulea spp. kamtschatica* (Elena variety), *m/z* 275.23. At the top is an MS scan in the range of 100–1700 m/z, at the bottom are fragmentation spectra (from top to bottom): MS2 of the protonated phloretin ion (275.23 *m/z*, red diamond), MS3 of the fragment 275.23→257.19 *m/z* and MS4 of the fragment 275.23→257.19→230.08 *m/z.* d) CID-spectrum of resveratrol from extracts of the *L. caerulea spp. kamtschatica* (wild form 1) berries, *m/z* 229.21. At the top is an MS scan in the range of 100–1700 m/z, at the bottom are fragmentation spectra (from top to bottom): MS2 of the protonated resveratrol ion (229.21 *m/z*, red diamond), MS3 of the fragment 229.21→179.16 *m/z* and MS4 of the fragment 229.21→179.16 →151.16 *m/z.* e) CID-spectrum of resveratrol from extracts of the *L. caerulea* (Tomichka variety) berries, *m/z* 229.21. At the top is an MS scan in the range of 100–1700 m/z, at the bottom are fragmentation spectra (from top to bottom): MS2 of the protonated resveratrol ion (229.21 *m/z*, red diamond), MS3 of the fragment 229.21→179.17 *m/z* and MS4 of the fragment 229.21→179.17→151.22 *m/z.*

**3.3. Metabolome profiles of the berries of the four *L. caerulea varieties***

The metabolome analysis of the berries harvested from the four varieties of *L. caerulea* resulted in the identification of 88 compounds (Figure 4a; Appendix 1). These metabolites were annotated to 39 compound classes (Figure 4b). The highest number of metabolites was detected in the extract from the berries of the Tomichka variety (57), followed by the Amfora (34), Volhova (32), and Goluboe (18) varieties. Seven metabolites, i.e. Herbacetin, kaempferol, 2,3,4,5,6-pentahydroxybenzoic acid, caffeic acid isoprenyl ester, L-Histidine, anonaine, and 3,4,8,9,10-Penthahydroxydibenzo[b,d]pyran-6-one were common to all four varieties (Appendix 1).

In addition to the highest number of detected metabolites, the Tomichka berry extract also contained 30 specific metabolites. These results indicated that the Tomichka berries are richer in metabolites such as flavonoids, amino acids, anthocyanins, coumarins, flavonols, hydroxycinnamic acid, and phenolic acids (Appendix 1).

Among others, the Amfora berry extract contained the second highest number (19) of exclusively detected metabolites. The Amfora berry metabolome was relatively more diverse than that of the Goluboe berries. It was composed of amino acid (L-histidine), anthocyanins, alkaloid, coumarins, flavan-3-ols, flavones, and flavonols. It also contained two omega-3-fatty acids (stearidonic acid and linolenic acid). Adenosine (ribonucleoside composite of adenine), sesquiterpene lactone (artemisinin C), vapiprost, and citric acid were the key components in the Amfora berries. Among them, the notable detection of apigenin, gallocatechin, citric acid, adenosine, and linolenic acid implies its beneficial health properties (Appendix 1).

While the Goluboe berry extract contained a limited number of metabolites, it contained four unique compounds, i.e. dihydroxy-tetramethoxy(iso)flavone, calycosin-7-O-beta-D-glucoside-6”-O-malonate, and pinosylvin, caffeoyl shikimic acid (Appendix 1).

However, the Volhova berry extract contained five exclusively accumulated compounds, i.e. a derivative of trihydroxy eicosatetraenoic acid, butin,3,4-O-dicaffeoylquinic acid, quercetin rhamnosyl hexoside, and monotropein. These results clearly indicated that the studied varieties contain a diverse range of metabolites. Considering the beneficial health properties of monotropein, i.e. the suppression of $H_2O_2$-evoked ROS production in osteoblasts (Ieri et al., 2013), it is a notable observation in the Volhova berry extract (Appendix 1).

**3.4. Metabolome profiles of berries of the six *L. caerulea spp. accessions***

The metabolome analysis of the berries harvested from the six accessions of *L. caerulea* ssp. *kamtschatica* resulted in the identification of 84 compounds (Figure 4c; Appendix 1). These metabolites were assigned to 27 compound classes (Figure 4d). The highest number of metabolites was detected in the Elena berry extract (35), followed by accessions wild No. 5 (34), wild No. 1 (26), wild No. 4 (19), and wild No. 2 and No. 3 (17 each). The berries of all six types of *L. caerulea spp. kamtschatica* studied accumulated compounds belonging to anthocyanins, flavan-3-ols, flavones, flavonols, and indole sesquiterpene alkaloid. Wild No. 1 was the richest in anthocyanins, followed by the Elena variety, wild No. 4 and No. 5, wild No. 2, and wild No. 3. Wild No. 5 was the richest in flavonols and phenolic acids.

The wild No. 1 berry metabolome was mostly composed of flavones, flavonols, flavan-3-ols, anthocyanins, hydroxycinnamic acid, phenolic acids, lignan and coumarin, amino acid, and indole sesquiterpene alkaloid. Notably, the presence of amino acid L-theanine and sespendole are important for their beneficial health and antimicrobial activity properties, respectively (Appendix 1).

The wild No. 2 berry metabolome showed a relatively less diverse compound class diversity. The extracts contained flavone, flavonol, flavone, flavan-3-ols, anthocyanins, ellagic acid (a hydroxybenzoic acid), tanshinone V (phenanthraquinone), and sespendole (Appendix 1).

The wild No. 3 berry metabolome, similar to that of wild No. 2, was less diverse. However, its composition was different from that of wild No. 2. In addition to flavone, flavonols, flavan-3-ols, and anthocyanin (only petunidin), several other compounds were detected, such as hydroxycinnamic acid, hydroxybenzoic acid, hydroxydodecenoid acid, vapiprost, and sespendole (Appendix 1).

The wild No. 4 berry metabolome was composed of flavone, flavanols, flavan-3-ols, anthocyanin, tannin (and ellagitannin), tricarboxylic acid, vapiprost, and sespendole (Appendix 1).

The wild No. 5 berry metabolome was the richest of the five wild accessions, as it contained flavones, flavonols, flavan-3-ols, anthocyanins, hydroxycinnamic acid, phenolic acids, L-histidine (and hydroxy decanoic acid), citric acid, vebonol, and sespendole (Appendix 1).

The Elena berry extract had the most diverse metabolome, as in addition to the above-mentioned compounds, it also included dihydrochalcone, stilbene, quinic acid, sebacic acid, caryophyllene oxide, atractylenolide II, hydroxy decanoic acid, and pheophorbide a (Appendix 1).

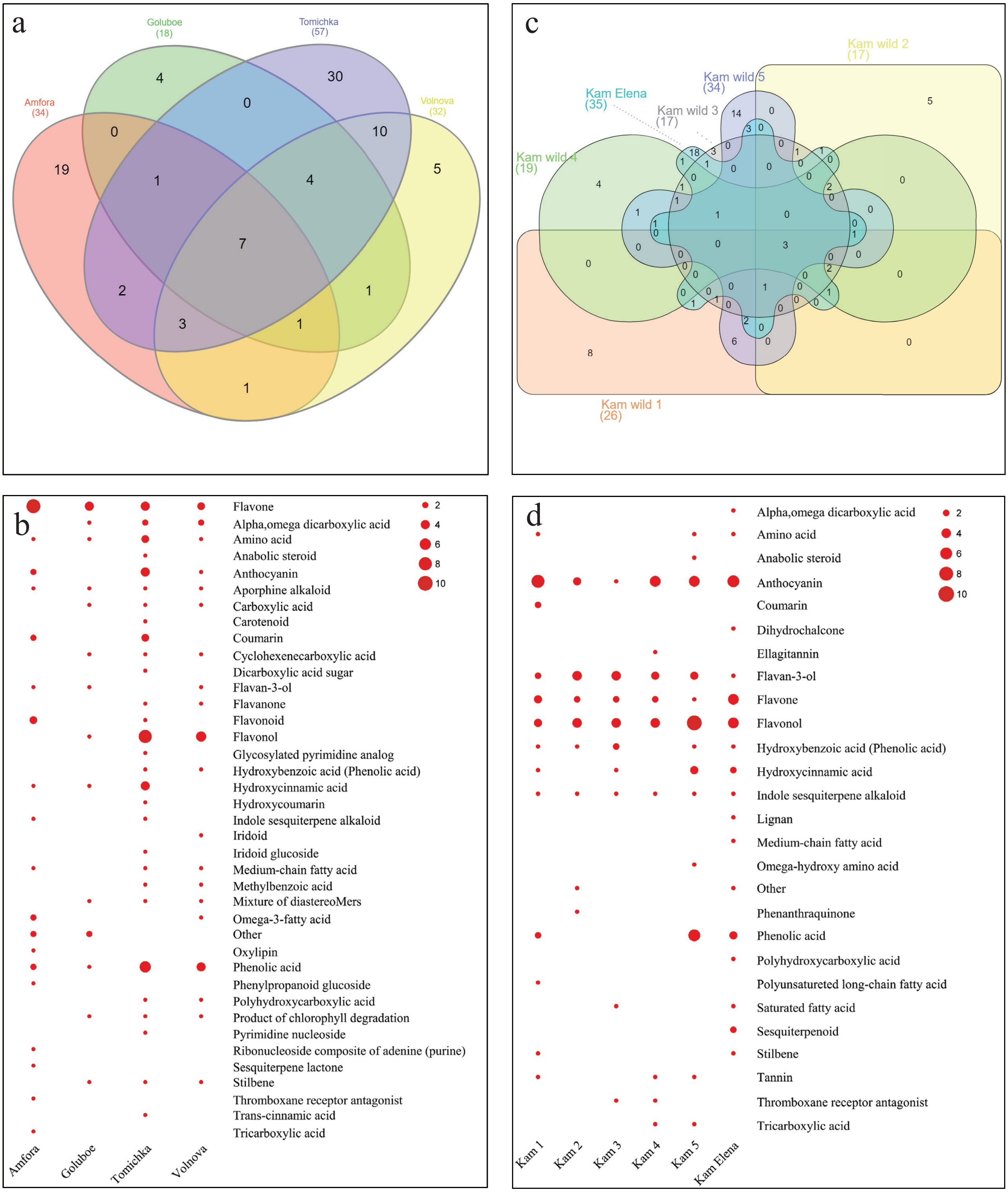


**Figure 4.** Metabolome composition of *L. caerulea* and *L. caerulea* spp. *kamtschatica.* a) Venn diagram showing the number of metabolites and b) scatter plot of the number of metabolites belonging to different compound classes detected in the four varieties of *L. caerulea.* c) Venn diagram showing the number of metabolites and d) scatter plot of the number of metabolites belonging to different compound classes detected in the six accessions of *L. caerulea* ssp. *kamtschatica.* The red circles in Figures b and d refer to the number of metabolites in each compound class. The absence of a circle indicates that there was no compound detected in that class. Kam 1–5 and Kam Elena in Figure d refer to the five wild accessions and variety of *L. caerulea* spp. *kamtschatica.*

**4. Discussion**

Honeysuckle fruits are source of flavonoids and anthocyanins, which impart health-promoting effects upon consumption. Earlier research on this species revealed how the accumulation patterns of different secondary metabolites, sugars, amino acids, and organic acids change during fruit development [29]. *Lonicera caerulea* L. has seven subspecies (Boyarskikh, 2020). To date, knowledge on the comparative metabolome compositions of these subspecies is scarce. However, owing to the reported health benefits, it is essential to explore the similarities and differences in their metabolome profiles. The current study reported the comparative metabolome analysis of the berries of two subspecies, i.e. *L. caerulea* L. subsp. *caerulea* and *L. caerulea* subsp. *kamtschatica.* For each subspecies, the available accessions and/or varieties were investigated via HPLC-ESI-MS and ESI-MS/MS analyses.

Honeysuckle berries contain organic acids, free amino acids, polyols, free fatty acids, monosaccharides, oligosaccharides, lignans and coumarins, phenolic acids, lipids, nucleotides and their derivatives, and, most importantly, flavonoids and anthocyanins (Lee et al., 2015; Shelenga et al., 2022). In this regard, the results herein, that the metabolome of *L. caerulea* varieties is composed of lignans, coumarins, flavonoids, stilbenes, phenolic acids, and anthocyanins (Figure 2), are consistent with the literature. Notably, the large proportion of the polyphenol class indicates the usefulness of both subspecies for studying their beneficial health impacts. This is because polyphenols are a highly functional class of compounds that have been linked to antioxidant, reduced risk of myocardial infarction, diabetes, heat stroke, inflammation, and improvement in blood pressure, antimicrobial, antibacterial effects (Rana et al., 2022). The common metabolites between the two subspecies indicated their collective usefulness. Contrarily, the detection of specific compounds within each subspecies indicated that the species differ in their metabolome composition, which is a novel observation in honeysuckle. Differences in the metabolome composition of subspecies exist in several plant species, e.g., pine (Rivas-Ubach et al., 2017), *japonica* and *indica* rice (Hu et al., 2014), brassica subspecies (Zheng et al., 2022), etc. Such differences are useful for breeding individual subspecies for the increased production of specific compounds, in addition to being helpful in subspecies identification at the metabolite level as well as metabolome-based genome-wide association (Wei et al., 2021). The presence of 16 anthocyanins in the two subspecies indicated that these are major pigments in *L. caerulea* (Guo et al., 2023). Differences in the composition of the anthocyanins can be associated with the ultimate color of the berries. For example, the presence of delphinidins, pelargonidins, and peonidins in *L. caerulea* corresponds to their fruit color, i.e. purple to dark purple. However, the combined presence of cyanidins, delphinidins, and peonidins in *L. caerulea* ssp. *kamtschatica* may be associated with the observable difference in their berries from those of *L. caerulea* (Figure 1). Notable factors in the color formation are copigmentation and temperature (Khoo et al., 2017). Since the two subspecies were grown at different locations, differences in the climate may have been a factor affecting the anthocyanin and other metabolite accumulation. The results herein, that within each subspecies, the accessions/varieties differed in their anthocyanin contents (Figure 2c), suggest that there may have been an effect resulting from their genetic background as well as the environment. This is consistent with the earlier reports that the anthocyanin content of berries can be different between related species and cultivars within a species (Ponder et al., 2021).

Apart from anthocyanins, the accumulation of other metabolites in the individual varieties/accessions highlighted their respective importance. The fact that the Tomichka berry extract had highest detected metabolites (as well as 30 specific compounds) among the *L. caerulea* varieties, indicated its usefulness in the food and health industries. Tomichka has been included in the State Register of Russia since 1987[22]. The results on its metabolite composition are useful knowledge for its usage in breeding for new *L. caerulea* varieties. Concomitantly, the detection of stearidonic acid, linolenic acid, adenosine, L-histidine, artemisinin C, vapiprost, and citric acid in Amfora indicated that its consumption will impart a range of health benefits (Walker et al., 2013; Thornthwaite et al., 2017). However, the presence of specific metabolites in other varieties, i.e. Goluboe and Volhova, also suggested that their consumption is useful for improving health, although their metabolome showed a limited number of variety-specific compounds. Particularly, the observation that the Volhova berries contained monotropein, indicated that their consumption might improve health. It has been reported that monotropein suppresses the $H_2O_2$-evoked ROS production in osteoblasts (Ieri et al., 2013). Here, it is important to note that the location it is grown at, the growth stage, and genetic background of the varieties can be notable factors responsible for such differences. This has been shown in other plant species, such as *Echinacea purpurea* (Xu et al., 2022), maize (Asiago et al., 2012), *Lycium barbarum* (Wang et al., 2020), etc. In the case of *L. caerulea* ssp. *kamtschatica*, there were fewer compound classes detected than in *L. caerulea* (Figure 4). This may have been due to either their different genetic makeup or the environment where they were grown (Ponder et al., 2021). Nevertheless, the Elena variety and other wild accessions in this subspecies offer a range of common

[2]https://bakcharopss.ru/catalog/ [accessed on 15 December 2023]

and specific compounds. Specifically, the polyphenol compositions of the studied variety and accessions highlight their potentially beneficial health impacts (Rana et al., 2022). Berries of the Elena variety and wild No. 1 can be good candidates for their use as parents for improved variety development as well as testing the beneficial health properties of the diverse range of compounds they contain. The L-theanine detected in wild No. 1 has been previously linked with disease prevention and health promoting activity (Williams et al., 2016). The commonly detected compound sespendole in the Elena variety and five wild accessions is a sesquiterpene and has been reported for its antibacterial activity (Kudo et al., 2018). Ellagic acid and tanshinone V were detected in wild No. 2. These two compounds have been linked with vascular health, and cardiovascular and therapeutic benefits (Larrosa et al., 2010), respectively. Similarly, the specific compounds identified in the other wild accessions and Elena variety indicated the usefulness of each accession/variety as a food and resource for the health industry. Taken together, it was concluded that the two subspecies differ in the metabolome profiles of their berries. Within each subspecies, the individual varieties and/or accessions also have different metabolome compositions.

Secondary metabolites are commonly found in fruit crops and are important for antioxidant defense and improving health in humans (Yao et al., 2004). The results herein finding 37 polyphenols and seven compounds from other groups highlighted that the health benefits of *L. caerulea* should be further explored. Among these, several compounds have been reported to have beneficial health effects. For example, 2'-hydroxygenistein can suppress [3]-dihydrotestosterone due to its receptors and offer greater antioxidant capacity than its other forms (Son et al., 2019). Among the flavonols, astragalin (antitumor activity) (Wang et al., 2021), myricetin (anticancer, antidiabetic, antiobesity, cardiovascular protection, osteoporosis protection, antiinflammatory, and hepatoprotective activity), kaempferol-3-*O*-glucoside (hepatoprotective activity) (Wang et al., 2015), and taxifolin-3-*O*-hexoside (antioxidant activity) have been reported for their health benefits. Similarly, the flavan-3-ols can act as cardio preventive, antioxidant, antiviral, anticarcinogen, antimicrobial, and neuroprotective agents upon consumption (Aron and Kennedy, 2008). However, the other detected compounds, such as hydroxy decenoic acid (bactericidal and antiinflammatory activity) (Yang et al., 2018), atractylenolide II (attenuation of wasting in chronic kidney disease) (Wang et al., 2019), and tanshinone V (antiantioxidant and anticancer activity) (Ansari et al., 2021) have been reported to have protective effects against several conditions. Therefore, their detection in the respective subspecies of *L. caerulea* contribute to the existing list of beneficial compounds in their berries.

## 5. Conclusions

The present study described a comparative metabolome profile of the berries of two subspecies of honeysuckle, i.e. *L. caerulea* and *L. caerulea ssp. kamtschatica*. The berries of the two subspecies differed in their metabolome composition either due to growing at different locations or owing to their different genetic backgrounds. The varieties and/or wild accessions within each subspecies also differed in terms of the berry metabolome profiles. The HPLC-ESI-MS and ESI-MS/MS analyses suggested that *L. caerulea* and *L. caerulea ssp. kamtschatica* berries are rich in polyphenols. The predominant classes of polyphenols in the berries of the two subspecies were flavonoids, flavanones, flavonols, flavan-3-ols, and anthocyanins. Additionally, they contained several other metabolite classes including phenolic acids, indole sesquiterpene alkaloids, iridoid glucosides, phenolic acids, phenylpropanoid glucosides, amino acids and derivatives, nucleotides and derivatives, omega-hydroxy amino acid, etc. Furthermore, more than 40 tentatively newly identified compounds were also determined from studied varieties/accessions.

## Conflicts of interest

The authors declare that there are no conflicts of interest.

## Author contributions

Conceptualization: NT, MAN, KG, SE, and MR; methodology: MR and MAN; software: MR; validation: MAN, MR, OC, and KG; formal analysis: MAN, ER, EP, AS, and MR; investigation: KG, NT, SE, and MR; resources: KG and MR; data curation: MAN, NT, AS, ER, EP, and OC; writing—original draft preparation: NT, MAN, and MR; writing:—review and editing: MAN, MR, and NT; visualization: MAN, MR, and NT; supervision: NT, and SE; and project administration: KG, MAN, SE, and MR. All the authors have read and approved the published version of the manuscript.

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**Appendix 1.** Approximate comparison of the chemical constituents identified in the *L. caerulea* and *L. caerulea ssp. kamtschatica* varieties obtained from two different regions.

| № | Class of compounds | Identification | Formula | Calculated mass | Observed mass [M-H]- | Observed mass [M+H]+ | MS/MS Stage 1 fragmentation | MS/MS Stage 2 fragmentation | MS/MS Stage 3 fragmentation | References |
|---|---|---|---|---|---|---|---|---|---|---|
| **1** | **Flavone** | **Apigenin** | $C_{15}H_{10}O_5$ | **270.2369** | | **271** | 225 | 179 | | *Lonicera henryi* (Jaiswal et al., 2014), *Lonicera japonica* (Cai et al., 2019), Andean blueberry (Aita et al., 2021), *Ribes meyeri* (Zhao et al., 2021) , |
| **2** | **Flavone** | **Trihydroxy(iso) flavone** | $C_{15}H_{10}O_5$ | **270.2369** | | **271** | 197 | 129 | | Propolis (Belmehdi et al., 2021) , |
| **3** | **Flavone** | **2'-Hydroxygenistein** | $C_{15}H_{10}O_6$ | **286.2363** | | **287** | 231 | 165 | | Mexican lupine species (Wojakowska et al., 2013) |
| **4** | **Flavone** | **Jaceosidin** [5,7,4'-trihydroxy-6',5'-dimethoxyflavone] | $C_{17}H_{14}O_7$ | **330.2889** | | **331** | 303; 203 | 203; 157 | 175 | *Artemisia argyi* (Chang et al., 2021), Mentha (Xu et al., 2017) |
| **5** | **Flavone** | **Cirsiliol** | $C_{17}H_{14}O_7$ | **330.2889** | **329** | | 229; 311 | 211 | 211 | *Juglans mandshurica* (Huo et al., 2018), *Inula viscosa* (Kheyar-Kraouche et al., 2018) |
| **6** | **Flavone** | **Pentahydroxy dimethoxyflavone** | $C_{17}H_{14}O_9$ | **362.2877** | | **363** | 344; 300; 256 | 238; 146 | | *Glottiphyllum linguiforme* (Hamed et al. 2021) |

**Appendix 1.** (Continued.)

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| 7 | **Flavone** | **Dihydroxy-tetramethoxy(iso) flavone** | $C_{19}H_{18}O_8$ | **374.3414** | | **375** | 345 | 245 | 175; 227 | Propolis (Belmehdi et al., 2021) |
| 8 | **Flavone** | **Luteolin 7-*O*-glucoside** [Cynaroside] | $C_{21}H_{20}O_{11}$ | **448.3769** | | **449** | 287 | 213 | 185 | *Lonicera henryi* (Jaiswal et al., 2014), *Lonicera japonica* (Cai et al., 2019) |
| 9 | **Flavone** | **Chrysoeriol O-hexoside** | $C_{22}H_{22}O_{11}$ | **462.4035** | | **463** | 445; 243 | | | *Triticum aestivum* (Wojakowska et al., 2013) |
| 10 | **Flavone** | **Diosmetin O-hexoside** | $C_{22}H_{22}O_{11}$ | **462.4035** | | **463** | 301 | 286 | 258 | Andean blueberry (Aita et al., 2021) |
| 11 | **Flavone** | **Formononetin-7-O-glucoside-6”-O-malonate** | $C_{25}H_{24}O_{12}$ | **516.4509** | | **517** | 271 | 243 | | *Astragali radix* (Zhang et al., 2015), (Huang et al., 2009)_ |
| 12 | **Flavone** | **Calycosin-7-O-beta-D-glucoside-6”-O-malonate** | $C_{25}H_{24}O_{13}$ | **532.4503** | | **533** | 287 | 273; 236 | | *Astragali radix* (Zhang et al., 2015), (Huang et al., 2009) |
| 13 | **Flavone** | **C-hexosyl-apigenin O-rhamnoside** | $C_{27}H_{30}O_{14}$ | **578.5187** | | **579** | 561; 337; 317 | 319; 262 | 161 | *Triticum aestivum* (Cavaliere et al., 2005) |
| 14 | **Flavone** | **Lonicerin** [Luteolin-7-O-Rhamnoside; Veronicastroside; Scolymoside] | $C_{27}H_{30}O_{15}$ | **594.5181** | | **595** | 449; 287 | 287 | 287; 153 | *Lonicera japonica* (Cai et al., 2019), *Exocarpium Citri Grandis* (Zeng et al., 2018) |

**Appendix 1.** (Continued.)

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| **15** | **Flavone** | **Chrysoeriol O-diglucoside** | $C_{28}H_{32}O_{16}$ | **624.5441** | | **625** | 301; 463 | 286 | 258 | Mexican lupine species (Wojakowska et al., 2013) |
| **16** | **Flavonol** | **Kaempferol** | $C_{15}H_{10}O_6$ | **286.2363** | | **287** | 269; 149 | 239; 181 | | *Lonicera japonica* (Cai et al., 2019), Andean blueberry (Aita et al., 2021), *Ribes meyeri* (Zhao et al., 2021), *Rhus coriaria* (Abu-Reidah et al., 2015) |
| **17** | **Flavone** | **Rhamnocitrin** | $C_{16}H_{12}O_6$ | **300.2629** | | **301** | 273 | 245 | 217; 177; 131 | *Astragali radix* (Zhang et al., 2015), *Lonicera caerulea* (Razgonova et al. 2023a) |
| **18** | **Flavonol** | **Quercetin** | $C_{15}H_{10}O_7$ | **302.2357** | | **303** | 257; 146 | 229 | 201; 145 | *Ribes meyeri* (Zhao et al., 2021), Propolis (Belmehdi et al., 2021), *Capsicum annuum* (Pascale et al., 2020) |
| **19** | **Flavone** | **Herbacetin [3,5,7,8-Tetrahydroxy-2-(4-hydroxyphenyl)-4H-chromen-4-one]** | $C_{15}H_{10}O_7$ | **302.2357** | | **303** | 203 | 175 | | *Lonicera caerulea* (Razgonova et al. 2023a), *Rhodiola rosea* (Zapesochnaya et al., 1985) |

**Appendix 1.** (Continued.)

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| **20** | **Flavonol** | **Isorhamnetin** [Isorhamnetol; Quercetin 3’-Methyl ether; 3-Methylquercetin] | $C_{16}H_{12}O_7$ | **316.2623** | **315** | | 283 | 255; 211 | 227 | Andean blueberry (Aita et al., 2021), *Spondias purpurea* (Engles et al., 2012) |
| **21** | **Flavonol** | **Myricetin** | $C_{15}H_{10}O_8$ | **318.2351** | | **319** | 273; 219 | 191 | 209 | Andean blueberry (Aita et al., 2021), Grape (Flamini, 2013), *Juglans mandshurica* (Huo et al., 2018) |
| **22** | **Flavonol** | **Astragalin** [Kaempferol 3-O-glucoside] | $C_{21}H_{20}O_{11}$ | **448.3769** | | **449** | 287 | 287; 229 | 203 | *Lonicera japonica* (Cai et al., 2019), *Ribes meyeri* (Zhao et al., 2021), *Juglans mandshurica* (Huo et al., 2018), *Spondias purpurea* (Engles et al., 2012), Bee-pollen (Mosic et al., 2019) |
| **23** | **Flavonol** | **Kaempferol-3-O-hexoside** | $C_{21}H_{20}O_{11}$ | **448.3769** | | **449** | 287 | 287; 231 | 230; 111 | Andean blueberry (Aita et al., 2021), *Punica granatum* (Mena 2012), *Rhus coriaria* (Abu-Reidah et al., 2015), *Cuphea ignea* (Ismail et al., 2022) |

**Appendix 1.** (Continued.)

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| **24** | **Flavonol** | **Quercetin 3-*O*- glucoside** [Isoquercitrin; Hirsutrin] | $C_{21}H_{20}O_{12}$ | **464.3763** | | **465** | 303 | 229; 165 | 201; 161 | *Lonicera Henryi*; (Jaiswal et al., 2014), *Lonicera japonica* (Cai et al., 2019), Andean blueberry (Aita et al., 2021), *Ribes meyeri* (Zhao et al., 2021), *Spondias purpurea* (Engles et al., 2012), *Rubus occidentalis* (Paudel et al., 2013) |
| **25** | **Flavonol** | **Taxifolin-3-O-hexoside** [Dihydroquercetin-3-O-hexoside] | $C_{21}H_{22}O_{12}$ | **466.3922** | **465** | | 285 | 241 | 197 | Chilean currants (Burgos-Edwards et al. 2018), Andean blueberry (Aita et al., 2021), *Euphorbia hirta* (Mekam et al., 2019) |
| **26** | **Flavonol** | **Kaempferol 3-O-rutinoside** | $C_{27}H_{30}O_{15}$ | **594.5181** | | **595** | 449; 287 | 287 | 287 | *Lonicera japonica* (Cai et al., 2019), *Ribes meyeri* (Zhao et al., 2021), *Spondias purpurea* (Engles et al., 2012) |
| **27** | **Flavonol** | **Kaempferol glucosyl-rhamnoside** | $C_{27}H_{30}O_{15}$ | **594.5181** | | **595** | 449; 287 | 287 | 287 | *Ribes nigrum* (Zhao et al., 2021) |
| **28** | **Flavonol** | **Quercetin 3-O-pentosyl hexoside** | $C_{26}H_{28}O_{16}$ | **596.4909** | | **597** | 303; 257; 211 | 257; 195; 165 | 229 | *Ferocactus pottsii* (Hamed et al., 2021), (Engles et al., 2012) *Spondias purpurea* |

**Appendix 1.** (Continued.)

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| 29 | **Flavonol** | **Rutin** (Quercetin 3-*O*-rutinoside) | $C_{27}H_{30}O_{16}$ | **610.5175** | | **611** | 303 | 257; 165 | 229 | *Lonicera Henryi* (Jaiswal et al., 2014), (Burgos-Edwards 2018), *Ribes magellanicum* (Burgos-Edwards 2018), *Lonicera japonica* (Cai et al., 2019), *Ribes meyeri* (Zhao et al., 2021), *Spondias purpurea* (Engles et al., 2012, ), *Rubus occidentalis* (Paudel et al., 2013) |
| 30 | **Flavonol** | **Kaempferol-3,7-Di-O-glucoside** | $C_{27}H_{30}O_{16}$ | **610.5175** | | **6111** | 287; 449 | 287; 213 | 213 | Rapeseed petals (Yin et al., 2019), *Taraxacum officinale* (Aabideen et al., 2020) |
| 31 | **Flavonol** | **Isorhamnetin 3-O-(6”-*O*-rhamnosyl-hexoside)** | $C_{28}H_{32}O_{16}$ | **624.5441** | | **625** | 317 | 302 | | *Lonicera henryi* (Jaiswal et al., 2014), Bee-pollen (Mosic et al., 2019) |
| 32 | **Flavonol** | **Kaempferol derivative** | $C_{27}H_{32}O_{17}$ | **628.5328** | **627** | | 465; 285 | 285 | 241 | *Cuphea ignea* (Ismail et al., 2022) |
| 33 | **Flavonol** | **Dimethylquercetin-3-*O*-dehexoside** | $C_{29}H_{34}O_{17}$ | **654.5701** | **653** | | 507; 353; 311 | 329 | 287; 190 | *Capsicum annuum* (Pascale et al.,2020) |
| 34 | **Flavonol** | **Quercetin deoxyhexosyl deoxyhexosyl hexoside** | $C_{33}H_{40}O_{20}$ | **756.6587** | **755** | | 300; 489; 737 | 271 | 243 | *Ribes meyeri* (Zhao et al., 2021) |

**Appendix 1.** (Continued.)

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| 35 | **Flavonol** | **Quercetin pentosyl hexoside hexoside** | $C_{32}H_{38}O_{21}$ | **758.6315** | | **758** | 670; 479; 319 | 415 | | *Ferocactus glaucescens* (Hamed et al., 2021) |
| 36 | **Flavonol** | **Derivative of Quercetin rhamnosyl hexoside** | $C_{36}H_{46}O_{22}$ | **830.7372** | **829** | | 609 | 301 | 300 | PubChem |
| 37 | **Flavan-3-ol** | **Epiafzelechin** [(epi) Afzelechin] | $C_{15}H_{14}O_5$ | **274.2687** | | **275** | 245; 219; 175 | 215; 193; 175; 157; 127 | 175; 157; 145 | *Alchorea cordifolia; Ferocactus glaucescens; Ferocactus herrerae* (Hamed et al., 2021), *Cassia abbreviata* (Sobeh et al., 2018) |
| 38 | **Flavan-3-ol** | **Catechin** | $C_{15}H_{14}O_6$ | **290.2681** | | **291** | 261; 157 | 191 | 173 | *Ribes magellanicum* (Burgos-Edwards et al., 2018), *Ribes meyeri* (Zhao et al., 2021) |
| 39 | **Flavan-3-ol** | **(Epi)-catechin** | $C_{15}H_{14}O_6$ | **290.2681** | | **291** | 273; 137 | | | *Vaccinium myrtillus* (Liu et al., 2014), Andean blueberry (Aita et al., 2021), *Carpobrotus edulis* (Senica et al. 2018), Grape (Flamini, 2013), *Radix polygoni multiflori* (Zhu et al., 2012), *Rubus occidentalis* (Paudel et al., 2013) |

**Appendix 1.** (Continued.)

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| **40** | **Flavan-3-ol** | **Gallocatechin** [+(-) Gallocatechin] | $C_{15}H_{14}O_{7}$ | **306.2675** | | **307** | 261; 243; 163; 137 | 187; 159 | 131 | *Glottiphyllum linguiforme* (Hamed et al. 2021), *Embelia* (Vijayan and Raghu, 2019), *Ribes meyeri* (Zhao et al., 2021) |
| **41** | **Flavan-3-ol** | **(Epi)-catechin derivative** | | **379** | | **379** | 261 | 233 | 151 | Pubchem |
| **42** | **Flavan-3-ol** | **(Epi)-afzelechin derivative** | $C_{18}H_{16}O_{10}$ | **392.3136** | | **393** | 275; 245; 215 | 245; 175 | 175; 127 | *Zostera marina* (Vijayan and Raghu, 2019) |
| **43** | **Flavan-3-ol** | **(Epi)-catechin derivative** | $C_{18}H_{16}O_{11}$ | **408.313** | | **409** | 291; 275 | 261; 242; 208; 173 | 244; 214; 191; 173; 160; 124 | PubChem |
| **44** | **Flavan-3-ol** | **(Epi)-catechin derivative** | | **424** | | **425** | 291 | 261; 191 | 191 | PubChem |
| **45** | **Flavan-3-ol** | **(epi)Catechin O-hexoside** | $C_{21}H_{24}O_{11}$ | **452.4087** | | **453** | 289; 129 | 129 | 111 | Andean blueberry (Aita et al., 2021) |
| **46** | **Flavan-3-ol** | **(Epi)gallocatechin-(epi) catechin dimer** | $C_{30}H_{26}O_{13}$ | **594.5286** | | **595** | 577; 409; 247 | 229 | 183 | Grape (Flamini, 2013) Carao tree seeds (Marcia Fuentes et al., 2021) |
| **47** | **Flavanone** | **Naringenin** [Naringetol; Naringenine] | $C_{15}H_{12}O_{5}$ | **272.5228** | | **273** | 153; 189 | 111 | | *Andean blueberry* (Aita et al., 2021) *G. linguiforme* ; *Mexican lupine species [51]; Exocarpium, Citri Grandis* (Zeng 2018) Rapeseed petals (Yin et al., 2019) |
| **48** | **Flavanone** | **Butin [7,3',4'-Trihydroxyflavanone]** | $C_{15}H_{12}O_{5}$ | **272.0681** | | **273** | 153 | 171 | 153 | *Ribes meyeri* (Zhao et al., 2021) |

**Appendix 1.** (Continued.)

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| **49** | **Tannin** | **Proanthocyanidin B1** [Procyanidin Dimer B1] | $C_{30}H_{26}O_{12}$ | **578.5202** | | **579** | 409; 291 | 287 | 245 | *Vaccinium myrtillus* (Liu et al., 2014), Andean blueberry (Aita et al., 2021), Blackberry (Wang et al., 2016) strawberry (Aaby et al., 2012) |
| **50** | **Tannin** | **Proanthocyanidin B-type** | $C_{30}H_{26}O_{13}$ | **594.5196** | | **595** | 287; 449 | 213 | | *Actinidia* (Chen et al., 2021) |
| **51** | **Ellagitannin** | **Di-O-galloyl-HHDP-glucose** [Heterophylliin A; Pedunculagin II] | $C_{34}H_{26}O_{22}$ | **786.557** | | **786** | 599; 761 | 301 | | *Cuphea ignea* (Ismail et al., 2022), *Punica granatum* (Kachkoul et al., 2020) |
| **52** | **Anthocyanin** | **Anthocyanidin [cyanidin chloride; Cyanidin]** | $C_{15}H_{11}O_{6+}$ | **287.2442** | | **287** | 286; 270; 247; 205 | 221 | 201 | Andean blueberry (Aita et al., 2021), *Ferocactus herrerae* (Hamed et al., 2021), *Phoenix dactylifera* (Said et al., 2017) |
| **53** | **Anthocyanin** | **Delphinidin** | $C_{15}H_{11}O_{7}$ | **303.2436** | | **303** | 257; 165 | 229 | | *A. cordifolia* [70]; Wines (Fermo 2021, ) |
| **54** | **Anthocyanin** | **Petunidin** | $C_{16}H_{13}O_{7+}$ | **317.2702** | | **318** | 256 | 238; 113 | 238 | *A. cordifolia; C. edulis* (Senica et al. 2018) |
| **55** | **Anthocyanin** | **Pelargonidin-3-O-glucoside (callistephin)** | $C_{21}H_{21}O_{10}$ | **433.3854** | | **431** | 257; 331 | 227 | 215 | Strawberry (Aaby et al., 2012) *Rubus ulmifolius* (Da Silva and 34-43 2019,); Black currant (Elderberry Burgos-Edwards et al., 2018) |

**Appendix 1.** (Continued.)

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| **56** | **Anthocyanin** | **Cyanidin-3-O-glucoside** [Cyanidin 3-O-beta-D-Glucoside; Kuromarin] | $\mathbf{C_{21}H_{21}O_{11}+}$ | **449.3848** | | **449** | 287 | 213 | 185 | *Ribes magellanicum* (Burgos-Edwards et al., 2018); Black currant (Burgos-Edwards et al. 2018), Gooseberry, Chokeberry, Elderberry, Red currant (Wang 2016); *Berberis ilicifolia; Berberis empetrifolia; Ribes maellanicum; Ribes cucullatum; Myrteola nummalaria; Gaultheria mucronata; Gaultheria antarctica; Rubus geoides; Fuchsia magellanica* (Ruiz et al., 2013) |
| **57** | **Anthocyanin** | **Cyanidin-3-O-beta-galactoside** | $\mathbf{C_{21}H_{21}O_{11}}$ | **449.3848** | | **449** | 287 | 287; 213 | 185 | Rapeseed petals (Yin et al., 2019), *Gaultheria mucronata* (Ruiz et al., 2013), Black soybean (Xu et al., 2017) |

**Appendix 1.** (Continued.)

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| 58 | **Anthocyanin** | **Peonidin-3-O-glucoside** | $C_{22}H_{23}O_{11+}$ | **463.4114** | | **463** | 301 | 286 | 258 | Andean blueberry (Aita et al., 2021), Black currant (Elderberry Burgos-Edwards et al., 2018), Gooseberry (Wang 2016), *Berberis ilicifolia; Berberis empetrifolia* (Ruiz et al., 2013), Black soybean (Xu et al., 2017) |
| 59 | **Anthocyanin** | **Delphinidin 3-O-glucoside** | $C_{21}H_{21}O_{12+}$ | **465.3905** | | **465** | 303 | 257; 165 | 229; 201 | *Ribes magellanicum* (Burgos-Edwards et al., 2018), Rapeseed petals (Yin et al., 2019), Black currant (Wang et al., 2016), *Berberis ilicifolia; Berberis empetrifolia; Ribes maellanicum; Ribes cucullatum; Myrteola nummalaria* (Ruiz et al., 2013) |
| 60 | **Anthocyanin** | **Delphinidin 3-acetylglucoside** [Delphinidin-3-O-(6-O-acetyl)glucoside] | $C_{23}H_{23}O_{13+}$ | **507.4209** | | **507** | 303 | 257 | 229 | Grape (Flamini, 2013) Wines (Fermo et al., 2021) |
| 61 | **Anthocyanin** | **Pelargonidin 3-O-(6-O-malonyl-beta-D-glucoside)** | $C_{24}H_{23}O_{13}$ | **519.4388** | | **519** | 271 | 243 | 197 | *Lonicera caerulea* (Razgonova et al., 2023a), Strawberry (Aaby et al., 2012) |

**Appendix 1.** (Continued.)

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| 62 | **Anthocyanin** | **Cyanidin-3-O-rutinoside** [Keracyanin; Antirrhinin; Sambucin] | $C_{27}H_{31}O_{15}$ | **595.526** | | **595** | 287; 449 | 213 | | *Ribes magellanicum* (Burgos-Edwards et al., 2018), *Berberis ilicifolia; Berberis empetrifolia; Ribes maellanicum; Ribes cucullatum* (Ruiz et al., 2013) |
| 63 | **Anthocyanin** | **Delphinidin 3-*O*-Beta-*D*-sambubioside** | $C_{26}H_{29}O_{16}$ | **597.4989** | | **597** | 303; 465; 229 | 229; 165 | 201; 172 | Red currant [104] |
| 64 | **Anthocyanin** | **Peonidin 3-O-rutinoside** | $C_{28}H_{33}O_{15}$ | **609.5526** | | **609** | 463; 301 | 286 | | *Gaultheria ucronate; Gaultheria antarctica* (Ruiz et al., 2013) |
| 65 | **Anthocyanin** | **Peonidin 3-*O*-(6-*O*-*p*-coumaroyl)glucoside** | $C_{31}H_{29}O_{13}$ | **609.554** | | **609** | 301; 542 | 258 | | Grape (Flamini, 2013)<br>Wines (Fermo et al., 2021) |
| 66 | **Anthocyanin** | **Delphinidin 3-O-rutinoside** | $C_{27}H_{31}O_{16}$ | **611.5254** | | **611** | 303 | 257; 165 | 229 | Black currant (Elderberry Burgos-Edwards et al., 2018) *Berberis ilicifolia; Berberis empetrifolia; Ribes maellanicum; Ribes cucullatum* (Ruiz et al., 2013) |
| 67 | **Anthocyanin** | **Cyanidin 3,5-O-diglucoside** | $C_{27}H_{31}O_{16}$ | **611.5335** | | **611** | 287; 449 | 213 | 185 | Grape (Flamini, 2013),<br>Rapeseed petals (Yin et al., 2019) |
| 68 | **Anthocyanin** | **Petunidin-3-rutinoside** | $C_{28}H_{33}O_{16}$ | **625.552** | | **625** | 317; 479 | 302; 139 | 274; 229; 153 | Black currant (Elderberry Burgos-Edwards et al., 2018), *Berberis ilicifolia; Berberis empetrifolia* (Ruiz et al., 2013) |

**Appendix 1.** (Continued.)

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| **69** | **Hydroxybenzoic acid (Phenolic acid)** | **Protocatechuic acid** | $C_7H_6O_4$ | **154.1201** | | **155** | 127 | | | *Lonicera japonica* (Cai et al., 2019), *Ribes meyeri* (Zhao et al., 2021) |
| **70** | **Hydroxycinnamic acid** | **Caffeic acid** | $C_9H_8O_4$ | **180.1574** | | **181** | 135 | 119 | | *Lonicera japonica* (Cai et al., 2019), *Ribes meyeri*; *Rubus occidentalis* (Paudel et al., 2013) |
| **71** | **Methylbenzoic acid** | **Methylgallic acid** [Methyl gallate] | $C_8H_8O_5$ | **184.1461** | | **185** | 139 | 111 | | Andean blueberry (Aita et al., 2021); Grape (Flamini 2013, ) ; *Lonicera caerulea* [23] |
| **72** | **Hydroxycinnamic acid** | **3,4-Dihydroxyhydrocinnamic acid [Dihydrocaffeic acid]** | $C_9H_{10}O_4$ | **182.1733** | | **183** | 155 | 127 | **145** | Chilean currants (Burgos-Edwards 2018, ) |
| **73** | **Trans-cinnamic acid** | **Ferulic acid** | $C_{10}H_{10}O_4$ | **194.184** | **193** | | 176 | 132 | | *Lonicera japonica* (Cai et al., 2019), Andean blueberry (Aita et al., 2021); *Juglans mandshurica* (Huo et al., 2018,) |
| **74** | **Phenolic acid** | **Hydroxy methoxy dimethylbenzoic acid** | $C_{10}H_{12}O_4$ | **196.1999** | | **197** | 160 | 151 | | *Ferocactus herrerae; Ferocactus glaucescens* (Hamed et al., 2021) |
| **75** | **Phenolic acid** | **2,3,4,5,6-pentahydroxybenzoic acid** | $C_7H_6O_7$ | **202.1183** | | **203** | 156 | 129 | | *Jatropha* (Zengin et al., 2021) |
| **76** | **Hydroxycinnamic acid** | **Hydroxyferulic acid** | $C_{10}H_{10}O_5$ | **210.1834** | | **211** | 193 | 75; 147 | 157; 129 | Andean blueberry (Aita et al., 2021), *Rosa davurica* (Razgonova et al., 2022) |
| **77** | **Hydroxycinnamic acid** | **Sinapic acid** [trans-Sinapic acid] | $C_{11}H_{12}O_5$ | **224.21** | | **225** | 207; 179 | 151; 123 | 123 | Andean blueberry (Aita et al., 2021), Rapeseed petals (Yin et al., 2019) |

**Appendix 1.** (Continued.)

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| **78** | **Hydroxybenzoic acid (Phenolic acid)** | **Ellagic acid** [Benzoaric acid; Elagostasine; Lagistase; Eleagic acid] | $C_{14}H_6O_8$ | **302.1926** | **301** | | 257 | 229 | 201 | *Punica granatum* (Mena et al., 2012), Grape (Flamini, 2013), *Ribes meyeri* (Zhao et al., 2021), *Rubus occidentalis* (Paudel et al., 2013), Strawberry (Aaby et al., 2012) |
| **79** | **Phenolic acid** | **p-Coumaroylquinic acid** | $C_{16}H_{18}O_8$ | **338.3093** | | **339** | 321; 121 | 320 | | *Ribes magellanicum* (Burgos-Edwards et al., 2018), *Vaccinium myrtillus* (Liu et al., 2014), Andean blueberry (Aita et al., 2021), *Ribes meyeri* (Zhao et al., 2021) |
| **80** | **Phenolic acid** | **6-Hydroxy-3-methoxy-4-O-beta-D-glucopyranoside** | $C_{14}H_{20}O_{10}$ | **348.3026** | **347** | | 301; 165 | 165; 137 | | Actinidia (Chen et al., 2021) |
| **81** | **Hydroxycinnamic acid;** | **Chlorogenic acid** [3-O-Caffeoylquinic acid] | $C_{16}H_{18}O_9$ | **354.3087** | **353** | | 191 | 127 | | *Lonicera Henryi* (Jaiswal et al., 2014), *Ribes magellanicum* (Burgos-Edwards et al., 2018), *Lonicera japonica* (Cai et al., 2019), *Vaccinium myrtillus* (Liu et al., 2014), Andean blueberry (Aita et al., 2021) |

**Appendix 1.** (Continued.)

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| **82** | **Hydroxycinnamic acid** | **Neochlorogenic acid** [5-O-Caffeoylquinic acid] | $C_{16}H_{18}O_{9}$ | **354.3088** | **353** | | 191 | 173 | 126 | *Lonicera Henryi* (Jaiswal et al., 2014), *Ribes magellanicum* (Burgos-Edwards et al., 2018), *Lonicera japonica* (Cai et al., 2019), *Vaccinium myrtillus* (Liu et al., 2014), Andean blueberry (Aita et al., 2021) |
| **83** | **Hydroxycinnamic acid;** | **3-*O*-Hydroxydihydrocaffeoylquinic acid** | $C_{16}H_{20}O_{10}$ | **372.324** | **371** | | 191 | 173; 127 | | *Lonicera Henryi* (Jaiswal et al., 2014) |
| **84** | **Phenolic acid** | **Caffeoylquinic acid derivative** | | **382.6633** | **381** | | 179; 135 | 135 | | *Vaccinium myrtillus* (Liu et al., 2014) |
| **85** | **Phenolic acid** | **Ferulic acid-O-hexoside derivative** | $C_{21}H_{22}O_{11}$ | **450.3928** | **449** | | 269; 151 | 225; 151 | | *Cuphea ignea* (Ismail et al., 2022) Strawberry (Aaby et al., 2012) |
| **86** | **Flavonoid** | **p-Coumaroylhexose-4-O-hexoside** | $C_{25}H_{28}O_{10}$ | **488.4838** | | **489** | 327 | 299; 253 | 253; 225 | *Gmelina arborea* (N'gaman-Kouassi et al., 2016) |
| **87** | **Phenolic acid** | **Dicaffeoyl shiikimic acid** | $C_{25}H_{22}O_{11}$ | **498.4356** | | **499** | 163; 319 | 145 | 117 | Andean blueberry (Aita et al., 2021) |
| **88** | **Phenolic acid** | **3,4-O-dicaffeoylquinic acid [Isochlorogenic acid B]** | $C_{25}H_{24}O_{12}$ | **516.4509** | **515** | | 353 | 191 | 173 | *Lonicera Henryi* (Jaiswal et al., 2014), *Lonicera japonica* (Cai et al., 2019), *Artemisia argyi* (Chang et al., 2021) |

**Appendix 1.** (Continued.)

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| **89** | **Phenolic acid** | **4,5-O-dicaffeoylquinic acid** [Isochlorogenic acid C] | $C_{25}H_{24}O_{12}$ | **516.4509** | **515** | | 353 | 191 | 171 | *Lonicera Henryi* (Jaiswal et al., 2014), *Lonicera japonica* (Cai et al., 2019), *Artemisia argyi* (Chang et al., 2021) |
| **90** | **Phenolic acid** | **p-Coumaroyl malonyldihexose** | | **574.8314** | | **575** | 413; 335; 188 | 395; 340; 226; 188 | 346; 290; 211 | *Vaccinium myrtillus* (Liu et al., 2014) |
| **91** | **Phenolic acid** | **Feruloyl-O-p-coumaroyl-O-caffeoylshikimic acid** | | **676** | | **677** | 513; 367 | 349; 266 | | *Phoenix dactylifera* (Said et al., 2017) |
| **92** | **Phenolic acid** | **Dicaffeoylferuoylquinic acid** | | **692.22** | | **693** | 353; 261 | 335; 261; 135 | 243; 149 | *Artemisia annua* (Han et al., 2008) |
| **93** | **Dihydrochalcone** | **Phloretin** [Dihydronaringenin; Phloretol] | $C_{15}H_{14}O_5$ | **274.2687** | | **275** | 257 | 230 | 229 | *Glottiphyllum linguiforme* (Hamed et al., 2021); *Punica granatum* (Mena et al., 2012) |
| **94** | **Stilbene** | **Pinosylvin** [ 3,5-Stilbenediol; Trans-3,5-Dihydroxystilbene] | $C_{14}H_{12}O_2$ | **212.2439** | | **213** | 167; 139 | 139 | | *Pinus resinosa* (Simard et al., 2008), *Pinus sylvestris* (Ekeberg et al., 2006) |
| **95** | **Stilbene** | **Resveratrol** [trans-Resveratrol] | $C_{14}H_{12}O_3$ | **228.2433** | | **229** | 211 | 183; 127 | 138 | *Alchorea cordifolia; Ferocactus glaucescens; Ferocactus herrerae* (Hamed et al., 2021), *Embelia* (Vijayan et al., 2019), Grape (Flamini, 2013), *Radix polygoni multiflori* (Zhu et al., 2012) |

**Appendix 1.** (Continued.)

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| **96** | **Hydroxycoumarin** | **Umbelliferone** [Skimmetin; Hydragin] | $C_9H_6O_3$ | **162.1421** | | **163** | 145 | 117 | | *Lonicera caerulea* (Razgonova et al., 2023a), *Zostera marina* (Razgonova et al., 2022), *Actinidia* (Chen et al., 2021) |
| **97** | **Coumarin** | **4-Methylesculetin** [4-Methyl-6,7-Dihydroxycoumarin] | $C_{10}H_8O_4$ | **192.1681** | | **193** | 147 | 129 | 110 | *Artemisia annua* (Zhu et al., 2013) |
| **98** | **Coumarin** | **Fraxetin** | $C_{10}H_8O_5$ | **208.1675** | | **209** | 191 | 117 | | *Embelia* (Vijayan and Raghu, 2019), Actinidia (Chen et al., 2021), *Jatropha* (Zengin et al., 2021) |
| **99** | **Coumarin** | **3,4/6,8-Dihydro-5,7-dihydroxy-2-oxo-2H-1-benzopyran-3-acetic acid** | $C_{11}H_{10}O_6$ | **238.1935** | | **239** | 221 | 203 | 185 | Actinidia (Chen et al., 2021) |
| **100** | **Coumarin** | **Umbelliferone hexoside** | $C_{15}H_{16}O_8$ | **324.2827** | | **325** | 289; 127 | 271; 127 | 253; 146 | *Glottiphyllum linguiforme* (Hamed et al. 2021) |
| **101** | **Coumarin** | **7-(beta-D-Glucopyranoside/galactopyranoside)-2-oxo-2H-1-benzopyran-4-acetic acid** | $C_{17}H_{18}O_{10}$ | **382.3188** | | **383** | 163; 365 | 145 | | Actinidia (Chen et al., 2021) |
| **102** | **Lignan** | **Syringaresinol** | $C_{22}H_{26}O_8$ | **418.4436** | | **419** | 255 | 239 | 211 | Magnolia (Guo et al., 2019), *Annona montana* (Liaw et al., 2005) |
| | **OTHERS** | | | | | | | | | |
| **103** | **Amino acid** | **L-Histidine** | $C_6H_9N_3O_2$ | **155.1546** | | **156** | 129 | 110 | | *Lonicera japonica* (Cai et al., 2019), *Camellia kucha* (Qin 2020), *Actinidia deliciosa* (Razgonova et al., 2023) |

**Appendix 1.** (Continued.)

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| **104** | **Amino acid** | **L-theanine** | $C_7H_{14}N_2O_3$ | **174.1977** | | **175** | 157; 129 | 129; 115 | | *Camellia kucha* (Qin et al., 2020) |
| **105** | **Amino acid** | **L-Arginine** | $C_6H_{14}N_4O_2$ | **174.201** | | **175** | 130 | 111 | | *Lonicera japonica* (Cai et al., 2019), *Hylocereus polyrhizus* (Wu et al., 2019) |
| **106** | **Omega-hydroxy amino acid** | **Hydroxy decenoic acid** | $C_{10}H_{18}O_3$ | **186.2481** | | **187** | 145 | 127 | | *Ferocactus glaucescens* (Hamed et al., 2021) |
| **107** | **Tricarboxylic acid** | **Citric acid** | $C_6H_8O_7$ | **192.1235** | **191** | | 111; 173 | | | *Punica granatum* (Mena et al., 2012) |
| **108** | **Polyhydroxycarboxylic acid** | **Quinic acid** | $C_7H_{12}O_6$ | **192.1666** | **191** | | 111; 173 | 111 | | *Lonicera japonica* (Cai et al., 2019), Andean blueberry (Aita et al., 2021), *Ribes meyeri* (Zhao et al., 2021) |
| **109** | **Alpha, omega dicarboxylic acid** | **Sebacic acid [Decanedioic acid]** | $C_{10}H_{18}O_4$ | **202.2475** | | **203** | 185 | 139 | 111; 157 | *Jatropha* (Zengin et al., 2021) |
| **110** | | **4-Dihydroxy-3-methoxy-benzenepropanoic acid** | $C_{10}H_{12}O_5$ | **212.1993** | | **213** | 193; 167; 139; 119 | | | *Actinidia* (Chen et al., 2021) |
| **111** | **Saturated fatty acid** | **Hydroxydodecenoic acid** | $C_{12}H_{22}O_3$ | **214.3013** | | **215** | 208 | 186 | | *Lonicera caerulea* (Razgonova et al., 2023a), *Jatropha* (Zengin et al., 2021) |
| **112** | **Sesquiterpenoid** | **Caryophyllene oxide** [Caryophyllene-alpha-oxide] | $C_{15}H_{24}O$ | **220.3505** | **219** | | 173; 111 | 111 | | *Rosa davurica* (Razgonova et al., 2022), *Ledum palustre* (Razgonova et al., 2023b) |
| **113** | **Carboxylic acid** | **Myristoleic acid** [Cis-9-Tetradecanoic acid] | $C_{14}H_{26}O_2$ | **226.355** | | **227** | 209; 165 | 121 | | *Ferocactus glaucescens* (Hamed et al., 2021), *Maackia amurensis* (Razgonova et al., 2023c) |

**Appendix 1.** (Continued.)

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| 114 | **Sesquiterpenoid** | **Atractylenolide II** [Asterolide; 2-Atractylenolide] | $C_{15}H_{20}O_2$ | **232.3181** | | **233** | 216 | 160 | 132 | *Atractylodes macrocephalae rhizoma* (Huang et al., 2018), Chinese herbal formula Jian-Pi-Yi-Shen pill (Wang et al., 2020) |
| 115 | **Pyrimidine nucleoside** | **Cytidine** | $C_9H_{13}N_3O_5$ | **243.2166** | | **244** | 225; 179 | 179 | 151 | *Lonicera japonica* (Cai et al., 2019) |
| 116 | **Glycosylated pyrimidine analog** | **Uridine** | $C_9H_{12}N_2O_6$ | **244.2014** | | **245** | 145 | 117 | | *Lonicera japonica* (Cai et al., 2019) |
| 117 | **Medium-chain fatty acid** | **Hydroxy dodecanoic acid** | $C_{12}H_{22}O_5$ | **246.3001** | | **247** | 229; 201 | 187 | 159; 145 | *Ferocactus glaucescens* (Hamed et al., 2021) |
| 118 | | **Caffeic acid isoprenyl ester** | $C_{14}H_{16}O_4$ | **248.2744** | | **249** | 203 | 157 | 129 | *Lonicera caerulea* (Razgonova et al., 2023a) |
| 119 | **Sesquiterpene lactone** | **Artemisinin C** | $C_{15}H_{20}O_3$ | **248.3175** | | **249** | 202; 157; 125 | 157; 185 | 129 | *Artemisia annua* (Zhu et al., 2013) |
| 120 | **Polyunsaturated long-chain fatty acid** | **Hexadecadienoic acid** | $C_{16}H_{28}O_2$ | **252.3923** | | **253** | 145; 244 | 127 | | *Rhus coriaria* (Abu-Reidah et al., 2015) |
| 121 | **Aporphine alkaloid** | **Anonaine** | $C_{17}H_{15}NO_2$ | **265.3065** | | **266** | 249 | 203 | 157 | *Rosa rugosa* (Razgonova et al., 2022), Magnolia (Guo et al., 2019) |
| 122 | **Ribonucleoside composite of adenine (purine)** | **Adenosine** | $C_{10}H_{13}N_5O_4$ | **267.2413** | | **268** | 250 | 204; 158 | 157 | *Lonicera japonica* (Cai et al., 2019), *Rosa acicularis* (Razgonova et al., 2022), Huolisu Oral Liquid (Yin et al., 2021) |
| 123 | | **3,4,8,9,10-Penthahydroxydibenzo [b,d]pyran-6-one** | $C_{13}H_8O_7$ | **276.1984** | | **277** | 203 | 157 | 129 | *Terminalia arjuna* (Singh et al., 2015) |

**Appendix 1.** (Continued.)

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| **124** | **Omega-3-fatty acid** | **Stearidonic acid** [6,9,12,15-Octadecatetraenoic acid; Moroctic acid] | $C_{18}H_{28}O_2$ | **276.4137** | | **277** | 261 | 215; 115 | 129 | *Glottiphyllum linguiforme* (Hamed et al. 2021), *Rhus coriaria* (Abu-Reidah et al., 2015), *Jatropha* (Zengin et al., 2021), (Yang et al., 2015), *Salviae Miltiorrhizae* (Yang et al., 2015) |
| **125** | **Omega-3-fatty acid** | **Linolenic acid** (Alpha-Linolenic acid; Linolenate) | $C_{18}H_{30}O_2$ | **278.4296** | | **279** | 261 | 219 | 163 | Jatropha (Zengin et al., 2021), *Pinus sylvestris* (Ekeberg et al., 2006), *Maackia amurensis* (Razgonova et al., 2023c), *Salviae Miltiorrhizae* (Yang et al., 2015) |
| **126** | **Mixture of diastereomers** | **Fructose-leucine** | $C_{12}H_{23}NO_7$ | **293.3135** | | **294** | 276 | 258 | 210 | *Lonicera caerulea* (Razgonova et al., 2023a) |
| **127** | **Phenanthraquinone** | **Tanshinone V** | $C_{19}H_{22}O_4$ | **314.3765** | **313** | | 212; 113 | 113; 185 | | Huolisu Oral Liquid (Yin et al., 2021) |
| **128** | **Cyclohexenecarboxylic acid** | **Coumaroyl shiikimic acid** | $C_{16}H_{16}O_7$ | **320.294** | | **321** | 219; 173 | 201; 173 | 155 | Andean blueberry (Aita et al., 2021) |
| **129** | **Oxylipin** | **13- Trihydroxy-Octadecenoic acid** [THODE] | $C_{18}H_{34}O_5$ | **330.4596** | **329** | | 229; 171 | 210 | 209; 183 | *Phoenix dactylifera* (Said et al., 2017), *Jatropha* (Zengin et al., 2021) |
| **130** | **Alpha, omega-dicarboxylic acid** | **Eicosatetraenedioic acid** | $C_{20}H_{30}O_4$ | **334.4498** | **333** | | 287; 197; 151 | 151 | | *Glottiphyllum linguiforme* (Hamed et al. 2021) |

**Appendix 1.** (Continued.)

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| 131 | **Cyclohexenecarboxylic acid** | **Caffeoyl shikimic acid** | $C_{16}H_{16}O_8$ | **336.2934** | | **337** | 273; 173 | 128 | | *Ribes meyeri* (Zhao et al., 2021) |
| 132 | | **Sophoraisoflavone A** | $C_{20}H_{16}O_6$ | **352.3374** | | **353** | 335 | 317; 243; 137 | 191 | Chinese herbal formula Jian-Pi-Yi-Shen pill (Wang et al., 2020) |
| 133 | **Alpha,omega-dicarboxylic acid** | **Trihydroxy eicosatetraenoic acid** | $C_{20}H_{32}O_5$ | **352.4651** | | **353** | 261 | 243 | 159 | *Ferocactus glaucescens* (Hamed et al., 2021) |
| 134 | **Dicarboxylic acid sugar** | **Caffeoyl gluconic acid** | $C_{15}H_{18}O_{10}$ | **358.2974** | | **359** | 340; 312; 284; 228; 196 | | | *Ribes meyeri* (Zhao et al., 2021) |
| 135 | **Iridoid** | **Monotropein** | $C_{16}H_{22}O_{11}$ | **390.3393** | | **391** | 373; 329; 251; 187 | 311; 202 | 203 | *Vaccinium myrtillus* (Liu et al., 2014) |
| 136 | **Tricarboxylic acid** | **Citric acid derivative** | | **392** | **391** | | 373; 217 | 143 | | *Punica granatum (Mena et al., 2012)* |
| 137 | **Anabolic steroid** | **Vebonol** | $C_{30}H_{44}O_3$ | **452.6686** | | **453** | 435; 210 | 226; 336 | 210 | *Rhus coriaria* (Abu-Reidah et al., 2015) |
| 138 | **Phenylpropanoid glucoside** | **Grayanoside A** [Hydroxyphenylethyl feruoyl glucopyranoside] | $C_{24}H_{28}O_{10}$ | **476.4731** | **475** | | 375; 275 | 347; 275; 175 | 247; 175 | Andean blueberry (Aita et al., 2021) |
| 139 | **Thromboxane receptor antagonist** | **Vapiprost** | $C_{30}H_{39}NO_4$ | **477.635** | | **478** | 337 | 263; 121 | 119 | *Rhus coriaria* (Abu-Reidah et al., 2015), *Hylosereus polyrhizus* (Wu et al., 2019) |
| 140 | **Indole sesquiterpene alkaloid** | **Sespendole** | $C_{33}H_{45}NO_4$ | **519.7147** | | **520** | 184 | 125 | | *Rhus coriaria* (Abu-Reidah et al., 2015) |
| 141 | **Iridoid glucoside** | **p-coumaroyl-6,7-dihydromonotropein** | $C_{25}H_{30}O_{13}$ | **538.4979** | | **540** | 373; 229; 179 | 179 | | *Vaccinium myrtillus* (Ieri et al., 2013), *Vaccinium* (Heffels and 2017), *Cranberry* (Wang et al., 2018) |

**Appendix 1.** (Continued.)

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| **142** | **Carotenoid** | **Zeaxanthin** [All-Trans-Zeaxanthin; Anchovyxanthin] | $C_{40}H_{56}O_2$ | **568.8714** | | **570** | 552; 412; 184 | 534; 317; 184 | 487; 404; 321; 149 | Sarsaparilla (Delgado-Pelayo and Hornero-Mendez, 2012), Human blood samples (Zoccali et al., 2018) |
| **143** | **Product of chlorophyll degradation** | **Pheophorbide a** | $C_{35}H_{36}N_4O_5$ | **592.6841** | | **593** | 533 | 461 | 433 | PubChem |
| **144** | **Iridoid** | **p-Coumaroyl monotropein hexoside** | | **698.881** | | **699** | 537; 347; 259 | 375; 259; 185 | | *Vaccinium myrtillus* (Ieri et al., 2013) |
| **145** | **Product of chlorophyll degradation** | **Pheophytin A** | $C_{55}H_{74}N_4O_5$ | **871.1999** | | **872** | 593 | 533 | 461 | *Physalis peruviana* (Etzbach et al., 2018), Capsicum (Pascale et al., 2020) |