

Article

Maackia amurensis Rupr. et Maxim.: Supercritical CO₂ Extraction and Mass Spectrometric Characterization of Chemical Constituents

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Abstract: Three types of extraction were used to obtain biologically active substances from the heartwood of *M. amurensis*: supercritical CO₂ extraction, maceration with EtOH, and maceration with MeOH. The supercritical extraction method proved to be the most effective type of extraction, giving the highest yield of biologically active substances. Several experimental conditions were investigated in the pressure range of 50–400 bar, with 2% of ethanol as co-solvent in the liquid phase at a temperature in the range of 31–70 °C. The most effective extraction conditions are: pressure of 100 bar and a temperature of 55 °C for *M. amurensis* heartwood. The heartwood of *M. amurensis* contains various polyphenolic compounds and compounds of other chemical groups with valuable biological activity. Tandem mass spectrometry (HPLC-ESI—ion trap) was applied to detect target analytes. High-accuracy mass spectrometric data were recorded on an ion trap equipped with an ESI source in the modes of negative and positive ions. The four-stage ion separation mode was implemented. Sixty-six different biologically active components have been identified in *M. amurensis* extracts. Twenty-two polyphenols were identified for the first time in the genus *Maackia*.

Keywords: *Maackia amurensis*; CO₂ extraction; tandem mass spectrometry; polyphenols; bioactive compounds



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1. Introduction

Maackia amurensis Rupr. et Maxim. is the only representative of the Fabaceae family in the flora of the Russian Far East. Probably, this species can be considered a relic of the Tertiary flora, which survived in more severe climatic conditions than the species of the genera *Cladrastis* and *Sophora*. The distribution area of *Maackia amurensis* is in the Amur River basin and in the south of Primorsky Krai, Russia. The natural reserves of this plant are large and actively self-renewal [1–3]. A close species to *maackia* is *M. amurensis* Rupr. et Maxim. var. *buergeri* (Maxim.) C.K. Schneider (Figure 1). However, its chemical composition differs sharply from that of the Far Eastern species, *M. amurensis* [2–5]. Until 1985, the only data on the chemical composition of Russian *maackia* were data on alkaloids contained in the bark and green parts of the plant. In the subsequent detailed chemical study of alcoholic extracts of heartwood, it was shown that the main components of *maackia* are plant polyphenols [3–5].

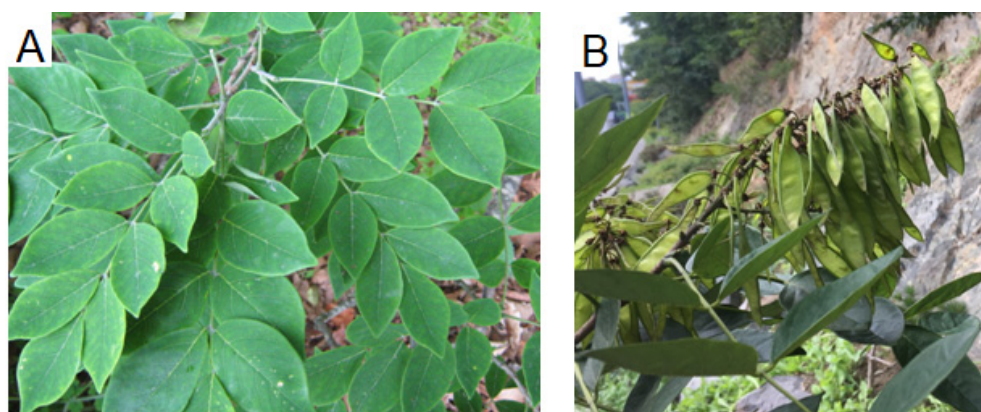


Figure 1. (A) *Maackia amurensis* L.; (B) fruits of *Maackia amurensis* species. Photo taken by N.P. Mishchenko (August 2020).

These include isoflavones: genistein, daidzein, retusin, afromosin, formononetin, orobol, tectorigenin, 3-hydroxyvestiton, pterocarpan maackiain, medicarpin [5–7]. The peculiarity of *Maackia amurensis* growing in Primorye is the high content of monomeric stilbenes resveratrol and piceatannol and isoflavonstilben maackiasin in its wood [5,6]. These polyphenols were not found in the variety *Maackia amurensis* (var. buergeri) growing in Japan [1].

In addition to monomeric stilbenes and isoflavones, the polar fractions of *Maackia amurensis* extracts contain oligomeric stilbenes maackin, scirpusin A, scirpusin B, maackin A (XVII), and stilbenolignan maackolin [8,9].

The polyphenolic complex from *M. amurensis* heartwood, called Maksar[®] preparation, is registered in the Russian Federation as a hepatoprotective medicine (P N003294/01). Maksar[®] increases the body's antioxidant system activity and reduces the lipid peroxidation level. Its application in clinical practice showed that this drug is effective for treating liver fatty dystrophy. It prevents the increase in total serum lipid content and the development of hyperlipoproteinemia in experimental animals. Maksar[®] also possesses antithrombogenic, antiplatelet, and antitumor properties [10,11]. Recently, new research has been carried out which shows that stilbenolignan maackolin may be a good candidate as a SARS-CoV-2 Mpro inhibitor in vivo studies [12].

The use of supercritical fluids in food material applications and more broadly in the food industry began in the late 1960s and probably represents the most successful application of supercritical fluids to date. The “green technology” of supercritical CO₂ extraction using high pressures is an excellent technique for obtaining natural thermolabile compounds. In addition, there are no residues of organic solvents in the products, which occurs with conventional extraction methods—conventional solvents can be toxic, for example, in the case of methanol and hexane. Easy removal of the solvent from the final product, a high selectivity, and the use of moderate temperatures in the extraction process are the main attractive factors of SFE, leading to a significant increase in research for applications in the food and pharmaceutical industries [13].

Chemical reactions that have made the greatest contribution to food technologies were enzyme-catalyzed reactions [14], hydrogenations designed to control particular trans isomers occurring in lipid mixtures [15], and hydrolysis conducted in the presence of enzymes or a medium such as subcritical water [16]. Considerable activity in producing fine particles for use in the pharmaceutical industry began in the 1990s. In the last three decades, focus on the development of technologies was displaced by the combination of SCF technologies in the food industry and the obtainment of bioactive agents from natural matrixes [17,18].

In this research, supercritical CO₂ extraction, MeOH maceration, and EtOH maceration of the samples of *M. amurensis* were used to obtain an effective amount of biologically active substances. We used a tandem mass spectrometry to carry out a phytochemical study

involving a detailed metabolomic analysis of *M. amurensis*. The bark of *M. amurensis* was collected during expedition work near Ussuri River, Primorsky Krai, Russia (N 42°36′10″ E 131°10′55″), during the period from 1 to 20 August 2022.

2. Results

Three samples of wood substance of *M. amurensis* were subjected to supercritical CO₂ extraction under different extraction conditions. The applied supercritical pressures ranged from 150 to 400 bar, and the extraction temperature ranged from 31 to 65 °C. The co-solvent EtOH was used in an amount of 2% of the total amount of solvent. A pronounced extraction extremum is shown in the 3D graph (Figure 2). The best extraction conditions for *M. amurensis* (heartwood) were the following: pressure of 100 bar and temperature at 55 °C. The total yield of biologically active substances under these extraction conditions was 4.3 mg per 100 mg of supercritical CO₂ extract. The structural identification of each compound was carried out on the basis of their accurate mass and MS/MS fragmentation via the HPLC–ESI–ion trap–MS/MS. A total of 66 compounds were identified in extracts of *M. amurensis* based on their accurate MS and fragment ions by searching online databases and the references.

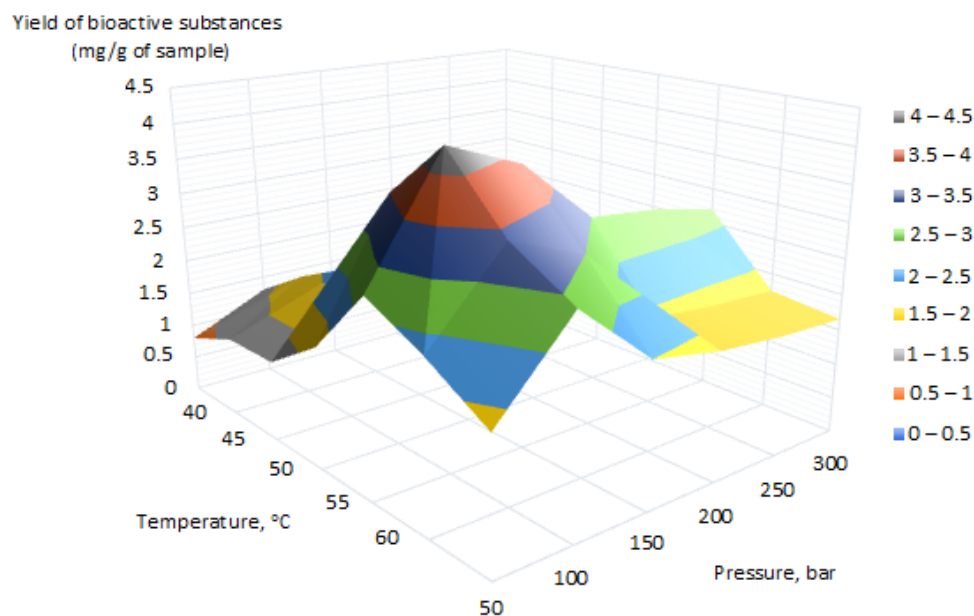


Figure 2. 3D graph data of supercritical CO₂ extraction. Complex yield of biologically active substances from CO₂ extracts of wood substance of *M. amurensis*.

The research data presented in Figure 2 show the presence of a confident maximum of supercritical CO₂ extraction in the pressure range of 100 to 150 bar and temperature range from 50 °C to 55 °C. In this range, the highest yield of biologically active compounds from the plant matrix of *M. amurensis* is observed. It should be noted that during the experiment, the extraction time was also small—1 h; therefore, what can we say about the effectiveness of the applied method of supercritical CO₂-extraction?

3. Discussion

The number of constituents tentatively identified via tandem mass spectrometry was 66 chemical compounds (54 compounds from the polyphenol group and 12 compounds from other chemical groups). All the identified polyphenols and compounds from other chemical groups, their molecular formulas, and MS/MS data for *M. amurensis* are summarized in Table A1 (Appendix A). Polyphenols are represented by the following chemical groups: flavones, flavonols, flavan-3-ols, flavanones, stilbenes, hydroxycoumarins. For the first time, 22 polyphenols were identified in *M. amurensis* heartwood. There are polyphenols:

flavones biochanin-A, 7-hydroxy-6,4'-dimethoxyisoflavone, trihydroxy methoxyflavone, cirsimaritin, dihydroxy-dimethoxy(iso)flavone, myricetin, cirsiolol, wightone, luteone, dihydroxy tetramethoxyflavanone, hydroxy hexamethoxyflavone, odoratin-*O*-hexoside, 6,4'-dimethoxyisoflavone-7-*O*-glucoside, genistein C-glucoside malonylated, calycosin-7-*O*-beta-D-glucoside-6''-*O*-malonate, chrysoeriol 8-C-glucoside malonylated, apigenin 7-C-glucosylidideoxyhexoside, flavanones methyl-liquiritigenin, liquiritigenin dimethyl ester, padmatin, etc.

Figures 3–6 show examples of the decoding spectra (collision-induced dissociation (CID) spectrum) of the ion chromatogram obtained using tandem mass spectrometry. The CID spectrum in negative ion modes of isoflavone 3-hydroxyvestitol from *M. amurensis* is shown in Figure 3.

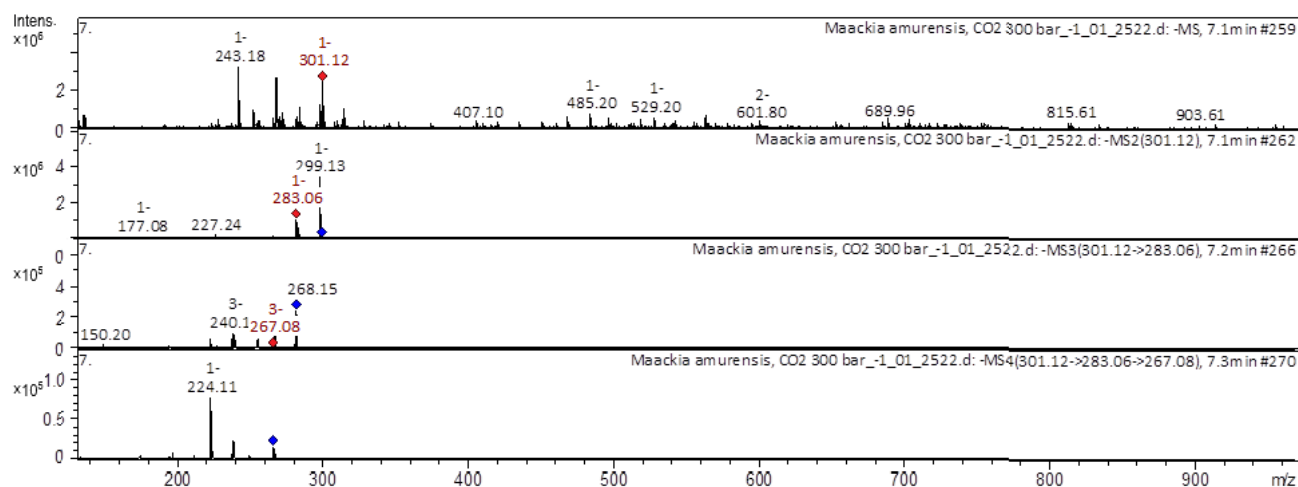


Figure 3. CID spectrum of 3-Hydroxyvestitol from *M. amurensis*, at m/z 275.01.

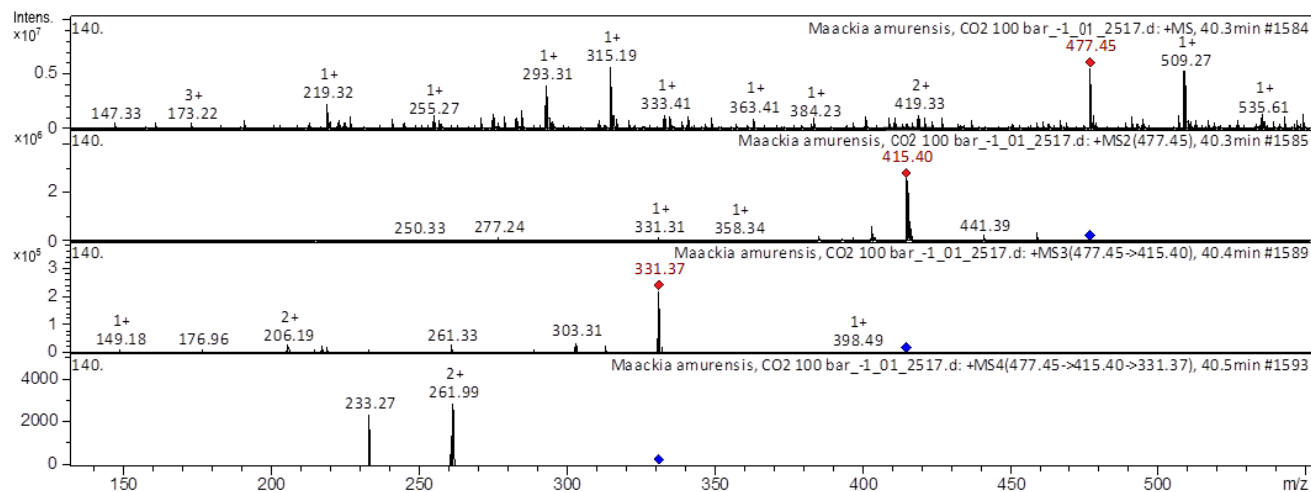


Figure 4. CID spectrum of odoratin-*O*-hexoside from *M. amurensis*, at m/z 477.45.

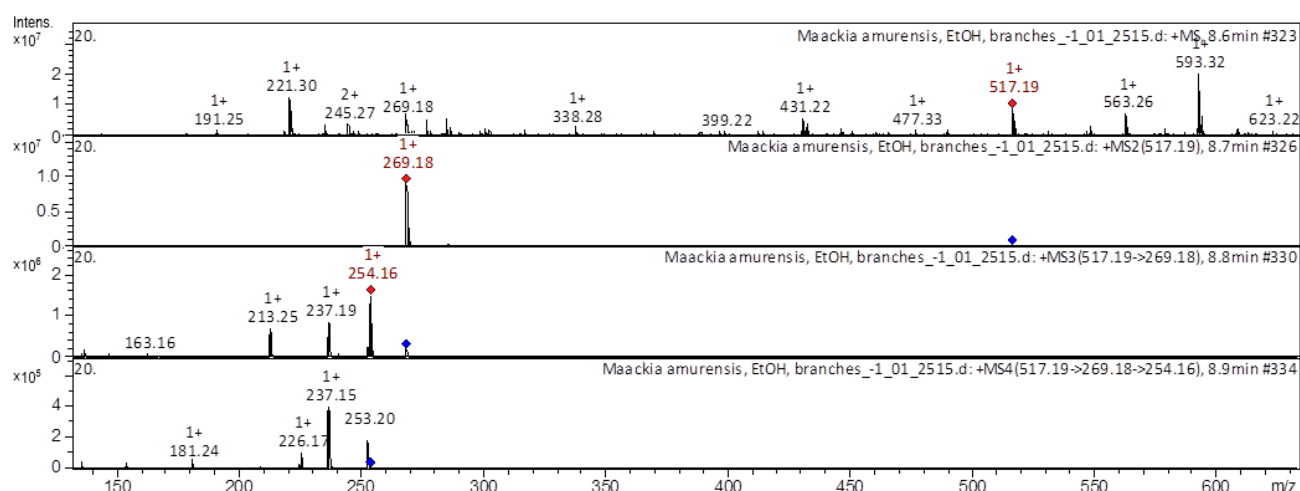


Figure 5. CID spectrum of formononetin-7-O-glucoside-6''-O-malonate from *M. amurensis*, at m/z 517.19.

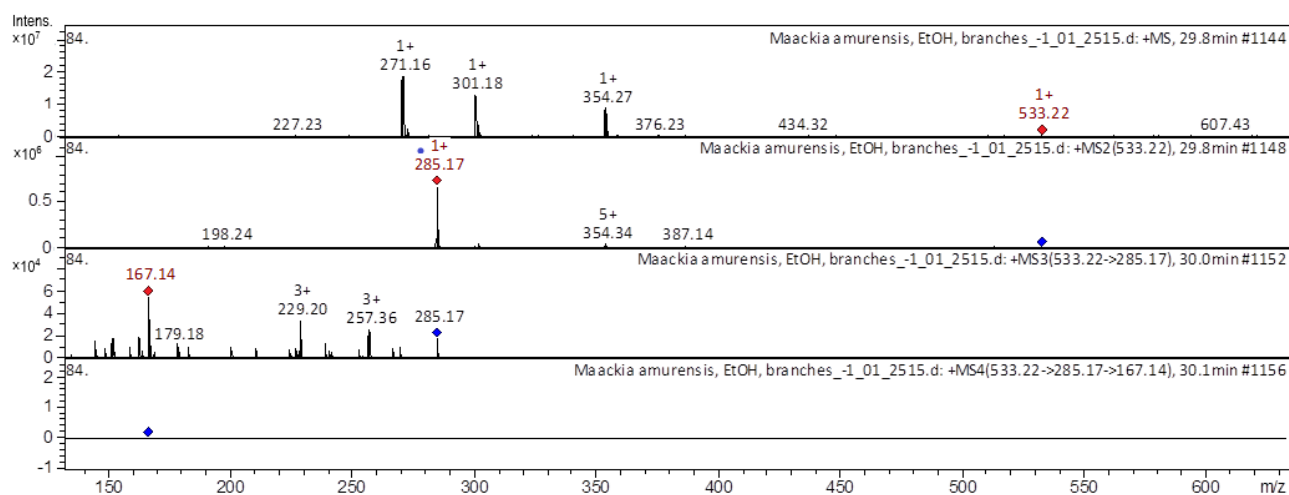


Figure 6. CID spectrum of calycosin-7-O-beta-D-glucoside-6''-O-malonate acid from *M. amurensis*, at m/z 533.22.

$[M+H]^+$ ion produced four fragment ions at m/z 299.13, m/z 283.13, m/z 227.24, and at m/z 177.08 (Figure 3). The fragment ion at m/z 283.06 produced three characteristic daughter ions at m/z 267.08, m/z 240.1, and m/z 150.2. The fragment ion at m/z 267.08 produced one characteristic ion at m/z 224.11. It was identified in the references in the extract from *M. amurensis* [5–7]. The following is a list of polyphenols found in extracts of the wood substance of *M. amurensis*; it should be noted separately that similar polyphenols are found in the *Astragalus* genus. The CID spectrum in positive ion modes of odoratin-O-hexoside from *M. amurensis* is shown in Figure 4.

$[M+H]^+$ ion produced five fragment ions at m/z 415.4, m/z 358.34, m/z 331.31, m/z 277.24, and at m/z 250.33 (Figure 4). The fragment ion with m/z 415.4 produced six characteristic daughter ions at m/z 331.37, m/z 303.31, m/z 261.33, m/z 206.19, m/z 176.96, and at m/z 149.18. The fragment ion at m/z 331.37 produced two characteristic daughter ions at m/z 261.99 and m/z 233.27; they were identified in extracts from *Astragali Radix* [19–21]. The CID spectrum in the positive ion mode of formononetin-7-O-glucoside-6''-O-malonate from *M. amurensis* is shown in Figure 5.

$[M-H]^+$ ion produced one fragment ion at m/z 269.18 (Figure 5). The fragment ion with m/z 269.18 produced four characteristic daughter ions at m/z 254.16, m/z 237.19, m/z 213.25, and at m/z 163.16. The fragment ion at m/z 254.16 formed three daughter ions with m/z 237.15,

m/z 226.17, and m/z 181.24; they were identified in extracts from *Astragali Radix* [19–21]. The CID spectrum in the positive ion mode of calycosin-7-*O*-beta-D-glucoside-6''-*O*-malonate from *M. amurensis* is shown in Figure 6.

$[M+H]^+$ ion produced four fragment ions with m/z 285.17, m/z 387.34, m/z 354.34, and m/z 198.24 (Figure 6). The fragment ion with m/z 285.17 formed four daughter ions with m/z 167.14, m/z 257.36, m/z 229.2, and m/z 179.18; they were identified in extract from *Astragali Radix* [19–21].

It should also be noted that a detailed analysis of the presence of polyphenols and biologically active substances from other chemical groups showed the highest number of flavonoids at supercritical CO₂ extraction at a pressure of 100 bar—43 compounds. Accordingly, with other types of extraction investigated in this study, such as maceration with ethanol (20 compounds), maceration with methanol (23 compounds), and supercritical CO₂-extraction at a higher extraction pressure (19 compounds), the yield efficiency of biologically active substances is much lower. (Table 1).

Table 1. Identified chemical constituents by tandem mass spectrometry in three types of extraction: supercritical CO₂ extraction, maceration with EtOH, maceration with MeOH.

Nº	Class of Compounds	Identified Compounds	MeOH Extraction	EtOH Extraction	Static CO ₂ Extraction	CO ₂ Extraction 100 Bar	CO ₂ Extraction 300 Bar
POLYPHENOLS							
1	Flavone	2'-Hydroxyformononetin [Xenognosin B]	+				
2	Flavone	Daidzein [4',7-Dihydroxyisoflavone; Daidzeol]	+			+	+
3	Flavone	Formononetin [Biochanin B; Formononetol]	+	+	+		
4	Flavone	Apigenin	+	+		+	+
5	Flavone	Genistein	+				+
6	Flavone	Calycosin [3'-Hydroxyformononetin]		+			+
7	Flavone	5-Methoxydaidzein	+	+	+	+	+
8	Flavone	Biochanin-A *		+			+
9	Flavone	Orobol	+		+	+	+
10	Flavone	7-Hydroxy-6,4'-dimethoxyisoflavone*				+	
11	Flavone	Afromosin [Castanin]			+	+	+
12	Flavone	Tectorigenin	+	+	+	+	+
13	Flavone	Trihydroxy methoxyflavone *				+	+
14	Flavone	3-Hydroxyvestiton				+	+
15	Flavone	Odoratin	+	+	+	+	+
16	Flavone	Cirsimaritin *				+	
17	Flavone	Dihydroxy-dimethoxy(iso)flavone *		+			
18	Flavone	Myricetin *				+	
19	Flavone	Cirsiliol *			+		
20	Flavone	Wightone [Erythrinin B] *	+	+		+	+
21	Isoflavone	Luteone *		+			
22	Flavone	Dihydroxy tetramethoxyflavanone *	+				
23	Flavone	Hydroxy hexamethoxyflavone *				+	
24	Flavone	Formononetin (Glycosylated and methylated)				+	
25	Flavone	Odoratin- <i>O</i> -hexoside *	+			+	
26	Flavone	6,4'-Dimethoxyisoflavone-7- <i>O</i> -glucoside *				+	
27	Flavone	Formononetin-7- <i>O</i> -glucoside-6''- <i>O</i> -malonate		+			
28	Flavone	Genistein C-glucoside malonylated *	+				
29	Flavone	Maackiasin					+
30	Flavone	Calycosin-7- <i>O</i> -beta-D-glucoside-6''- <i>O</i> -malonate *		+			
31	Flavone	Chrysoeriol 8-C-glucoside malonylated *					+
32	Flavone	Apigenin 7-C-glucosyldideoxyhexoside *		+			

Table 1. Cont.

№	Class of Compounds	Identified Compounds	MeOH Extraction	EtOH Extraction	Static CO ₂ Extraction	CO ₂ Extraction 100 Bar	CO ₂ Extraction 300 Bar
33	Isoflavone	Ononin derivative		+			
34	Flavone	Apigenin 6-C-[6''-acetyl-2''-O-deoxyhexoside]-glucoside		+			
35	Flavonol	Kaempferol	+				+
36	Flavonol	Quercetin				+	
37	Flavonoid	Di-O-galloyl-glucoside *				+	
38	Isoflavan	Vestitol				+	
39	Prenyl flavonoid	Prenyl naringenin *	+			+	
40	Flavan-3-ol	(epi)Catechin-5-O-D-glycopyranoside *				+	
41	Flavanone	Liquiritigenin	+	+		+	
42	Flavanone	Methyl-Liquiritigenin *	+			+	
43	Flavanone	Liquiritigenin dimethyl ester *			+	+	
44	Flavanone	Padmatin *				+	
45	Flavanone	Maackiaflavanone B				+	
46	Phenolic acid	Ferulic acid				+	
47	Stilbene	Resveratrol				+	
48	Stilbene	3-Hydroxyresveratrol [Piceatannol]		+		+	+
49	Stilbene	Piceatannol-3-O-glucoside [Quzhaqigan]		+			
50	Stilbenolignan	Maackolin				+	
51	Dimeric stilbene	Resveratrol-piceatannol *				+	
52	Dimeric stilbene	Scirpusin A				+	
53	Dimeric stilbene	Scirpusin B				+	
54	Hydroxycoumarin	Esculin *					+
OTHERS							
55	Omega-5 fatty acid	Myristoleic acid [Cis-9-Tetradecanoic acid] *	+	+		+	
56	Pterocarpan	Medicarpin				+	
57	Omega-3 fatty acid	Stearidonic acid *		+			
58	Omega 3-fatty acid	Linolenic acid *				+	
59	Pterocarpan	Maackiain [Inermin]	+	+			
60	Omega 3-fatty acid	Hydroxy linolenic acid *				+	
61	Higher-molecular-weight carboxylic acid	Oxo-nonadecanoic acid		+			
62	Oxylipins	13-Trihydroxy-Octadecenoic acid *				+	
63	Unsaturated fatty acid	Pentacosenoic acid *				+	
64	Anabolic steroid	Vebonol *				+	
65	Triterpenic acid	Ursolic acid *				+	
66	Product of chlorophyll degradation	Pheophytin A *	+	+		+	+

* Chemical compounds identified for the first time in *M. amurensis*.

Thus, it can be stated that as a result of the most detailed study using tandem mass spectrometry, new data on the content of biologically active substances in *M. amurensis* have been obtained.

M. amurensis extracts exhibited different DPPH scavenging effects compared to quercetin (Table 2). CO₂ extract obtained at 100 bar possessed the most considerable activity compared to quercetin, which is mainly due to the high content of monomeric and dimeric stilbenes. EtOH extract from *M. amurensis* was the least active, because the main components of this extract were glycosides of isoflavones, which are rather weak antioxidants.

Table 2. DPPH scavenging activity of *M. amurensis* extracts.

Compound	DPPH Scavenging Effect
	IC ₅₀ µg, 20 min
Quercetin	3.05 ± 0.12
MeOH extraction	22.26 ± 1.95
EtOH extraction	38.35 ± 4.09
Static CO ₂ extraction	30.11 ± 3.10
CO ₂ extraction 100 Bar	5.13 ± 0.42
CO ₂ extraction 300 Bar	15.32 ± 2.02

Data are presented as the mean values ± SEM, n = 3.

4. Materials and Methods

4.1. Materials

Wood substance of *M. amurensis* was collected during expedition work near Ussuri River, Primorsky Krai, Russia (N 42°36′10″ E 131°10′55″), during the period from 1 to 20 August 2022. All samples were morphologically authenticated according to the current standard of Russian Pharmacopeia [22].

4.2. Chemicals and Reagents

HPLC-grade acetonitrile was purchased from Fisher Scientific (Southborough, UK), MS-grade formic acid was from Sigma-Aldrich (Steinheim, Germany). Ultra-pure water was prepared from a SIEMENS ULTRA clear (SIEMENS water technologies, Munich, Germany), and all other chemicals were analytical grade.

4.3. Fractional Maceration

The fractional maceration technique was applied to obtain highly concentrated extracts [23]. From 500 g of the wood substance, 20 g of wood were randomly selected for maceration. The total amount of the extractant (ethyl alcohol of reagent grade) was divided into 3 parts, and the parts of plant were consistently infused with the first, second, and third parts. The solid–solvent ratio was 1:20. The infusion of each part of the extractant lasted 7 days at room temperature.

4.4. Extraction

SC-CO₂ extraction was performed using the SFE-500 system (Thar SCF Waters, Milford, CT, USA) supercritical pressure extraction apparatus. System options include: co-solvent pump (Thar Waters P-50 High Pressure Pump), for extracting polar samples; CO₂ flow meter (Siemens, Munich, Germany), to measure the amount of CO₂ being supplied to the system; and multiple extraction vessels, to extract different sample sizes or to increase the throughput of the system. The flow rate was 10–25 mL/min for liquid CO₂ and 1.00 mL/min for EtOH. Extraction samples of 100 g of wood substance of *M. amurensis* were used. The extraction time was counted after reaching the working pressure and equilibrium flow, and it was 60–90 min for each sample.

4.5. 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 program with two mobile phases (A, deionized water; B, acetonitrile with formic acid 0.1% v/v) was as follows: 0–2 min, 0% B; 2–50 min, 0–100% B; control washing 50–60 min 100% B. The entire HPLC analysis was performed with a UV-vis detector SPD-20A (Shimadzu, Kyoto, Japan) at a wavelength of 230 nm for identification compounds; the temperature was 50 °C, and the total flow rate 0.25 mL min^{−1}. The injection volume was 10 µL. Additionally, liquid chromatography was combined with a mass spectrometric ion trap to identify compounds.

4.6. Mass Spectrometry

MS analysis was performed on an ion trap amaZon SL (BRUKER DALTONIKS, Bremen, Germany) equipped with an ESI source in the negative ion mode. 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; and collision energy: 60 eV. An ion trap was used in the scan range m/z 100–1.700 for MS and MS/MS. The capture rate was one spectrum/s for MS and two spectrum/s for MS/MS. Data collection was controlled using Windows software for BRUKER DALTONIKS. All experiments were repeated three times. A four-stage ion separation mode (MS/MS mode) was implemented.

4.7. Antiradical Activity

We determined the DPPH (2,2-diphenyl-1-picrylhydrazyl) scavenging effect of extracts from *M. amurensis* heartwood. The extracts were added to DPPH solution in MeOH (10^{-4} M) at concentrations from 1 to 85 µg/mL. We kept the reacting mixture in the dark at room temperature for 20 min. Then, we measured the absorbance at 517 nm using a Shimadzu UV-1800 spectrophotometer (Shimadzu, Canby, OR, USA). We used Equation (1) to calculate the DPPH radical-scavenging effect (%):

$$\text{DPPH scavenging effect, \%} = \frac{A_0 - A_x}{A_0} \times 100, \quad (1)$$

where A_0 is the absorbance of DPPH solution without *M. amurensis* extracts (blank sample); A_x is the absorbance of DPPH solution in the presence of different concentrations of extracts.

Quercetin was used as a reference compound. All experiments were performed in triplicate. The half maximal inhibitory concentrations (IC_{50}) for extracts were calculated by plotting the DPPH scavenging effect (%) against the concentrations of *M. amurensis* extracts. IC_{50} values are given as the mean $\pm$ SEM.

5. Conclusions

Three types of extraction were used to obtain biologically active substances from the wood substance of *M. amurensis*: supercritical CO₂ extraction, maceration with EtOH, and maceration with MeOH. The supercritical extraction method proved to be the most effective type of extraction, giving the highest yield of biologically active substances. Several experimental conditions were investigated in the pressure range of 50–400 bar, with the used volume of co-solvent ethanol being 2% in the liquid phase at a temperature in the range of 31–70 °C. The most effective extraction conditions are: pressure of 100 bar and temperature at 55 °C for the wood substance of *M. amurensis*. The wood of *M. amurensis* contains various polyphenolic compounds and compounds of other chemical groups with valuable biological activity. Tandem mass spectrometry (HPLC-ESI—ion trap) was applied to detect target analytes. High-accuracy mass spectrometric data were recorded on an ion trap amaZon SL BRUKER DALTONIKS equipped with an ESI source in the mode of negative and positive ions. The four-stage ion separation mode was implemented. Sixty-six different biologically active components have been identified in *M. amurensis* extracts. Twenty-two polyphenols were identified for the first time in the genus *Maackia*.

These data could support future research for the production of a variety of pharmaceutical products containing ultra-pure extracts of *M. amurensis*. The richness of various biologically active compounds, including compounds of the polyphenol group and compounds of other chemical groups (amino acids, Omega fatty acids, sterols, triterpenoids, etc.), provides great opportunities for the design of new nutritional and dietary supplements based on extracts from this *Maackia* genus.

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Appendix A

Table A1. Compounds identified from the CO₂ extracts of *M. amurensis* in positive and negative ionization modes using HPLC–ion trap–MS/MS.

Nº	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
POLYPHENOLS										
1	Flavone	2'-Hydroxyformononetin [Xenognosin B]	C ₁₆ H ₁₂ O ₅	284.2635	283		270; 255; 185; 151	255; 150	169	<i>Maackia amurensis</i> [5–8]
2	Flavone	Daidzein [4',7-Dihydroxyisoflavone; Daidzeol]	C ₁₅ H ₁₀ O ₄	254.2375		255	227; 211; 199; 163; 145			<i>Maackia amurensis</i> [5–8]; <i>Hedyotis diffusa</i> [24]; Isoflavones [25]
3	Flavone	Formononetin [Biochanin B; Formononetol]	C ₁₆ H ₁₂ O ₄	268.2641		269	253	236; 153	209; 181	<i>Astragali Radix</i> [21–23]; Isoflavones [25]; Huolisu Oral Liquid [26]
4	Flavone	Apigenin [5,7-Dihydroxy-2-(4-Hydroxyphenyl)-4H-Chromen-4-One]	C ₁₅ H ₁₀ O ₅	270.2369	269		225	181	181; 155	<i>Dracocephalum palmatum</i> [27]; <i>Lonicera japonica</i> [28]; Andean blueberry [29]; Mexican lupine species [30]; <i>Dracocephalum</i> [31]
5	Flavone	Genistein [Pruneton; 4',5,5-Trihydroxyisoflavone; Sophoricol]	C ₁₅ H ₁₀ O ₅	270.2369		271	253; 225; 215; 201; 179; 153	151		<i>Maackia amurensis</i> [5–8]; Mexican lupine species [30]; Isoflavones [25]
6	Flavone	Calycosin [3'-Hydroxyformononetin]	C ₁₆ H ₁₂ O ₅	284.2635	283		268; 254; 224; 187	224; 195; 175	224	<i>Maackia amurensis</i> [5–8]; <i>Astragali radix</i> [21–23]; Huolisu Oral Liquid [26]
7	Flavone	5-Methoxydaidzein	C ₁₆ H ₁₂ O ₅	284.2635		285	229; 211; 177; 163	211; 197; 183; 153	153	<i>Maackia amurensis</i> [1,2,5,6]

Table A1. Cont.

Nº	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
8	Flavone	Biochanin-A [4'-Methylgenistein; 5,7-Dihydroxy-4'- Methoxyisoflavone] *	C ₁₆ H ₁₂ O ₅	284.2635		285	270; 229; 152	242; 152	213; 158	<i>Astragali radix</i> [21–23]
9	Flavone	Orobol [Isoluteolin; 5,7,3',4' - Tetrahydroxyisoflavone]	C ₁₅ H ₁₀ O ₆	286.2363	285		283; 173	268; 224	224	<i>Maackia amurensis</i> [1,2,5,6]
10	Flavone	7-Hydroxy-6,4'- dimethoxyisoflavone *	C ₁₇ H ₁₄ O ₅	298.2901		299	286; 269; 245; 223; 167	152		<i>Astragali radix</i> [21–23]
11	Flavone	Afromosin [Castanin]	C ₁₇ H ₁₄ O ₅	298.2901		299	284; 239	253; 213; 178; 152	225; 167	<i>Maackia amurensis</i> [1,2,5,6]
12	Flavone	Tectorigenin	C ₁₆ H ₁₂ O ₆	300.2629		301	286; 269; 245; 226; 175; 153	258; 240; 212; 187; 168; 153	229; 212; 184; 156	<i>Maackia amurensis</i> [1,2,5,6]
13	Flavone	Trihydroxy methoxyflavone *	C ₁₆ H ₁₂ O ₆	300.2629	299		284; 240; 177	240; 211; 176; 150	213; 196; 156	<i>A. cordifolia</i> [32]; <i>Rosmarinus officinalis</i> [33]
14	Flavone	3-Hydroxyvestiton	C ₁₆ H ₁₄ O ₆	302.2788	301		283; 299; 227; 177	267; 240; 150	224	<i>Maackia amurensis</i> [1,2,5,6]
15	Flavone	Odoratin	C ₁₇ H ₁₄ O ₆	314.2895		315	300; 287; 255; 193; 167	148		<i>Astragali radix</i> [21–23]
16	Flavone	Cirsimaritin [Scrophulein; 4',5-Dihydroxy-6,7- Dimethoxyflavone; 7-Methylcapillarisin] *	C ₁₇ H ₁₄ O ₆	314.2895	313		298; 269	283; 255; 239; 195	255; 211	<i>Rosmarinus officinalis</i> [33]; <i>Artemisia annua</i> [34]; <i>Ocimum</i> [35]
17	Flavone	Dihydroxy- dimethoxy(iso)flavone *	C ₁₇ H ₁₄ O ₆	314.2895		315	313; 298; 269; 189	269; 167	237; 213; 154	<i>Astragali radix</i> [21; 22; 23]; <i>Rosmarinus officinalis</i> [33]; <i>Propolis</i> [36]

Table A1. Cont.

Nº	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
18	Flavone	Myricetin *	C ₁₅ H ₁₀ O ₈	318.2351		319	291; 219; 143	191; 143	173	Andean blueberry [29]; <i>F. glaucescens</i> [32]; Propolis [36]; <i>Solanaceae</i> [37]
19	Flavone	Cirsiliol *	C ₁₇ H ₁₄ O ₇	330.2889	329		311; 249; 229; 171	153		<i>Ocimum</i> [35]
20	Flavone	Wightone [Erythrinin B] *	C ₂₀ H ₁₈ O ₅	338.3539		339	283	255; 237; 183; 165	183	Mexican lupine species [30]
21	Isoflavone	Luteone *	C ₂₀ H ₁₈ O ₆	354.3533		355	299	281; 229; 165	183	Mexican lupine species [30]
22	Flavone	Dihydroxy tetramethoxyflavanone *	C ₁₉ H ₂₀ O ₈	376.3573		377	359; 341; 231; 189	341; 313; 239; 173	323; 295; 229; 179	<i>G. linguiforme</i> [32]
23	Flavone	Hydroxy hexamethoxyflavone *	C ₂₁ H ₂₄ O ₉	420.4099	419		404; 389; 373; 329	373; 359; 202	358; 328	<i>F. pottsii</i> [32]
24	Flavone	Formononetin (Glycosylated and methylated)	C ₂₃ H ₂₄ O ₉	444.4313		445	293; 267; 235; 217; 179	183		<i>Triticum aestivum</i> L. [38,39]
25	Flavone	Odoratin-O-hexoside *	C ₂₃ H ₂₄ O ₁₁	476.4301		477	415; 358; 331; 277	331; 303; 261; 206	261; 233	<i>Astragali radix</i> [21–23]
26	Flavone	6,4'-Dimethoxyisoflavone-7-O-glucoside *	C ₂₃ H ₂₄ O ₁₀	460.4307		461	283; 257; 215; 179	265; 237; 221; 197; 175	247; 219; 191; 181	<i>Astragali radix</i> [21–23]
27	Flavone	Formononetin-7-O-glucoside-6''-O-malonate *	C ₂₅ H ₂₄ O ₁₂	516.4509		517	269	254; 237; 213; 163	253; 237; 226; 181	<i>Astragali radix</i> [21–23]
28	Flavone	Genistein C-glucoside malonylated *	C ₂₄ H ₂₂ O ₁₃	518.4237		519	415; 369; 331	331; 261; 206		Mexican lupine species [30]
29	Flavone	Maackiasin	C ₃₀ H ₂₂ O ₉	526.4903		527	283; 255; 212; 171	255; 229; 152	240; 212; 184; 171	<i>Maackia amurensis</i> [1,2,5,6]

Table A1. Cont.

№	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
30	Flavone	Calycosin-7-O-beta-D-glucoside-6''-O-malonate *	C ₂₅ H ₂₄ O ₁₃	532.4503		533	285; 198	257; 229; 179; 167		<i>Astragali radix</i> [21–23]
31	Flavone	Chrysoeriol 8-C-glucoside malonylated *	C ₂₅ H ₂₄ O ₁₄	548.4497		549	487; 459; 365; 333; 245	245; 219; 167		Mexican lupine species [30]
32	Flavone	Apigenin 7-C-glucosyldeoxyhexoside *	C ₂₇ H ₃₀ O ₁₃	562.5193		563	431; 269	254; 237; 213; 199; 163	253; 237; 225; 181	<i>Passiflora incarnata</i> [40]
33	Isoflavone	Ononin derivative	C ₂₇ H ₂₈ O ₁₅	592.5022		593	269	254; 237; 213	237; 226; 200	Isoflavones [25]
34	Flavone	Apigenin 6-C-[6''-acetyl-2''-O-deoxyhexoside]-glucoside *	C ₂₉ H ₃₂ O ₁₅	620.5554		621	561	533; 461	433	<i>Passiflora incarnata</i> [40]
35	Flavonol	Kaempferol [3,5,7-Trihydroxy-2-(4-hydro-xyphenyl)-4H-chromen-4-one]	C ₁₅ H ₁₀ O ₆	286.2363		287	269; 259; 229; 213; 177; 163; 153	213; 171; 152	198; 181; 153	<i>Lonicera japonica</i> [28]; Andean blueberry [29]; <i>Dracocephalum</i> [31]; <i>Rhus coriaria</i> (Sumac) [41]
36	Flavonol	Quercetin	C ₁₅ H ₁₀ O ₇	302.2357		303	285; 228; 165	229; 165	141	<i>Astragali radix</i> [21–23]; Propolis [36]; <i>Rhus coriaria</i> [41]
37	Flavonoid	Di-O-galloyl-glucoside *	C ₂₀ H ₂₀ O ₁₄	484.3644		485	331; 267; 225; 169	225; 199; 163	215; 197	<i>Rosa rugosa</i> [42]; <i>Rosa canina</i> [43]; <i>Euphorbia hirta</i> [44]
38	Isoflavan	Vestitol	C ₁₆ H ₁₆ O ₄	272.2958		273	255; 227; 179	227; 197	209	<i>Maackia amurensis</i> [1,2,5,6]
39	Prenyl flavonoid	Prenyl naringenin [8-Prenylnaringenin; Flavaprenyl] *	C ₂₀ H ₂₀ O ₅	340.3698		341	285; 221; 179; 153	267; 221; 179	249; 171	<i>A. cordifolia</i> [32]; Beer [45]; Hop Prenylflavonoids [46]

Table A1. Cont.

Nº	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
40	Flavan-3-ol	(epi)Catechin-5-O-D-glycopyranoside *	C ₂₁ H ₂₄ O ₁₁	452.4087		453	343; 315; 281; 269; 227	161; 151	143	Actinidia [47]
41	Flavanone	Liquiritigenin [4',7-Dihydroxyflavanone; 5-Deoxyflavanone]	C ₁₅ H ₁₂ O ₄	256.2534	255		237; 213; 187; 151	185; 169; 145		Bauninia championii [48]; Maackia amurensis [1,2,5,6]
42	Flavanone	Methyl-liquiritigenin [7-O-Methyl-liquiritigenin] *	C ₁₆ H ₁₄ O ₄	270.2800		271	243; 221; 183; 161	183; 173; 155	155	PubChem
43	Flavanone	Liquiritigenin dimethyl ester [4',7-Dimethoxyflavanone] *	C ₁₇ H ₁₆ O ₄	284.3065		285	257; 227	225; 197; 173		PubChem
44	Flavanone	Padmatin [7-Methoxy-3,3',4',5-tetrahydroxyflavanone] *	C ₁₆ H ₁₄ O ₇	318.2782	317		299; 287; 270; 193	284; 256; 240	283; 256; 240; 228	Propolis [36]
45	Flavanone	Maackiaflavanone B	C ₃₀ H ₃₄ O ₅	474.5880		475	457; 413; 389; 349; 301; 255; 173	173; 145		PubChem
46	Phenolic acid	Ferulic acid	C ₁₀ H ₁₀ O ₄	194.184		195				Astragali radix [21–23]; Actinidia [47]; Codonopsis Radix [49]
47	Stilbene	Resveratrol [trans-Resveratrol; 3,4',5-Trihydroxystilbene; Stilbentriol]	C ₁₄ H ₁₂ O ₃	228.2433		229	211; 183	183; 171; 155		Maackia amurensis [1,2,5,6]; Radix polygoni multiflori [50]; Embelia [51]
48	Stilbene	3-Hydroxyresveratrol [Piceatannol]	C ₁₄ H ₁₂ O ₄	244.2427	243		225; 201	225; 157; 197		Maackia amurensis [1,2,5,6]; G. linguiforme [32]; Vine stilbenoids [52]
49	Stilbene	Piacetannol-3-O-glucoside [Quzhaqigan] *	C ₂₀ H ₂₂ O ₉	406.3833		407	351; 333; 295; 229	333; 295; 217; 179	319; 265; 235; 200	PubChem

Table A1. Cont.

Nº	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
50	Stilbenolignan	Maackolin	C ₂₅ H ₂₄ O ₈	452.4533		453	343; 281; 161	315; 283; 222; 161	283; 251; 205; 161	<i>Maackia amurensis</i> [1,2,5,6]
51	Dimeric stilbene	Resveratrol-piceatannol *	C ₂₈ H ₂₂ O ₇	470.4701		471	377; 365; 343; 307; 267; 215	267; 249; 221	249; 221; 199	Vine stilbenoids [52]; vinery products [53]
52	Dimeric stilbene	Scirpusin A	C ₂₈ H ₂₂ O ₇	470.4701	469		345; 304; 241	317; 299; 275; 251; 223	315; 288; 258	<i>Maackia amurensis</i> [1,2,5,6]
53	Dimeric stilbene	Scirpusin B	C ₂₈ H ₂₂ O ₈	486.4695		487	377; 255; 231; 157	267; 249	249	<i>Maackia amurensis</i> [1,2,5,6]
54	Hydroxycoumarin	Esculin [Aesculin; Esculoside; Polichrome; Esculetin-6-O-glucoside] *	C ₁₅ H ₁₆ O ₉	340.2821		341	179; 165	151		<i>Artemisia annua</i> [34]; <i>A. cordifolia</i> [32]; <i>Actinidia</i> [47]; <i>Stevia rebaudiana</i> [54]
OTHERS										
55	Omega-5 fatty acid	Myristoleic acid [Cis-9-Tetradecanoic acid] *	C ₁₄ H ₂₆ O ₂	226.3550		227	209	139		<i>F. glaucescens</i> [32]; <i>Dracocephalum</i> [31]
56	Pterocarpan	Medicarpin [(+)-Medicarpin; Demethylhomopterocarpin; 3-Hydroxy-9-Methoxypterocarpan]	C ₁₆ H ₁₄ O ₄	270.2800		271	215; 181; 161	197; 187; 169; 159	169	<i>Maackia amurensis</i> [1,2,5,6]; <i>Astragali radix</i> [21–23]
57	Omega-3 fatty acid	Stearidonic acid [6,9,12,15-Octadecatetraenoic acid; Moroctic acid] *	C ₁₈ H ₂₈ O ₂	276.4137		277	177; 276; 259; 241; 219; 195; 149	161		<i>G. linguiforme</i> [32]; <i>Rhus coriaria</i> [41]; <i>Salviae Miltiorrhizae</i> [55]; <i>Jatropha</i> [56]
58	Omega 3-fatty acid	Linolenic acid (Alpha-Linolenic acid; Linolenate) *	C ₁₈ H ₃₀ O ₂	278.4296		279	219; 259	159		<i>Salviae Miltiorrhizae</i> [55]; <i>Jatropha</i> [56]; <i>Pinus sylvestris</i> [57]

Table A1. Cont.

Nº	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
59	Pterocarpan	Maakiain [Inermin]	C ₁₆ H ₁₂ O ₅	284.2635		285	283; 269; 252; 228; 200; 169	254; 238; 210		<i>Maackia amurensis</i> [1,2,5,6]
60	Omega 3-fatty acid	Hydroxy linolenic acid *	C ₁₈ H ₃₀ O ₃	294.4290		295	276; 248; 171	231; 221; 159		<i>A. cordifolia</i> [32]
61	Higher-molecular-weight carboxylic acid	Oxo-nonadecanoic acid *	C ₁₉ H ₃₆ O ₃	312.4873		313	298; 269	269; 252; 213; 165	269; 213; 181	<i>G. linguiforme</i> ; <i>F. pottsii</i> ; <i>A. cordifolia</i> [32]
62	Oxylipins	13-Trihydroxy-Octadecenoic acid [THODE] *	C ₁₈ H ₃₄ O ₅	330.4596	329		171; 311; 275; 229; 211; 201	311; 201; 171	183; 211	<i>Dracocephalum</i> [31]; <i>Bituminaria</i> [58]; <i>Brassica oleracea</i> [59]
63	Unsaturated fatty acid	Pentacosenoic acid *	C ₂₅ H ₄₈ O ₂	380.6474	379		361; 337; 319; 295; 255	343; 333; 302; 273; 250	343; 315; 301	<i>F. glaucescens</i> [32]
64	Anabolic steroid	Vebronol *	C ₃₀ H ₄₄ O ₃	452.6686		453	435; 417; 336; 302; 245	336; 309; 281; 243; 226; 209	209; 192; 147	<i>Rhus coriaria</i> [41]; <i>Rosa rugosa</i> [60]; <i>Zostera marina</i> [61]
65	Triterpenic acid	Ursolic acid *	C ₃₀ H ₄₈ O ₃	456.7003		457	411; 367; 323; 236; 189	393; 263; 163	348	<i>Hedyotis diffusa</i> [24]; <i>Ocimum</i> [35]
66	Product of chlorophyll degradation	Pheophytin A *	C ₅₅ H ₇₄ N ₄ O ₅	871.1999			593; 533	533; 461	461; 433	<i>Physalis peruviana</i> [62]; <i>Capsicum</i> [63]

* Chemical compounds identified for the first time in *M. amurensis*.

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