

**The Effects of Selected Extraction Methods and Natural Deep Eutectic Solvents on the Recovery of Active Principles from *Aralia elata* var. *mandshurica* (Rupr. & Maxim.) J. Wen: A Non-Targeted Metabolomics Approach**

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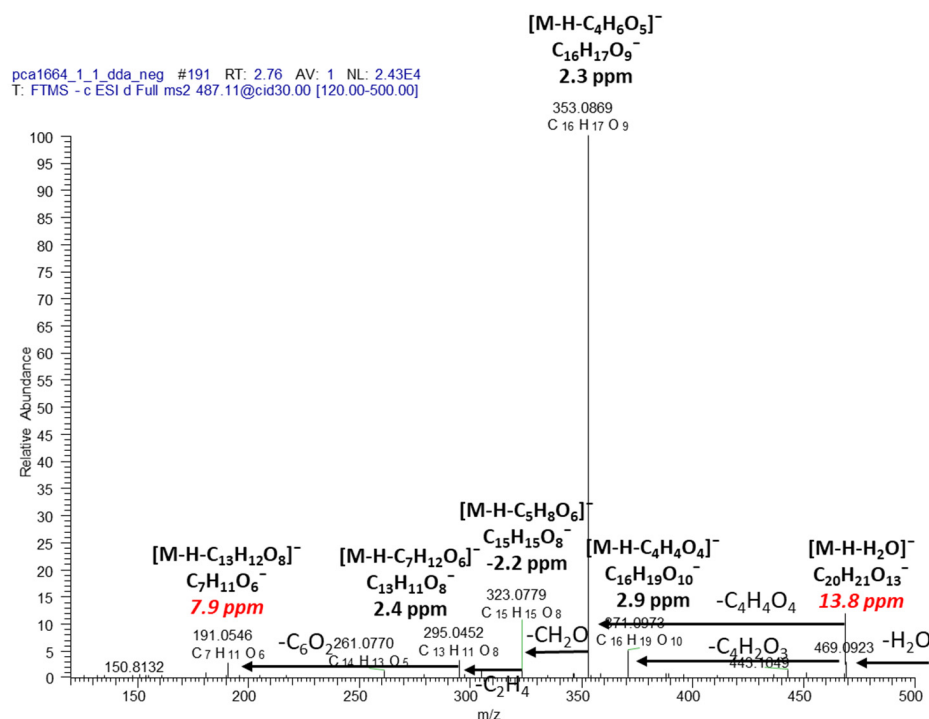
**Supplementary Information S1**

## Directory

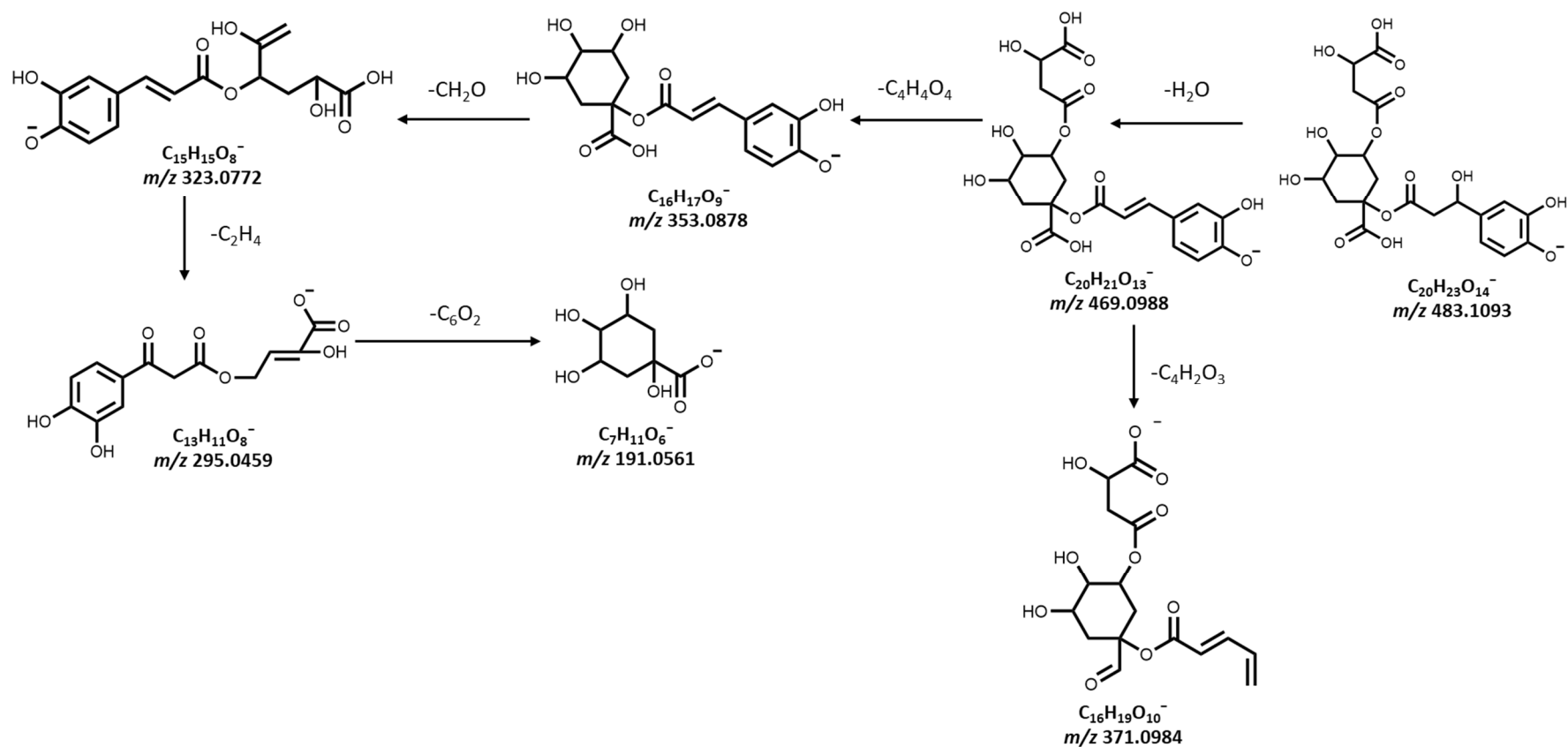
**Figures S1-12.** Secondary metabolites annotated by targeted MS/MS fragmentation patterns in *Aralia elata* var. *mandshurica* (Rupr. & Maxim.) J. Wen extracts in experiment of extractant comparison (sorbitol:malic acid vs choline chloride:malic acid) by reversed phase ultra-high-performance liquid chromatography—tandem mass spectrometry (RP-UHPLC-ESI-LIT-Orbitrap-MS/MS) in the negative ion mode. The MS/MS spectra of individual metabolites are listed as Figure S1 – S12.....3

**Figures S13-S34.** Secondary metabolites annotated by targeted MS/MS fragmentation patterns in *Aralia elata* var. *mandshurica* (Rupr. & Maxim.) J. Wen extracts in the experiment of extraction methods comparison (maceration vs vibrocavitator) by reversed phase ultra-high-performance liquid chromatography—tandem mass spectrometry (RP-UHPLC-ESI-LIT-Orbitrap-MS/MS) in the negative ion mode. The MS/MS spectra of individual metabolites are listed as Figure S13 – S34.....15

**Figures S1-S12.** Secondary metabolites annotated by targeted MS/MS fragmentation patterns in *Aralia elata* var. *mandshurica* (Rupr. & Maxim.) J. Wen extracts in experiment of extractant comparison (sorbitol:malic acid vs choline chloride:malic acid) by reversed phase ultra-high-performance liquid chromatography—tandem mass spectrometry (RP-UHPLC-ESI-LIT-Orbitrap-MS/MS) in the negative ion mode. The MS/MS spectra of individual metabolites are listed as Figure S1 – S12.

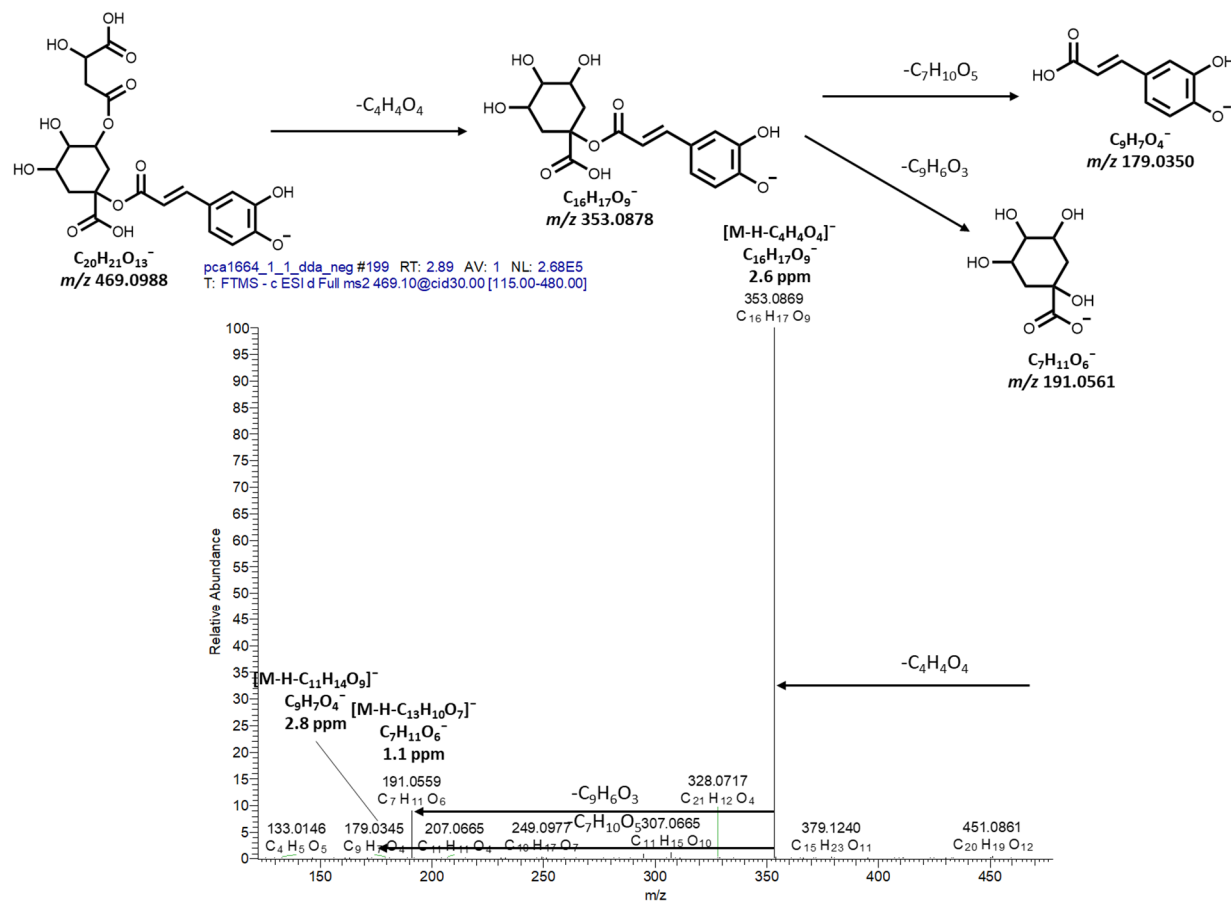


**Figure S1.** Tandem mass spectrum of  $m/z$  487.11 at  $t_R$  2.76 min corresponding to malonyl hydroxydihydrocaffeoylquinic acid (**1**), annotated in *Aralia elata* var. *mandshurica* (Rupr. & Maxim.) J. Wen extract. The spectrum was acquired with LIT-Orbitrap mass spectrometer operated in the negative product ion mode (collision energy 30 eV).

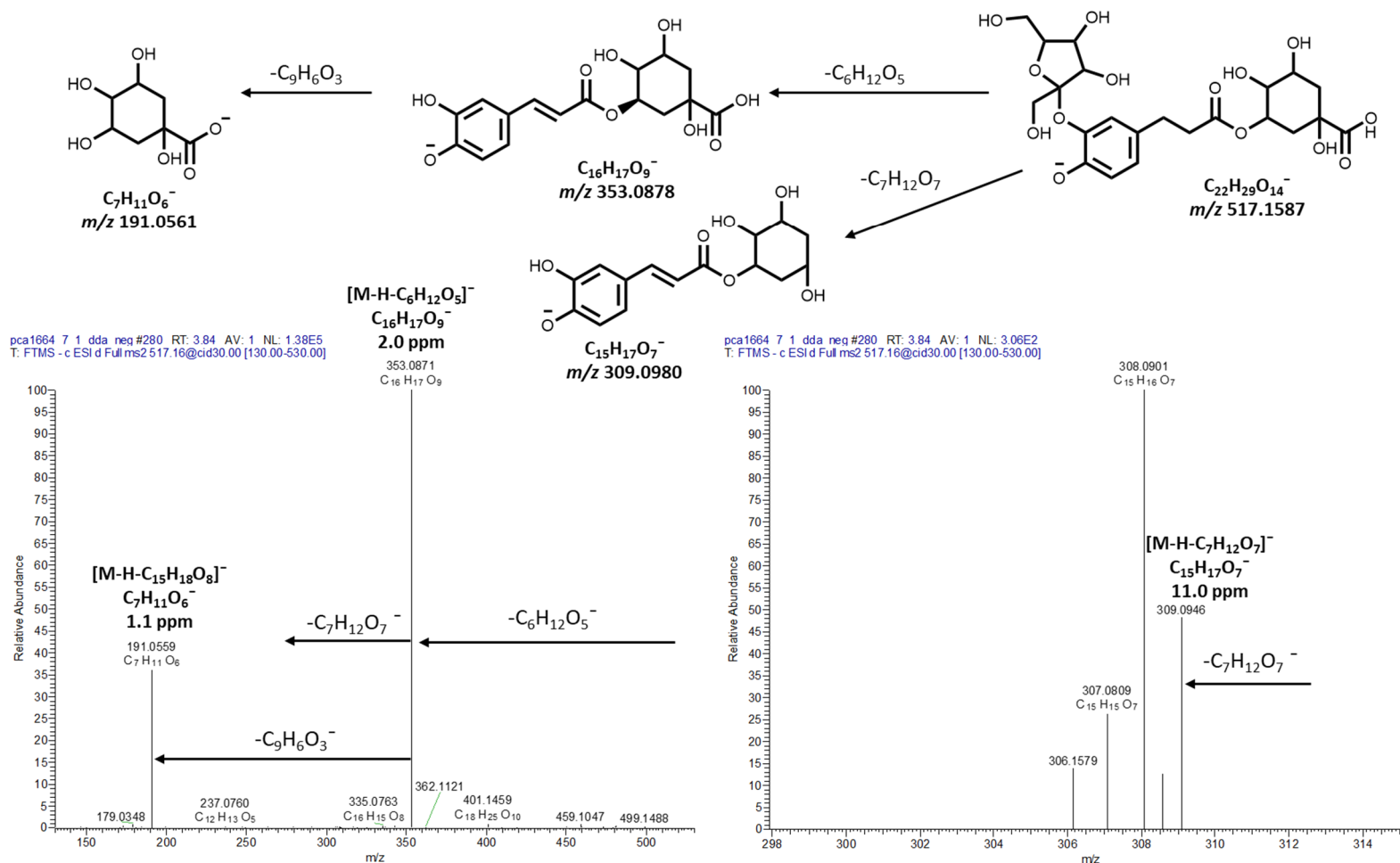


**Figure S2.** Proposed tandem mass spectrometric fragmentation patterns for the ion at  $m/z$  487.11 ( $[M-H]^-$ ,  $MS^2$ ) corresponding to malonyl hydroxy-dihydrocaffeoylquinic acid (1).



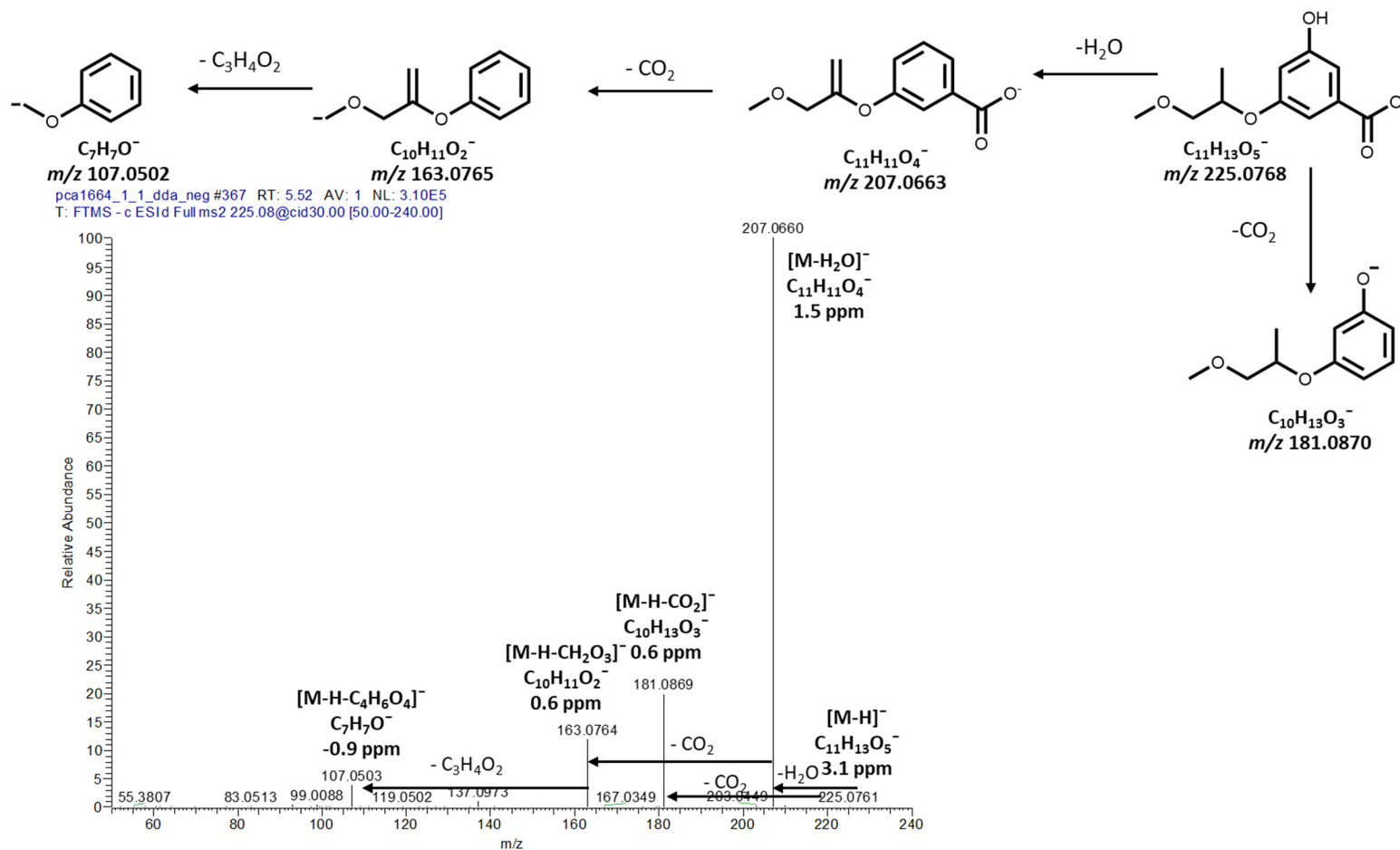


**Figure S3.** Tandem mass spectrum of  $m/z$  469.10 at  $t_R$  2.89 min corresponding to malonyl caffeoylquinic acid (2), annotated in *Aralia elata* var. *mandshurica* (Rupr. & Maxim.) J. Wen extract. The spectrum was acquired with LIT-Orbitrap mass spectrometer operated in the negative product ion mode (collision energy 30 eV). Structures shown are suggestions.

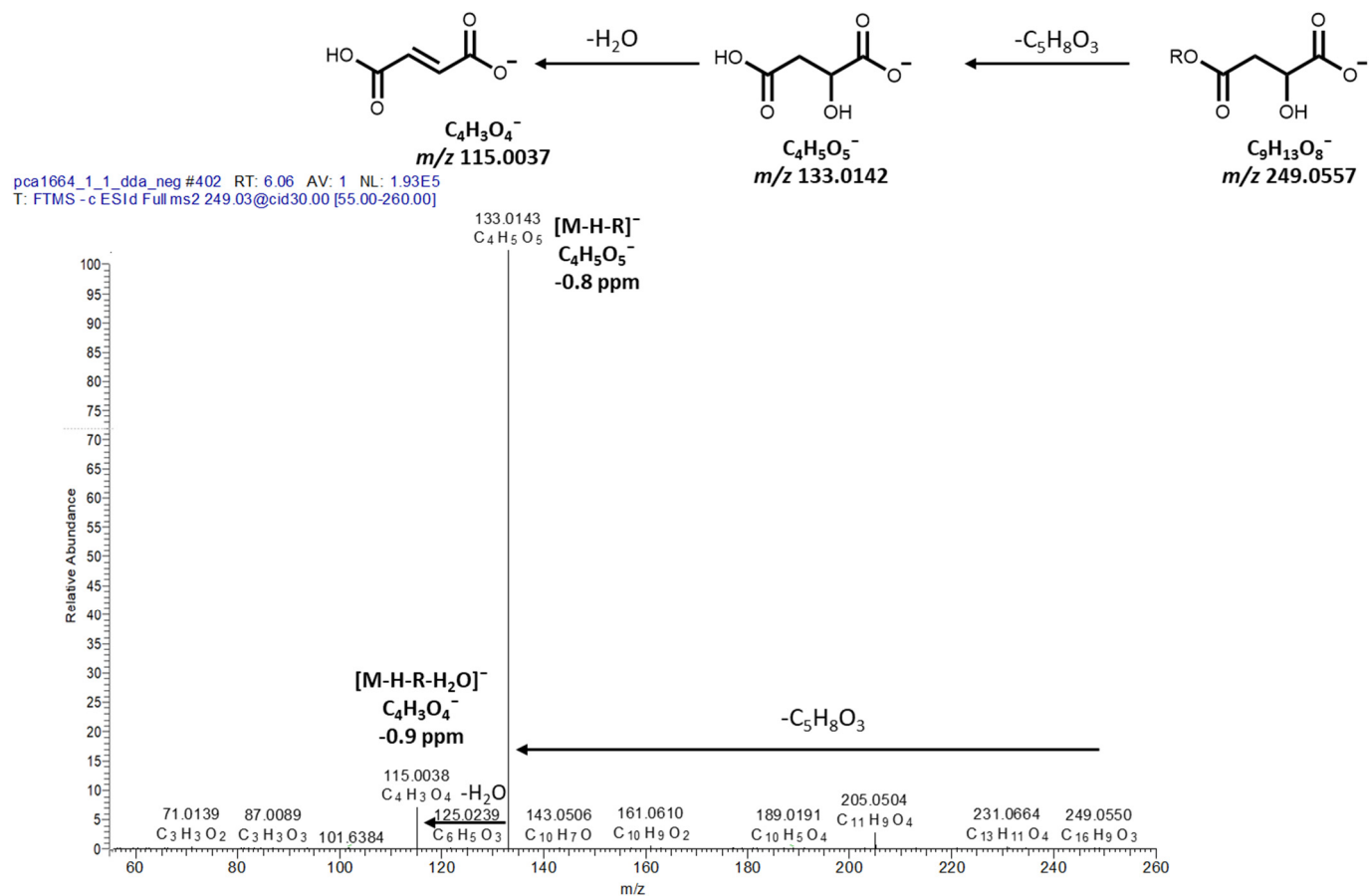


**Figure S4.** Tandem mass spectrum of  $m/z$  517.18 at  $t_R$  3.84 min corresponding to pentofuranosyl dihydrocaffeoylquinic acid (**3**), annotated in *Aralia elata* var. *mandshurica* (Rupr. & Maxim.) J. Wen extract. The spectrum was acquired with LIT-Orbitrap mass spectrometer operated in the negative product ion mode (collision energy 30 eV). Structures shown are suggestions.

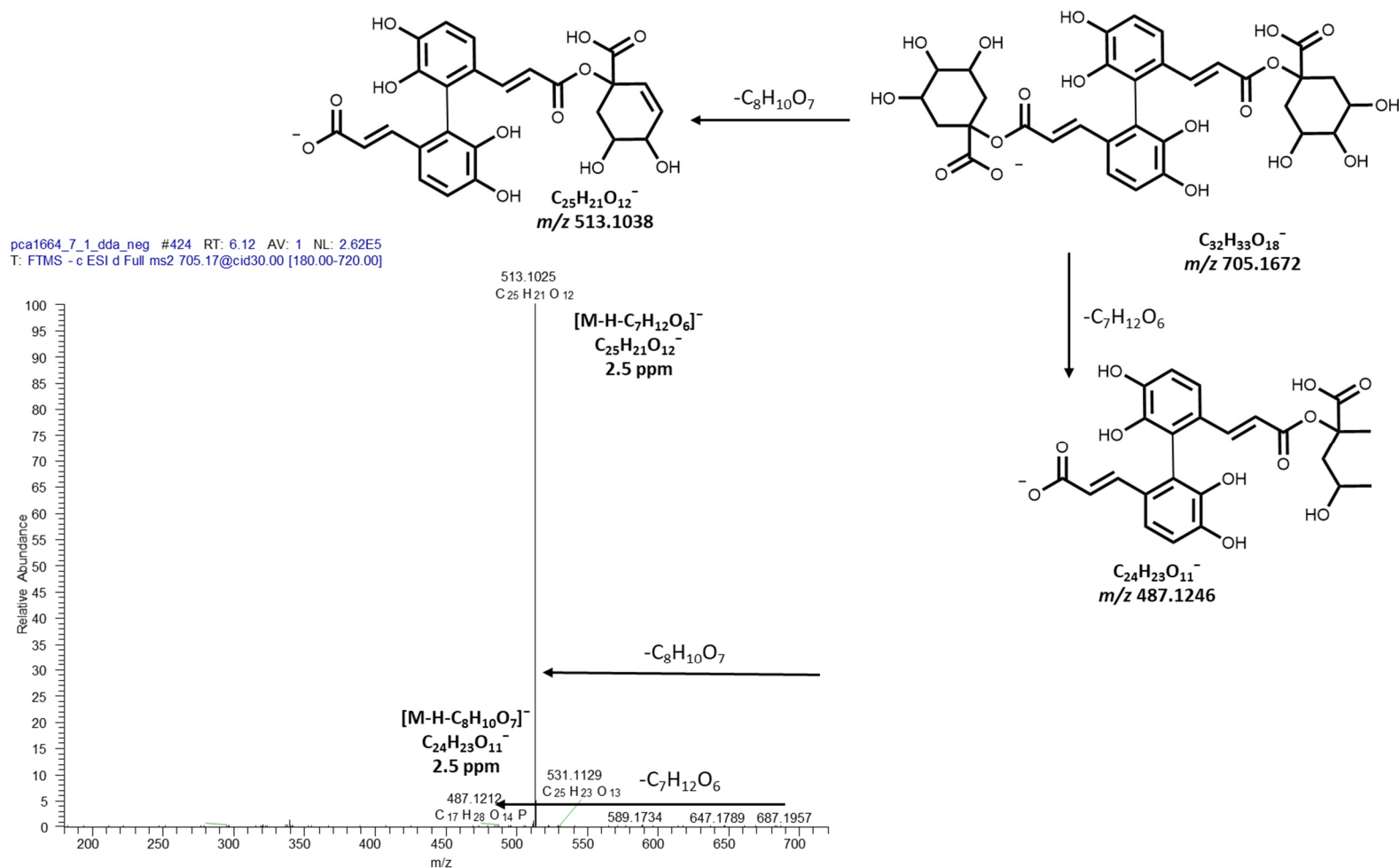




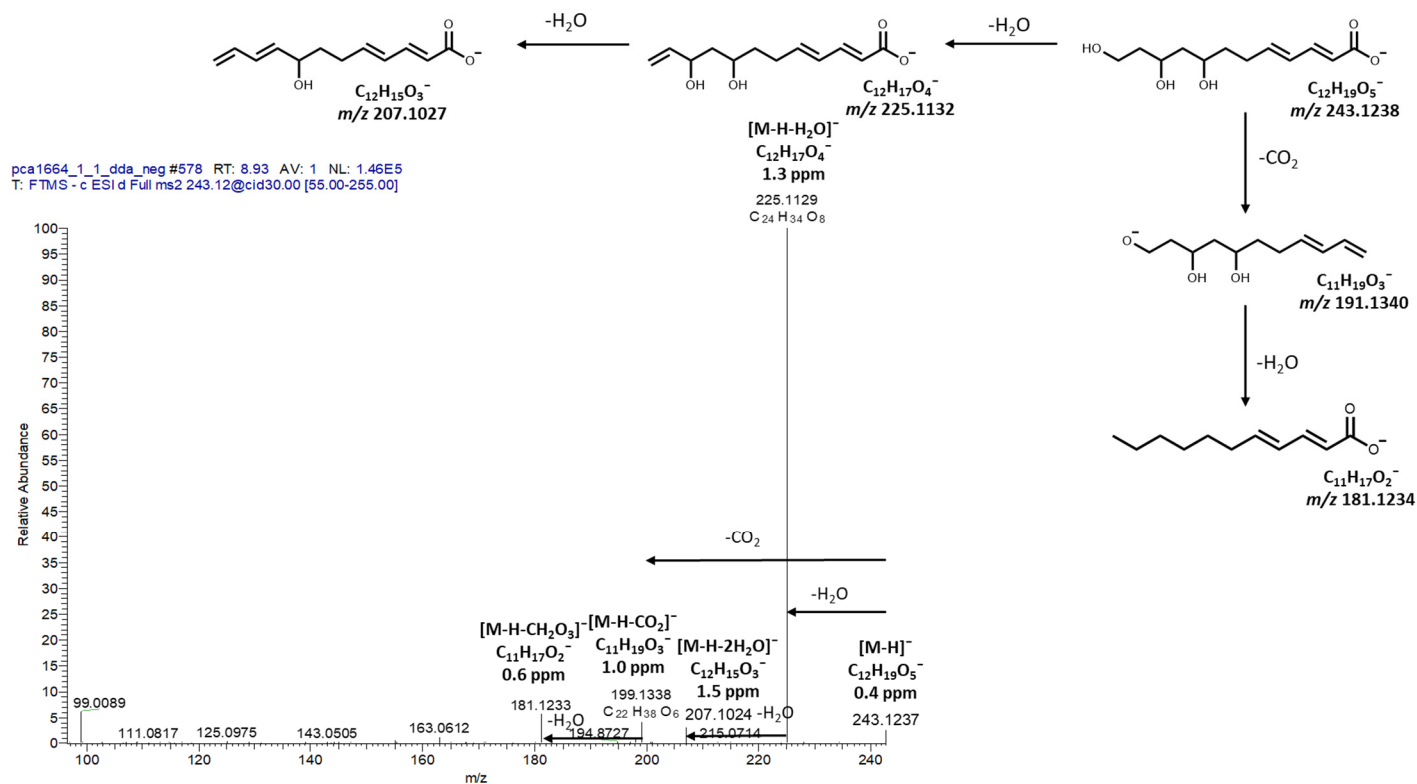
**Figure S6.** Tandem mass spectrum of  $m/z$  225.08 at  $t_R$  5.52 min corresponding to 3-hydroxy-5-(2-methoxy-1-methylethoxy)benzoate (**5**), annotated in *Aralia elata* var. *mandshurica* (Rupr. & Maxim.) J. Wen extract. The spectrum was acquired with LIT-Orbitrap mass spectrometer operated in the negative product ion mode (collision energy 30 eV). Structures shown are suggestions.



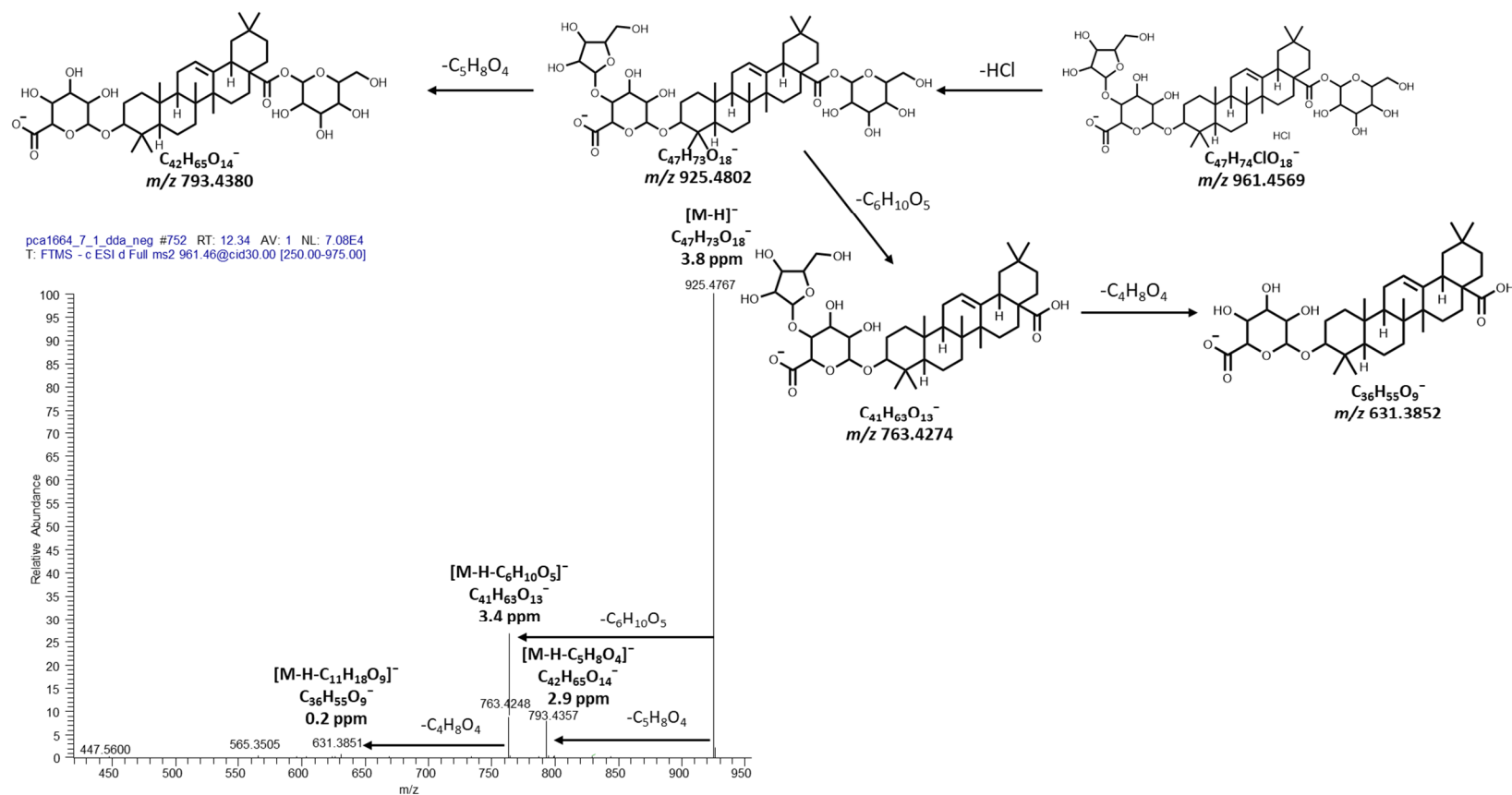
**Figure S7.** Tandem mass spectrum of  $m/z$  249.03 at  $t_R$  6.06 min corresponding to mallic acid derivatives (**6**), annotated in *Aralia elata* var. *mandshurica* (Rupr. & Maxim.) J. Wen extract. The spectrum was acquired with LIT-Orbitrap mass spectrometer operated in the negative product ion mode (collision energy 30 eV). Structures shown are suggestions.



**Figure S8.** Tandem mass spectrum of  $m/z$  705.17 at  $t_R$  6.12 min corresponding to caffeoylquinic acid dimer (7), annotated in *Aralia elata* var. *mandshurica* (Rupr. & Maxim.) J. Wen extract. The spectrum was acquired with LIT-Orbitrap mass spectrometer operated in the negative product ion mode (collision energy 30 eV). Structures shown are suggestions.

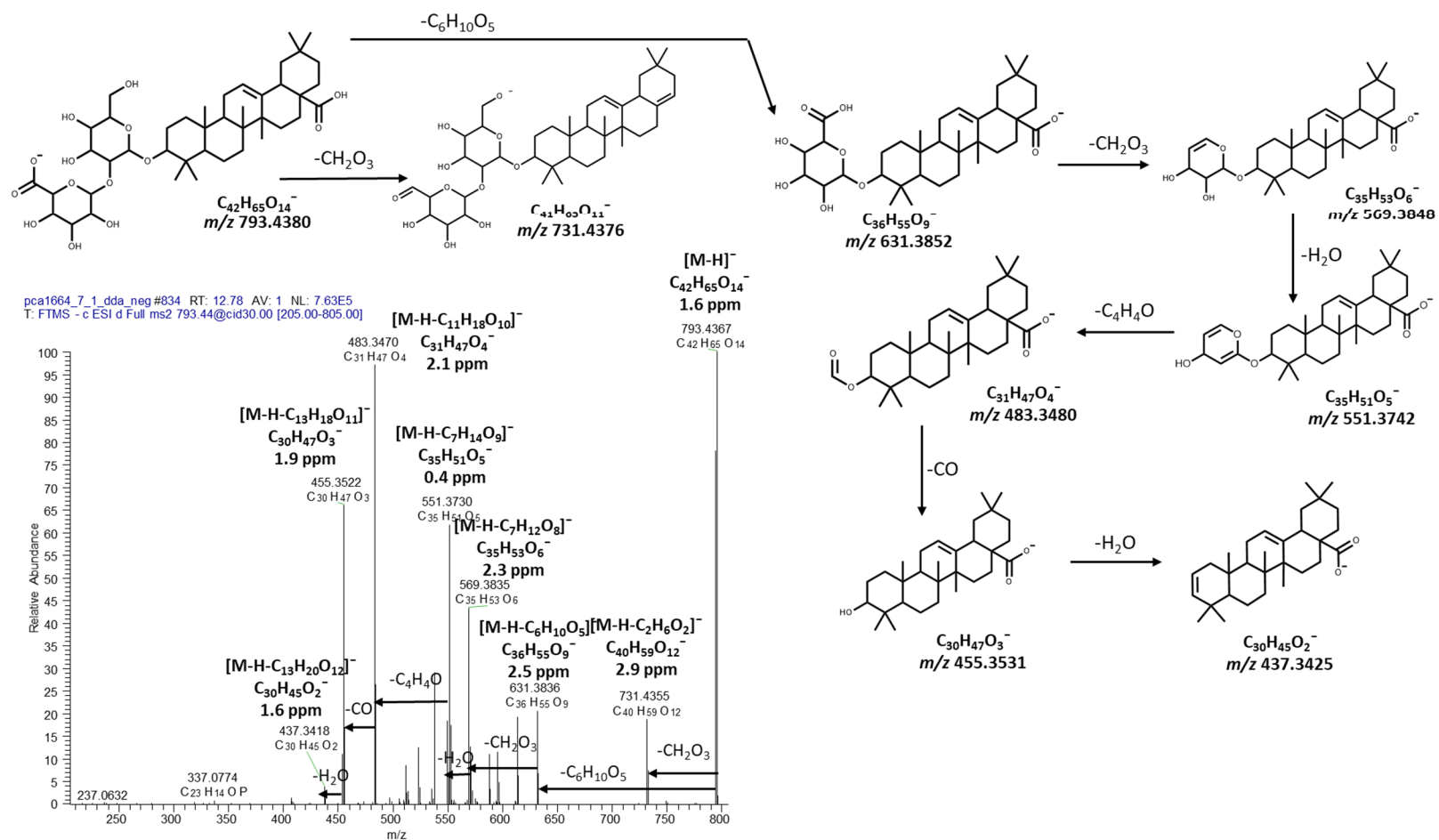


**Figure S9.** Tandem mass spectrum of  $m/z$  243.12 at  $t_R$  8.93 min corresponding to trihydroxy-dodecadienoic acid (**8**), annotated in *Aralia elata* var. *mandshurica* (Rupr. & Maxim.) J. Wen extract. The spectrum was acquired with LIT-Orbitrap mass spectrometer operated in the negative product ion mode (collision energy 30 eV). Structures shown are suggestions.

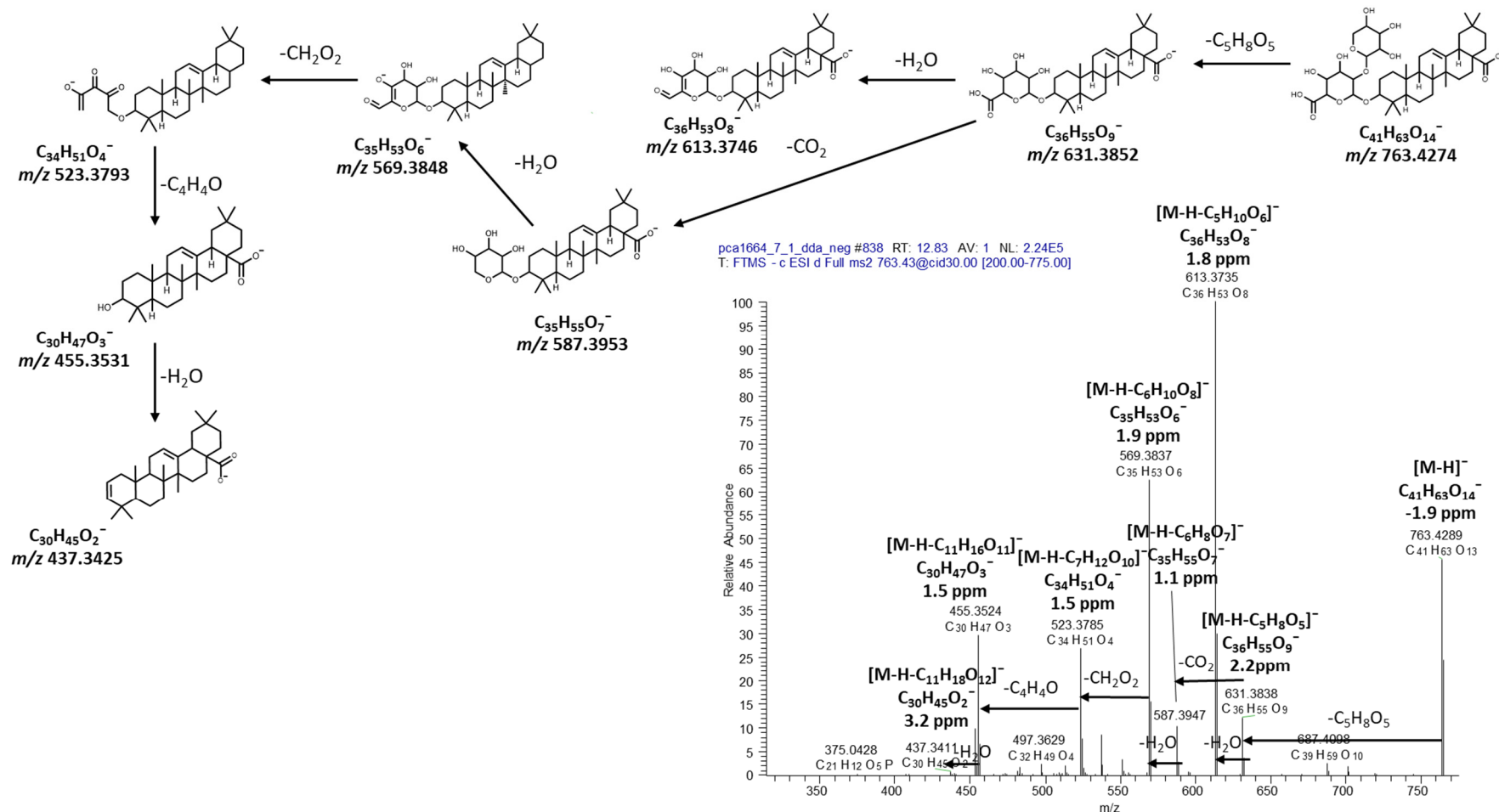


**Figure S10.** Tandem mass spectrum of  $m/z$  961.46 at  $t_R$  12.34 min corresponding to chikusetsusaponin IV (9), annotated in *Aralia elata* var. *mandshurica* (Rupr. & Maxim.) J. Wen extract. The spectrum was acquired with LIT-Orbitrap mass spectrometer operated in the negative product ion mode (collision energy 30 eV). Structures shown are suggestions.



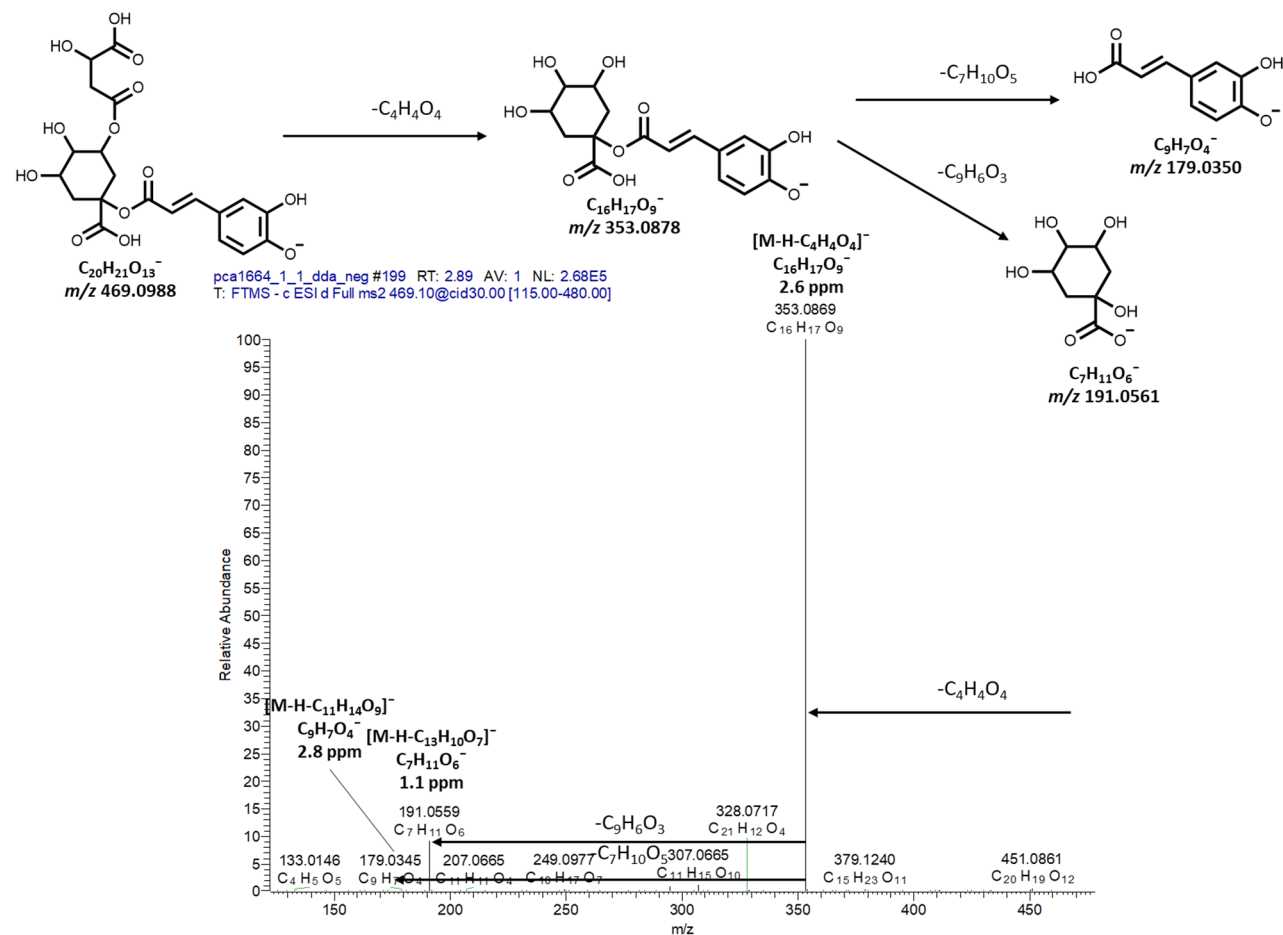


**Figure S11.** Tandem mass spectrum of  $m/z$  793.44 at  $t_R$  12.78 min corresponding to oleanolic acid-hexuronide-hexoside (**10**), annotated in *Aralia elata* var. *mandshurica* (Rupr. & Maxim.) J. Wen extract. The spectrum was acquired with LIT-Orbitrap mass spectrometer operated in the negative product ion mode (collision energy 30 eV). Structures shown are suggestions.

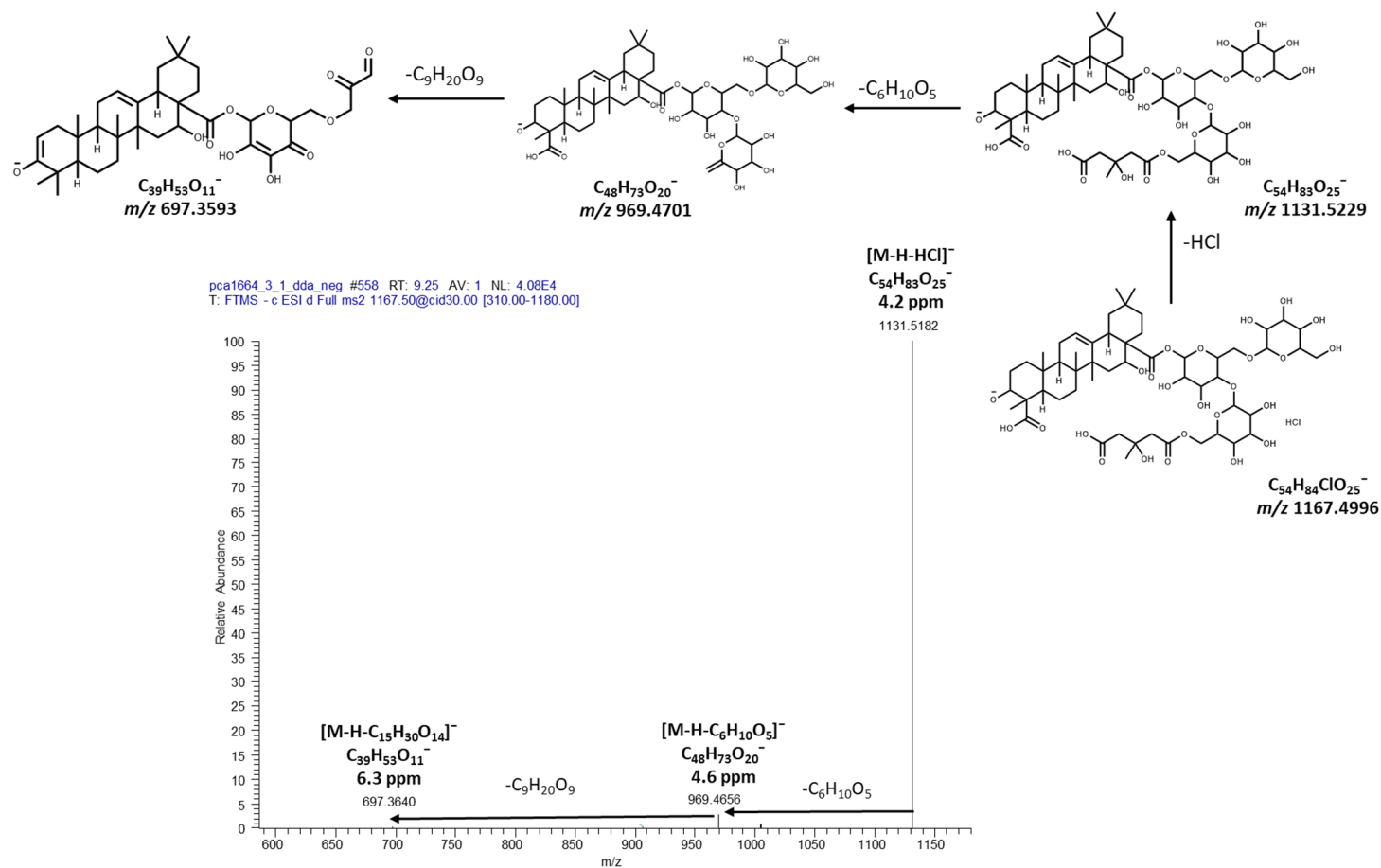


**Figure S12.** Tandem mass spectrum of  $m/z$  763.43 at  $t_R$  12.83 min corresponding to pseudoginsenoside Rp1 (11), annotated in *Aralia elata* var. *mandshurica* (Rupr. & Maxim.) J. Wen extract. The spectrum was acquired with LIT-Orbitrap mass spectrometer operated in the negative product ion mode (collision energy 30 eV). Structures shown are suggestions.

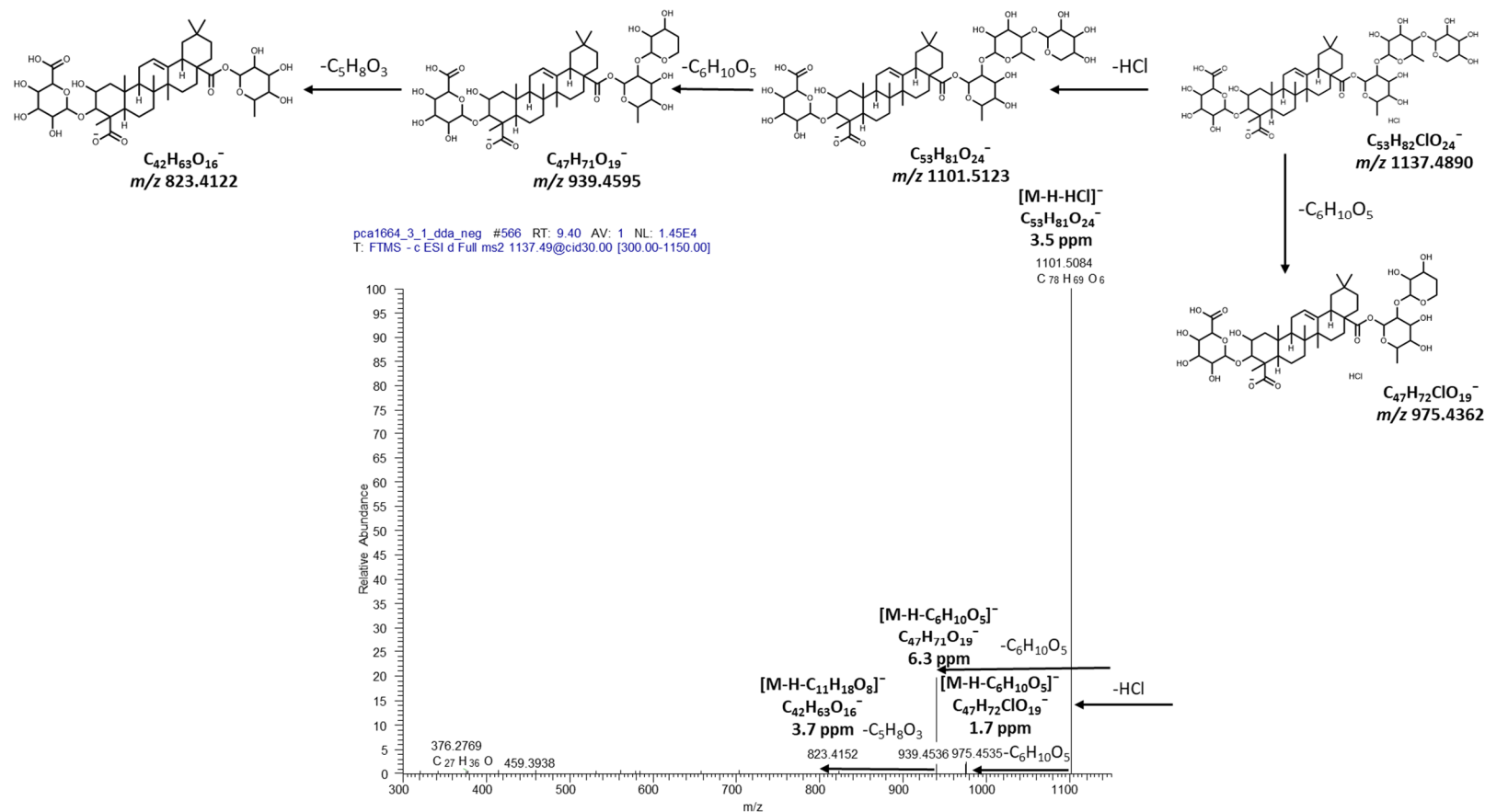
**Figures S13 – S34.** Secondary metabolites annotated by targeted MS/MS fragmentation patterns in *Aralia elata* var. *mandshurica* (Rupr. & Maxim.) J. Wen extracts in the experiment of extraction methods comparison (maceration vs vibrocavitator) by reversed phase ultra-high-performance liquid chromatography—tandem mass spectrometry (RP-UHPLC-ESI-LIT-Orbitrap-MS/MS) in the negative ion mode. The MS/MS spectra of individual metabolites are listed as Figure S13 – S34.



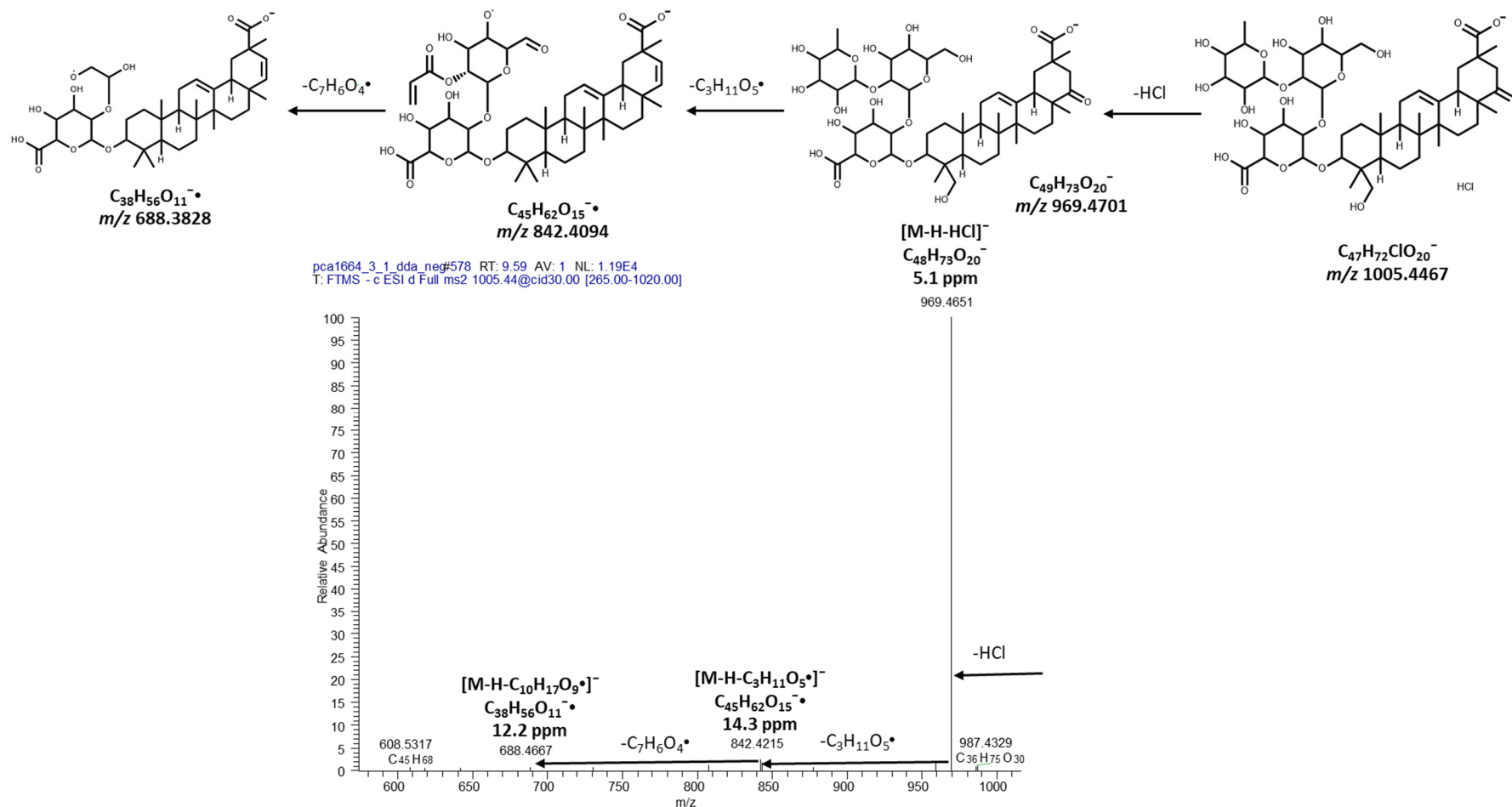
**Figure S13.** Tandem mass spectrum of  $m/z$  469.10 at  $t_R$  2.89 min corresponding to malonyl caffeoylquinic acid (12), annotated in *Aralia elata* var. *mandshurica* (Rupr. & Maxim.) J. Wen extract. The spectrum was acquired with LIT-Orbitrap mass spectrometer operated in the negative product ion mode (collision energy 30 eV). Structures shown are suggestions.



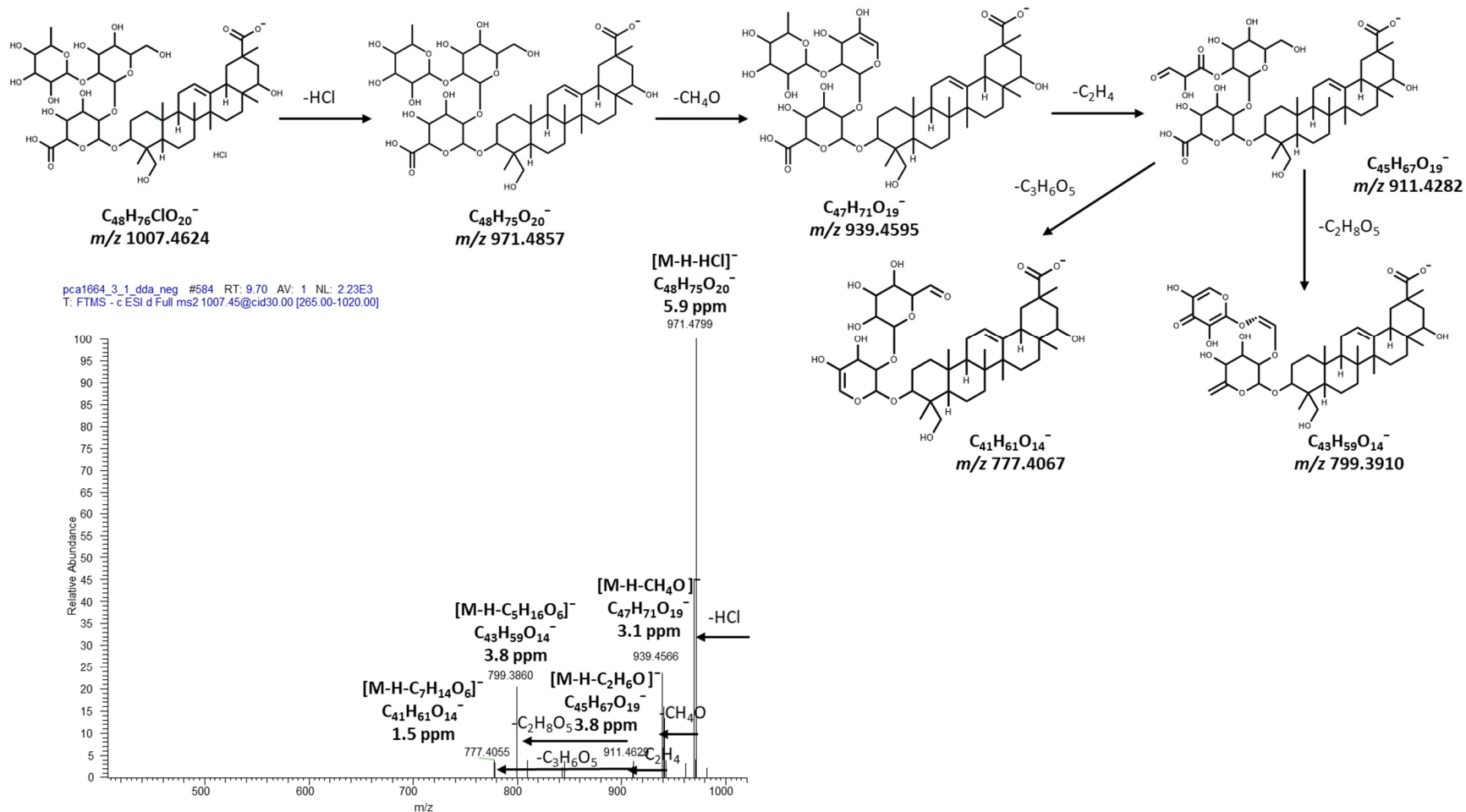
**Figure S14.** Tandem mass spectrum of  $m/z$  1167.50 at  $t_R$  9.25 min corresponding to 3,16-dihydroxyolean-12-en-23,28-dioic acid 28-O-[D-6-O-3-hydroxy-3-methylglutar-yl)-hexopyranosyl-(1 $\rightarrow$ 3)]-[D-hexopyranosyl-(1 $\rightarrow$ 6)]-D-hexopyranosyl ester (**13**), annotated in *Aralia elata* var. *mandshurica* (Rupr. & Maxim.) J. Wen extract. The spectrum was acquired with LIT-Orbitrap mass spectrometer operated in the negative product ion mode (collision energy 30 eV). Structures shown are suggestions.



**Figure S15.** Tandem mass spectrum of  $m/z$  1137.49 at  $t_R$  9.40 min corresponding to celosin I (**14**), annotated in *Aralia elata* var. *mandshurica* (Rupr. & Maxim.) J. Wen extract. The spectrum was acquired with LIT-Orbitrap mass spectrometer operated in the negative product ion mode (collision energy 30 eV). Structures shown are suggestions.

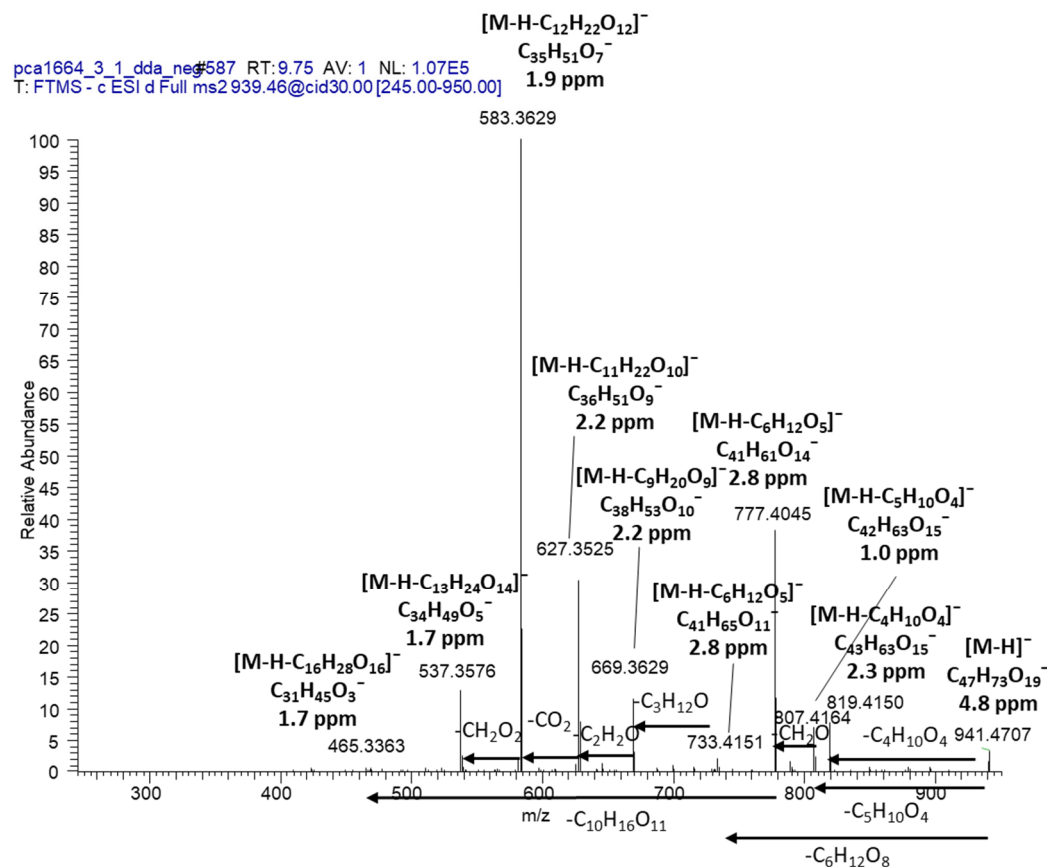


**Figure S16.** Tandem mass spectrum of  $m/z$  1005.44 at  $t_R$  9.59 min corresponding to 3-O-L-hexopyranosyl-(1→2)-D-hexopyranosyl-(1→2)-D-hexuronopyranosyl melilotigenin isomer 1 (**15**), annotated in *Aralia elata* var. *mandshurica* (Rupr. & Maxim.) J. Wen extract. The spectrum was acquired with LIT-Orbitrap mass spectrometer operated in the negative product ion mode (collision energy 30 eV). Structures shown are suggestions.

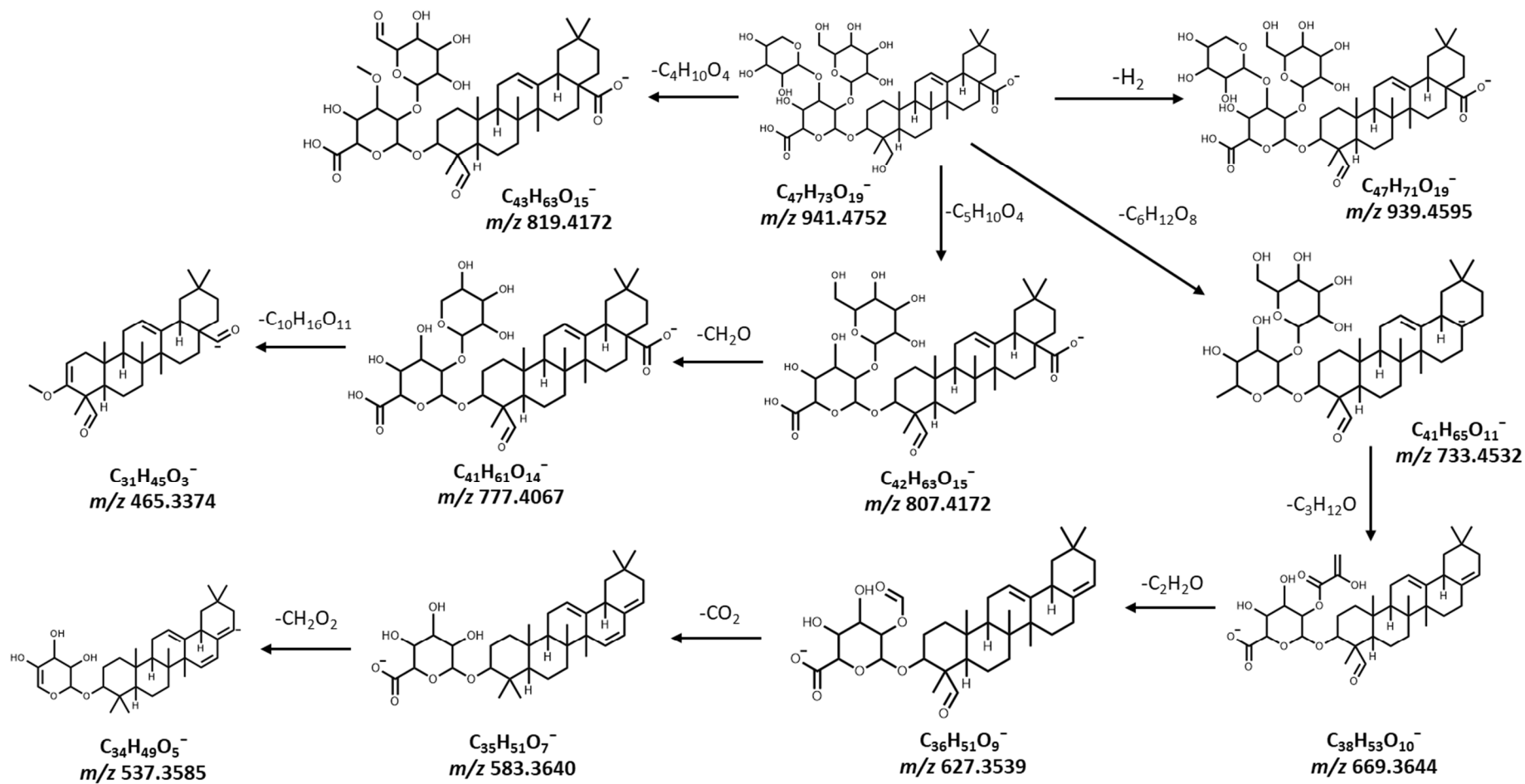


**Figure S17.** Tandem mass spectrum of  $m/z$  1007.45 at  $t_R$  9.70 min corresponding to sophoraflavoside II isomer 1 (16), annotated in *Aralia elata* var. *mandshurica* (Rupr. & Maxim.) J. Wen extract. The spectrum was acquired with LIT-Orbitrap mass spectrometer operated in the negative product ion mode (collision energy 30 eV). Structures shown are suggestions.

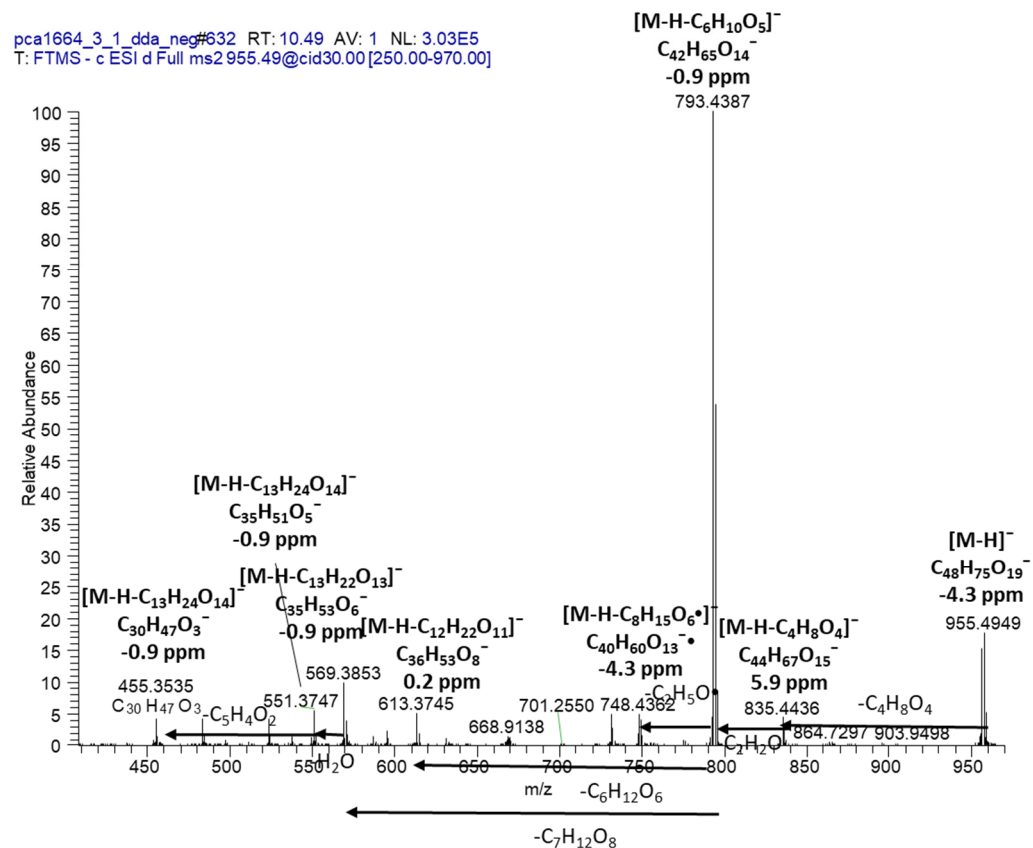




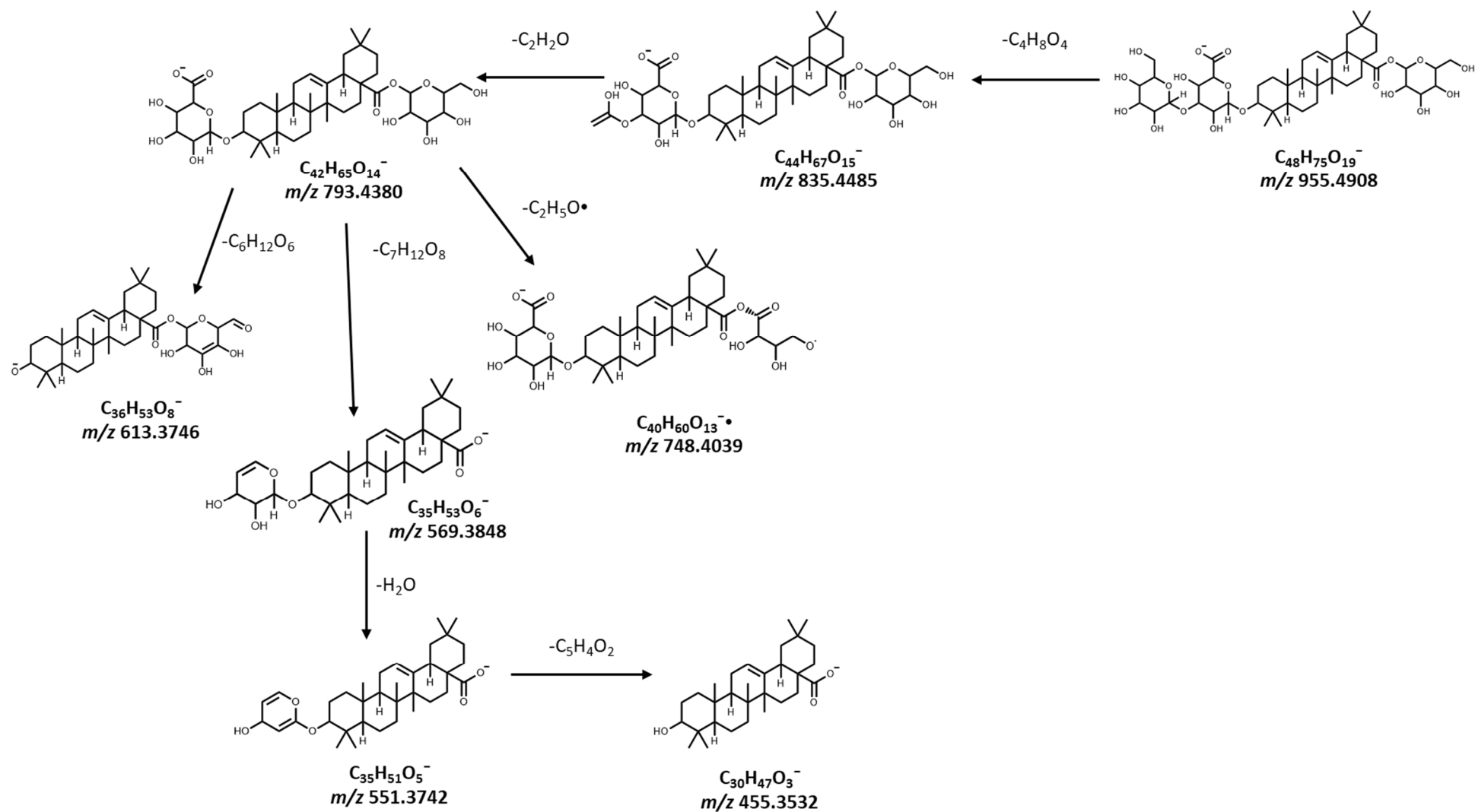
**Figure S18.** Tandem mass spectrum of  $m/z$  939.46 at  $t_R$  9.75 min corresponding to dihydrogypsogenin 3-*O*-pentopyranosyl-(1-2)-hexpyranox-yl-(1-3)- $\beta$ -D-hexuronopyranoside isomer 1 (**17**), annotated in *Aralia elata* var. *mandshurica* (Rupr. & Maxim.) J. Wen extract. The spectrum was acquired with LIT-Orbitrap mass spectrometer operated in the negative product ion mode (collision energy 30 eV).



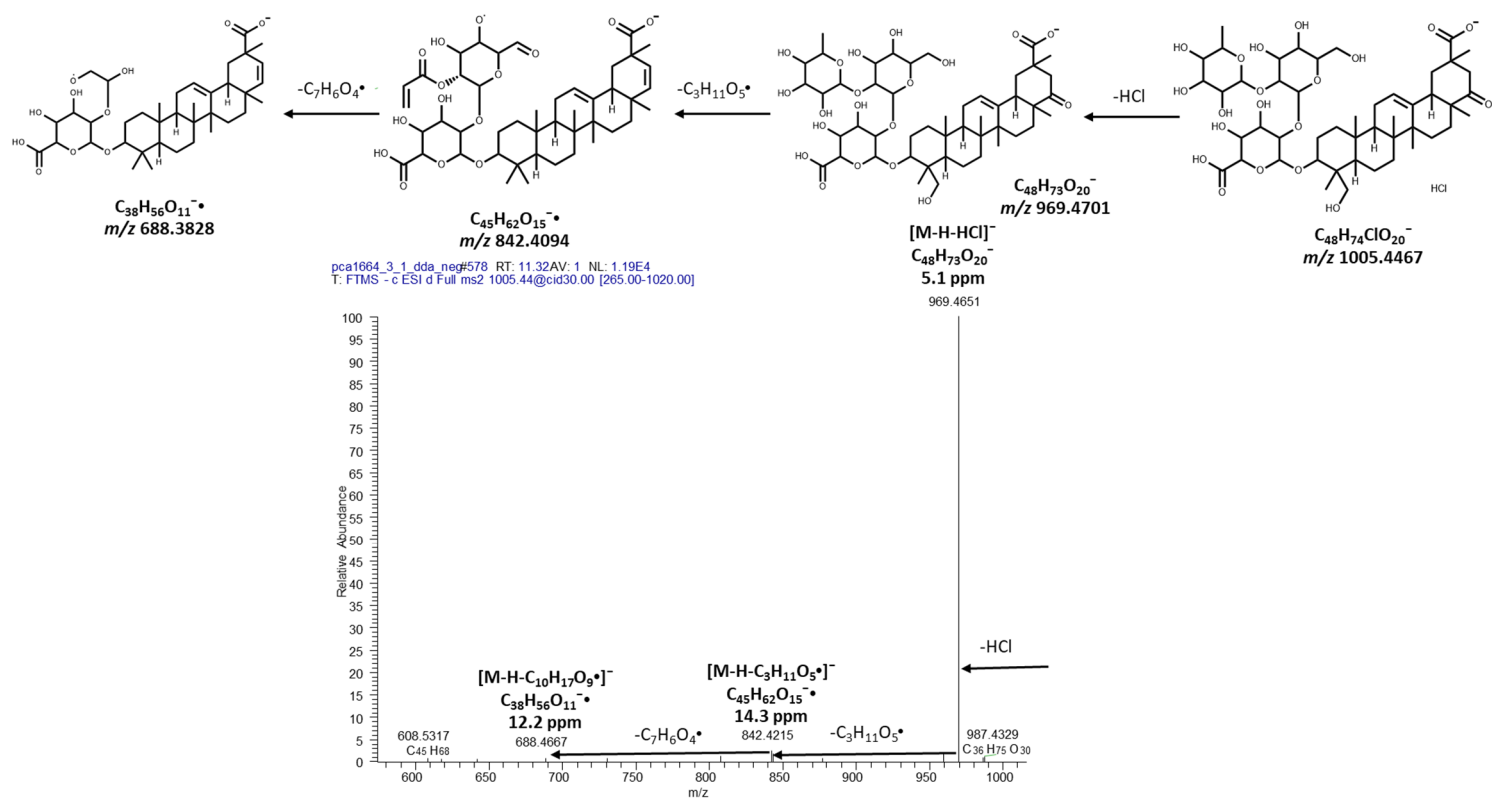
**Figure S19.** Proposed tandem mass spectrometric fragmentation patterns for the ion at  $m/z$  939.46 ( $[M-H]^-$ ,  $MS^2$ ) corresponding to dihydrogypsogenin 3-O-pentopyranosyl-(1-2)-hexpyranox-yl-(1-3)- $\beta$ -D-hexuronopyranoside isomer 1 (17).



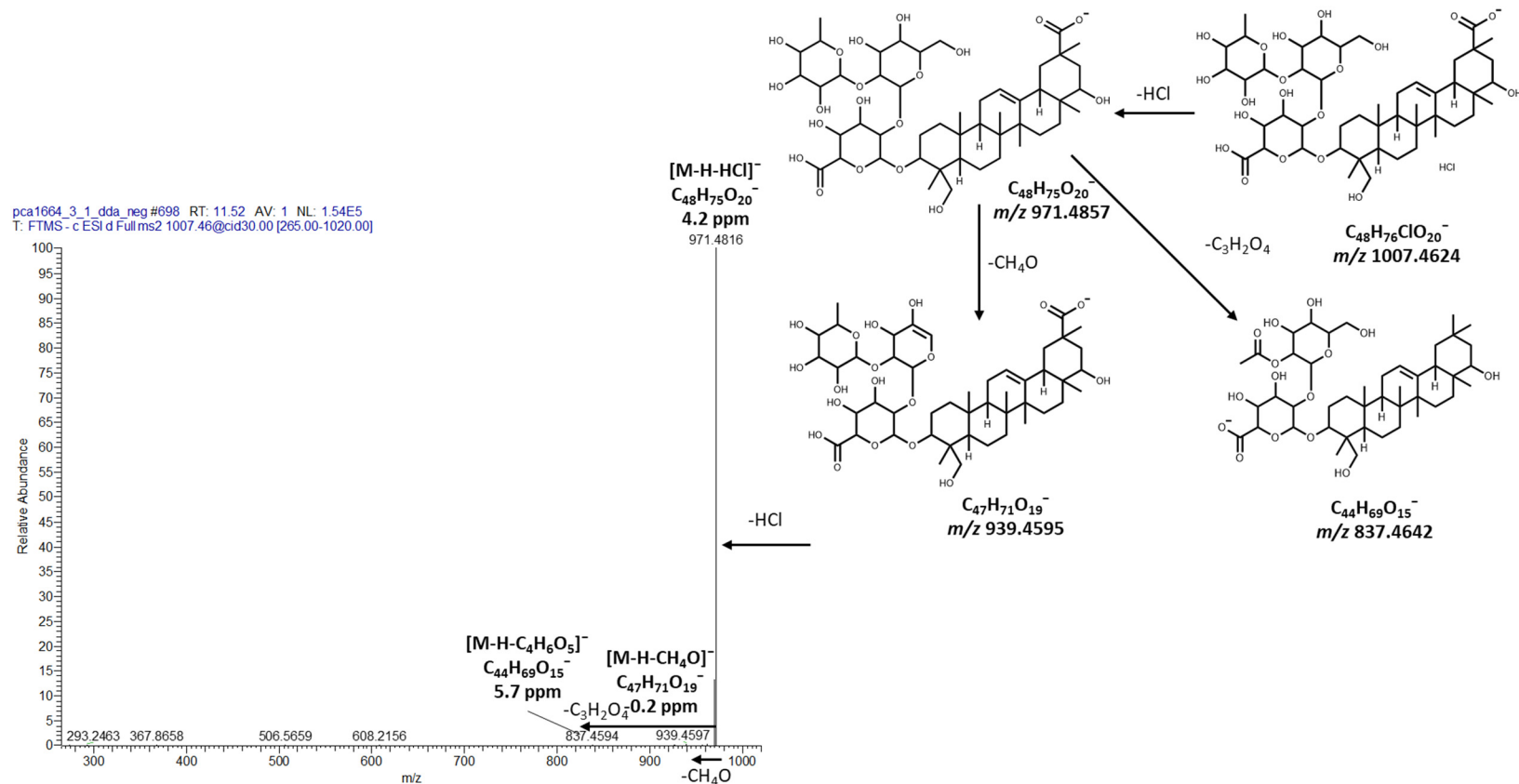
**Figure S20.** Tandem mass spectrum of  $m/z$  955.49 at  $t_R$  10.49 min corresponding to calendulaglycoside C (**18**), annotated in *Aralia elata* var. *mandshurica* (Rupr. & Maxim.) J. Wen extract. The spectrum was acquired with LIT-Orbitrap mass spectrometer operated in the negative product ion mode (collision energy 30 eV).



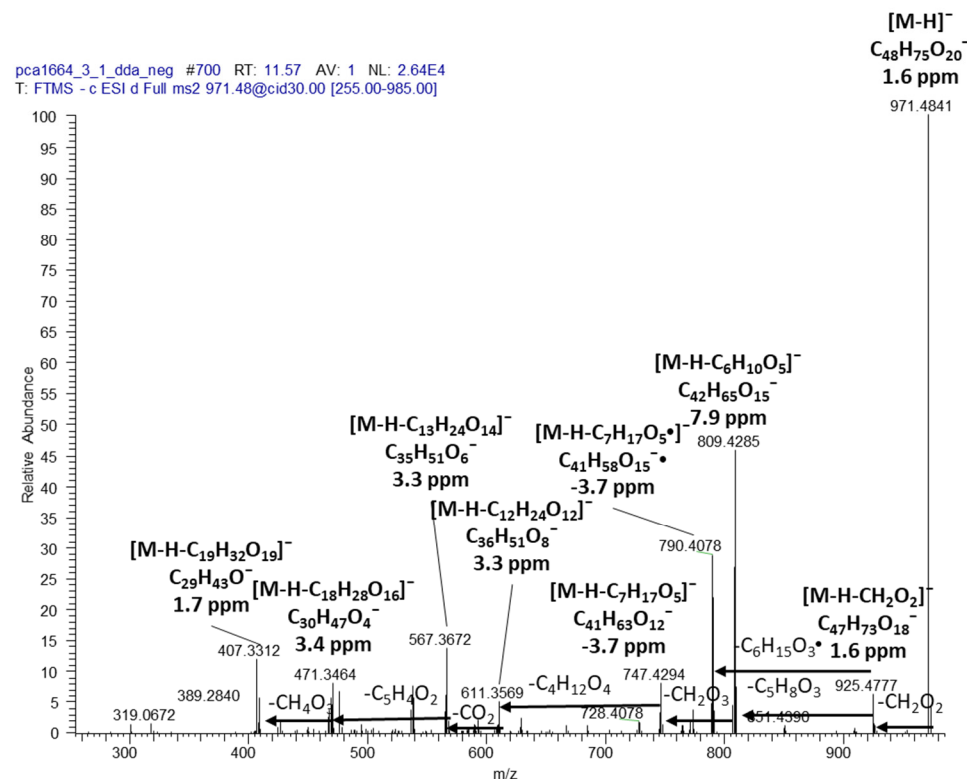
**Figure S21.** Proposed tandem mass spectrometric fragmentation patterns for the ion at  $m/z$  955.49 ( $[M-H]^-$ ,  $MS^2$ ) corresponding to calendulaglycoside C (18).



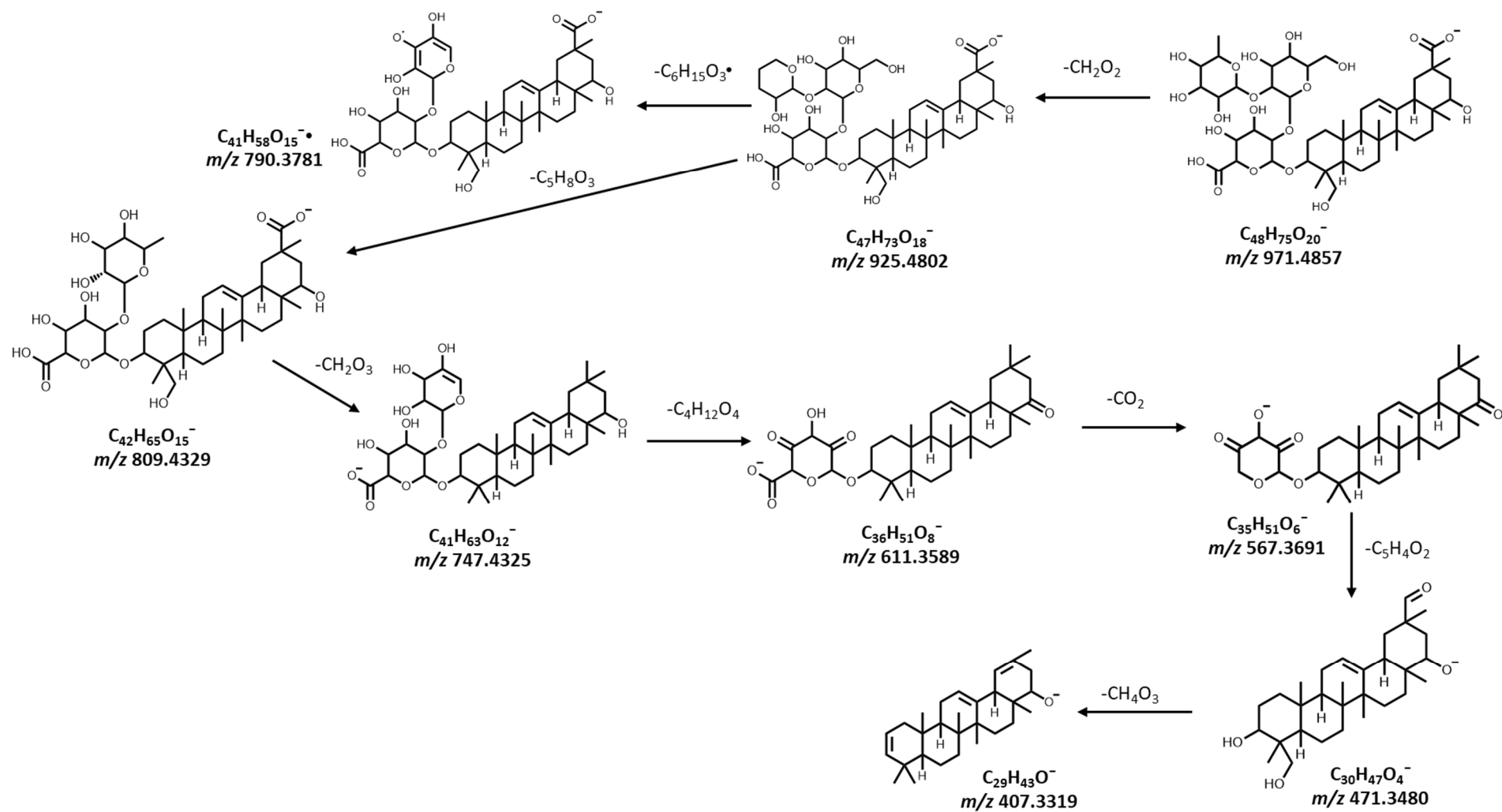
**Figure S22.** Tandem mass spectrum of  $m/z$  955.49 at  $t_R$  10.49 min corresponding to 3-*O*-hexopyranosyl-hexopyranosyl-hexuronopyranosyl melilotigenin isomer 2 (**19**), annotated in *Aralia elata* var. *mandshurica* (Rupr. & Maxim.) J. Wen extract. The spectrum was acquired with LIT-Orbitrap mass spectrometer operated in the negative product ion mode (collision energy 30 eV). Structures shown are suggestions.



**Figure S23.** Tandem mass spectrum of  $m/z$  1007.46 at  $t_R$  11.52 min corresponding to sophoraflavoside II isomer 2 (**20**), annotated in *Aralia elata* var. *mandshurica* (Rupr. & Maxim.) J. Wen extract. The spectrum was acquired with LIT-Orbitrap mass spectrometer operated in the negative product ion mode (collision energy 30 eV). Structures shown are suggestions.

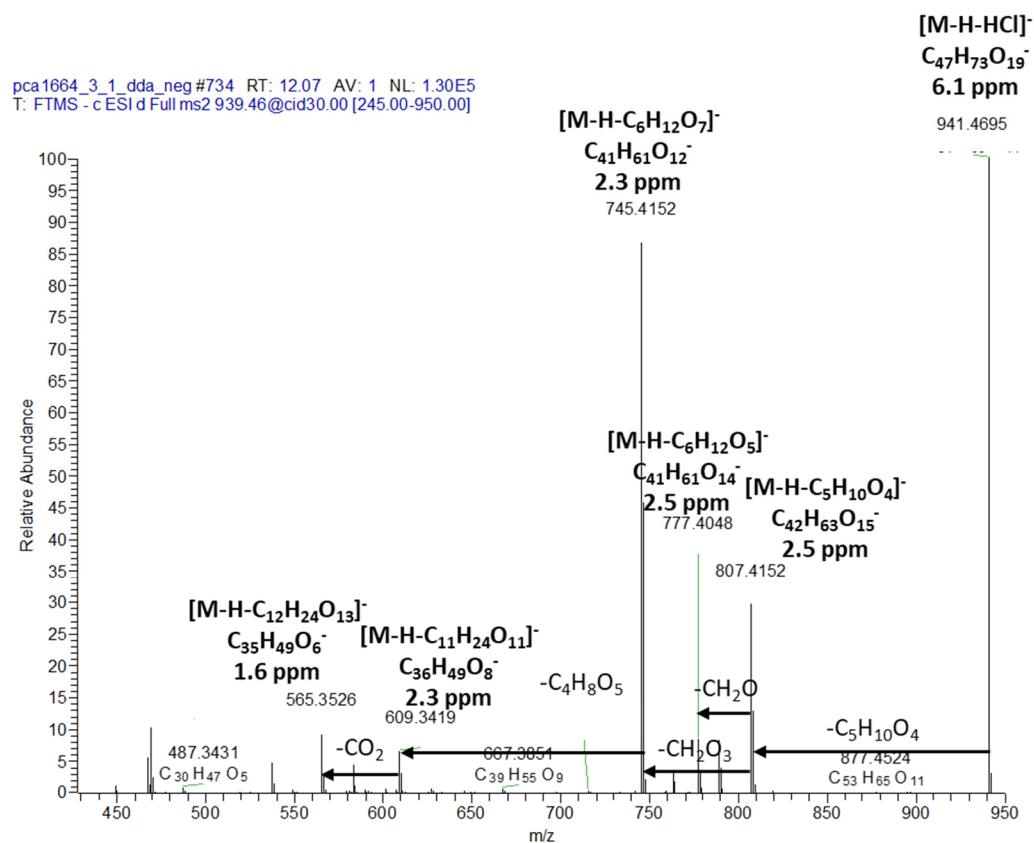


**Figure S24.** Tandem mass spectrum of  $m/z$  971.48 at  $t_R$  11.57 min corresponding to sophoraflavoside II isomer 3 (**21**), annotated in *Aralia elata* var. *mandshurica* (Rupr. & Maxim.) J. Wen extract. The spectrum was acquired with LIT-Orbitrap mass spectrometer operated in the negative product ion mode (collision energy 30 eV).

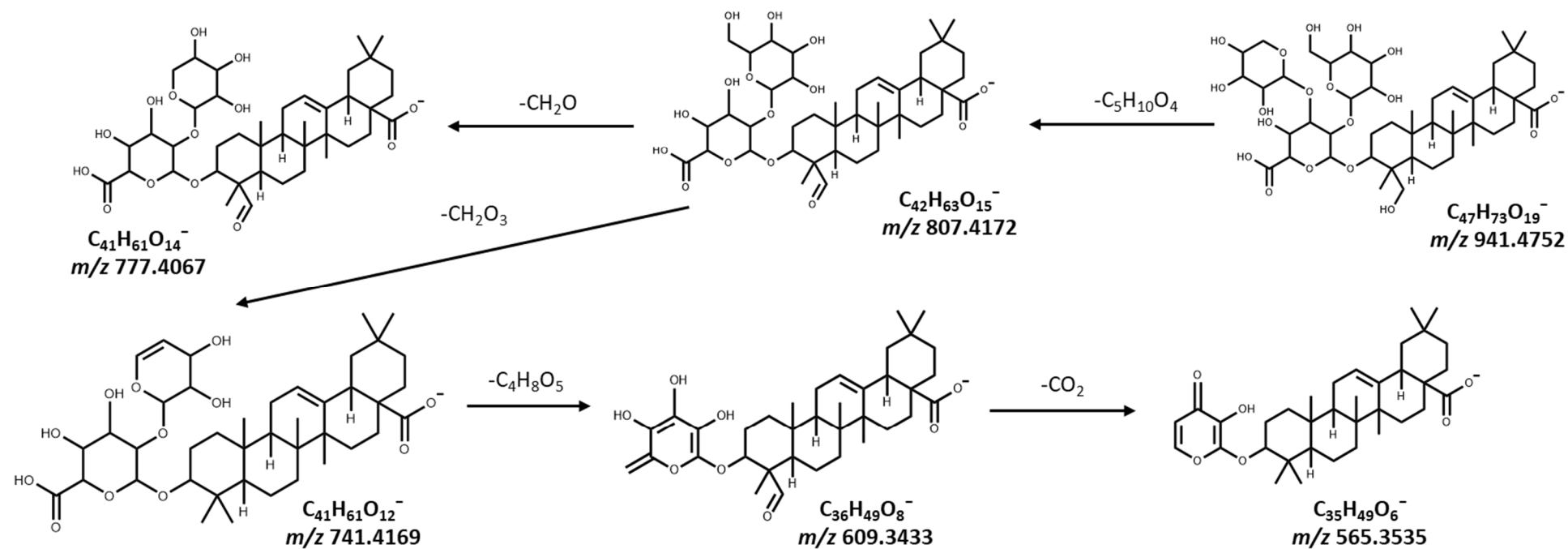


**Figure S25.** Proposed tandem mass spectrometric fragmentation patterns for the ion at  $m/z$  971.48 ( $[M-H]^-$ ,  $MS^2$ ) corresponding to sophoraflavoside II isomer 3 (**21**).

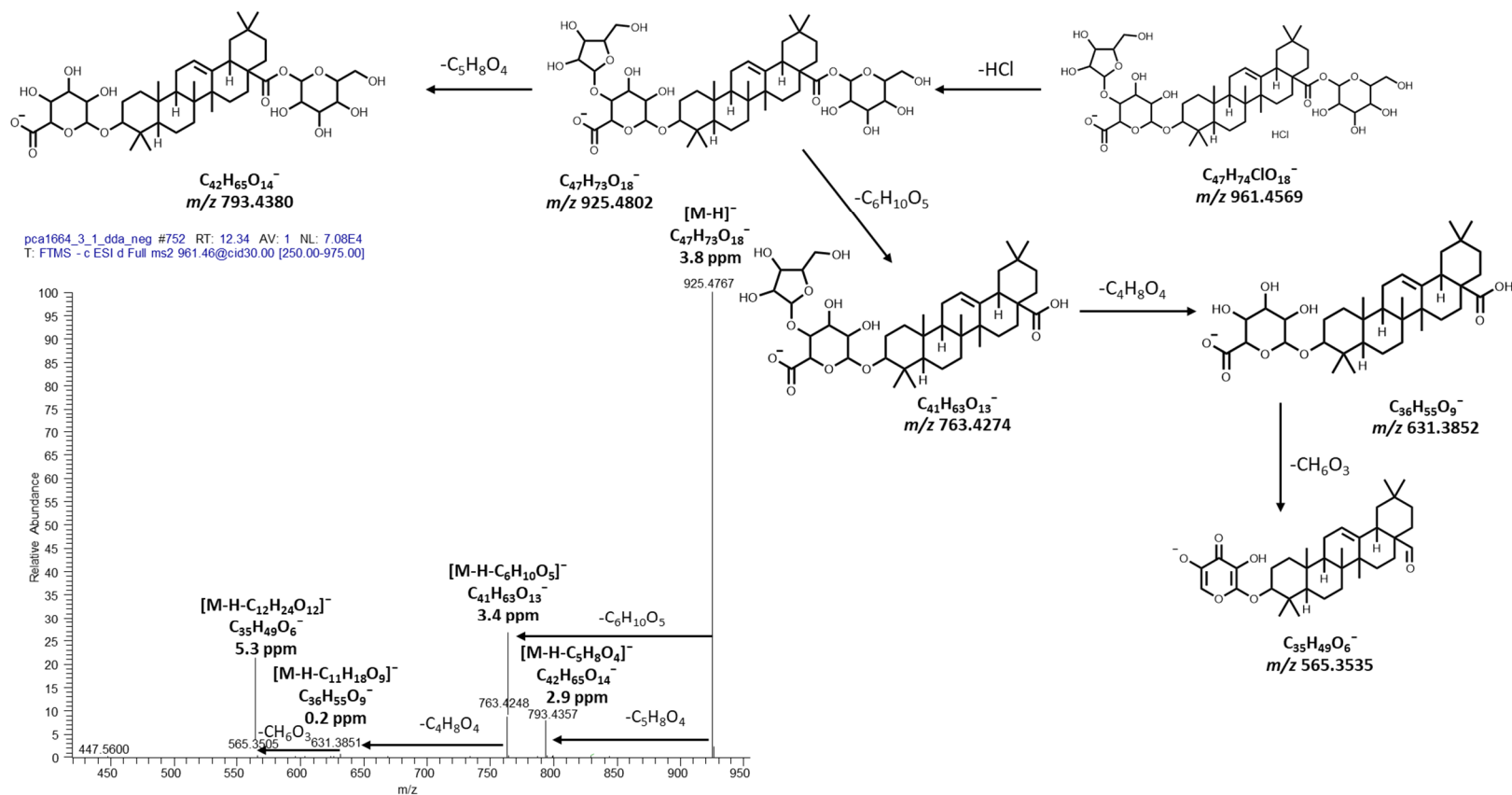




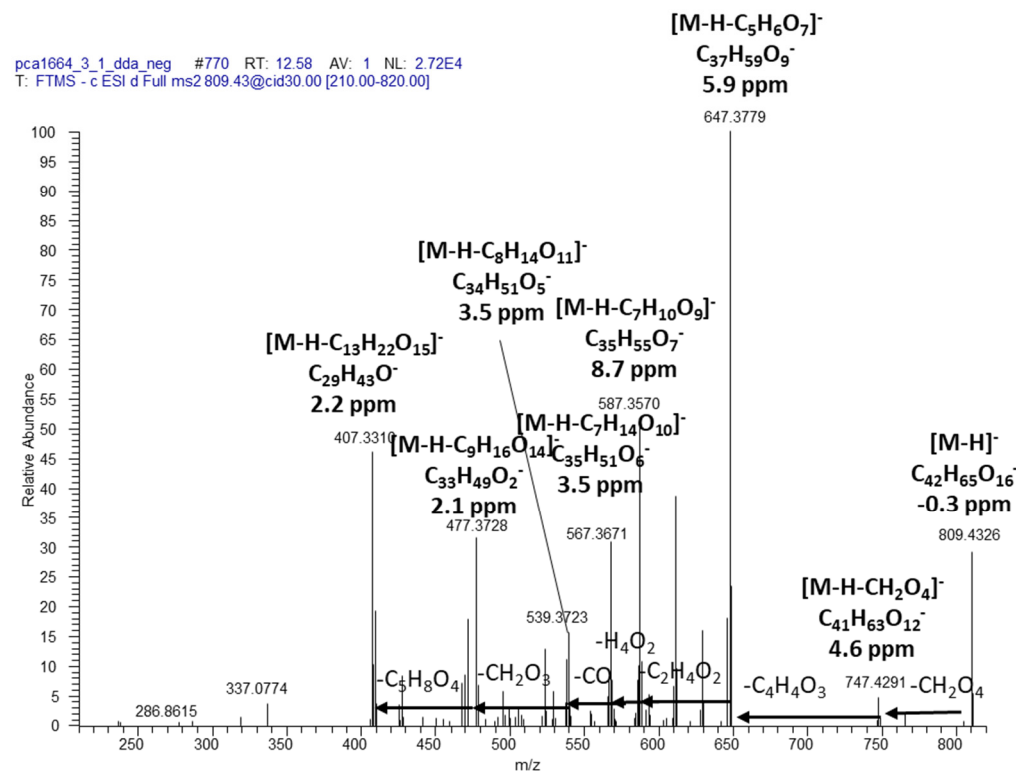
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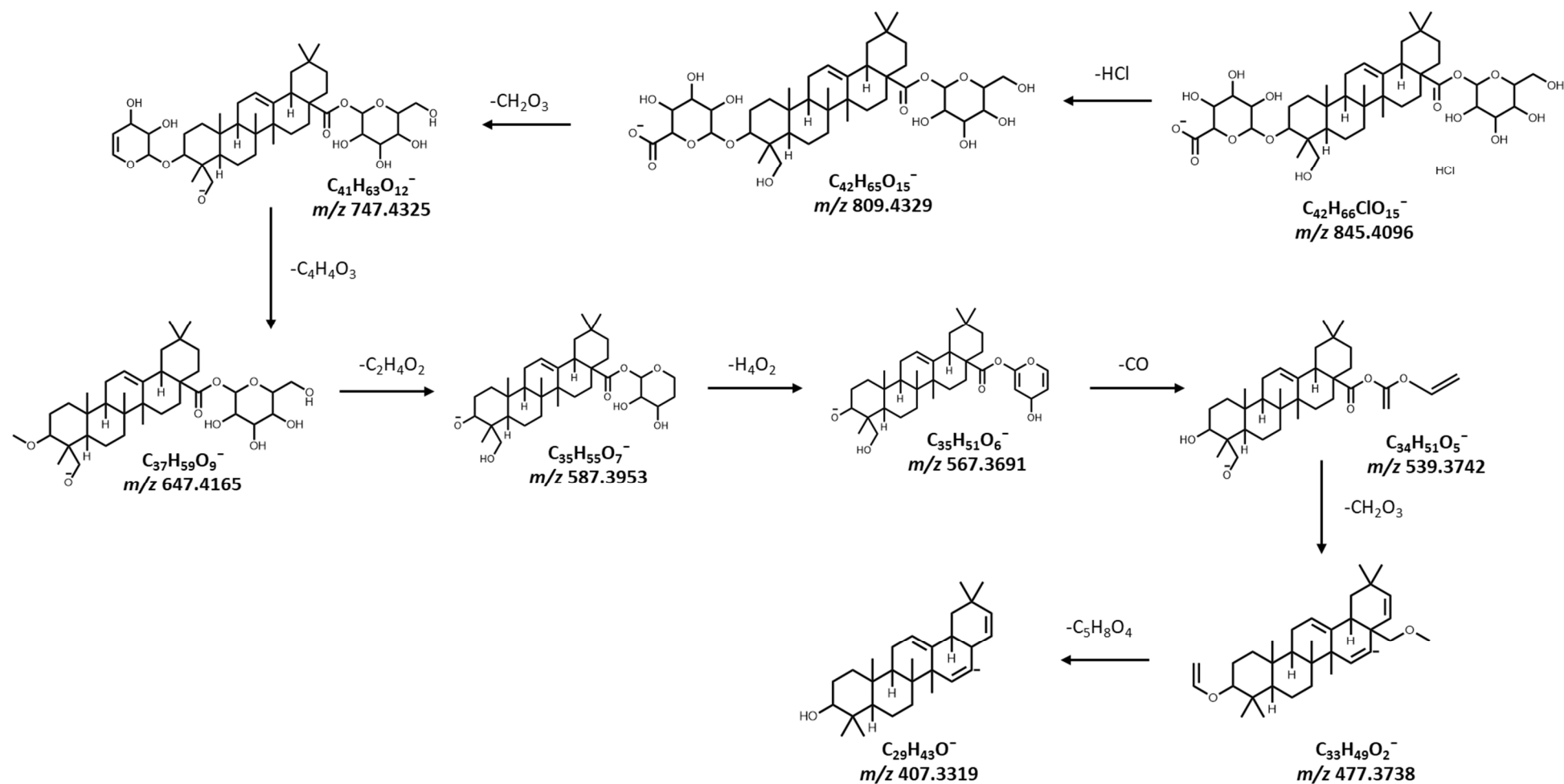
**Figure S27.** Proposed tandem mass spectrometric fragmentation patterns for the ion at  $m/z$  939.46 ( $[M-H]^-$ ,  $MS^2$ ) corresponding to dihydrogypsogenin 3-O-pentopyranosyl-hexpyranoxyl-hexuronopyranoside isomer 2 (**22**).



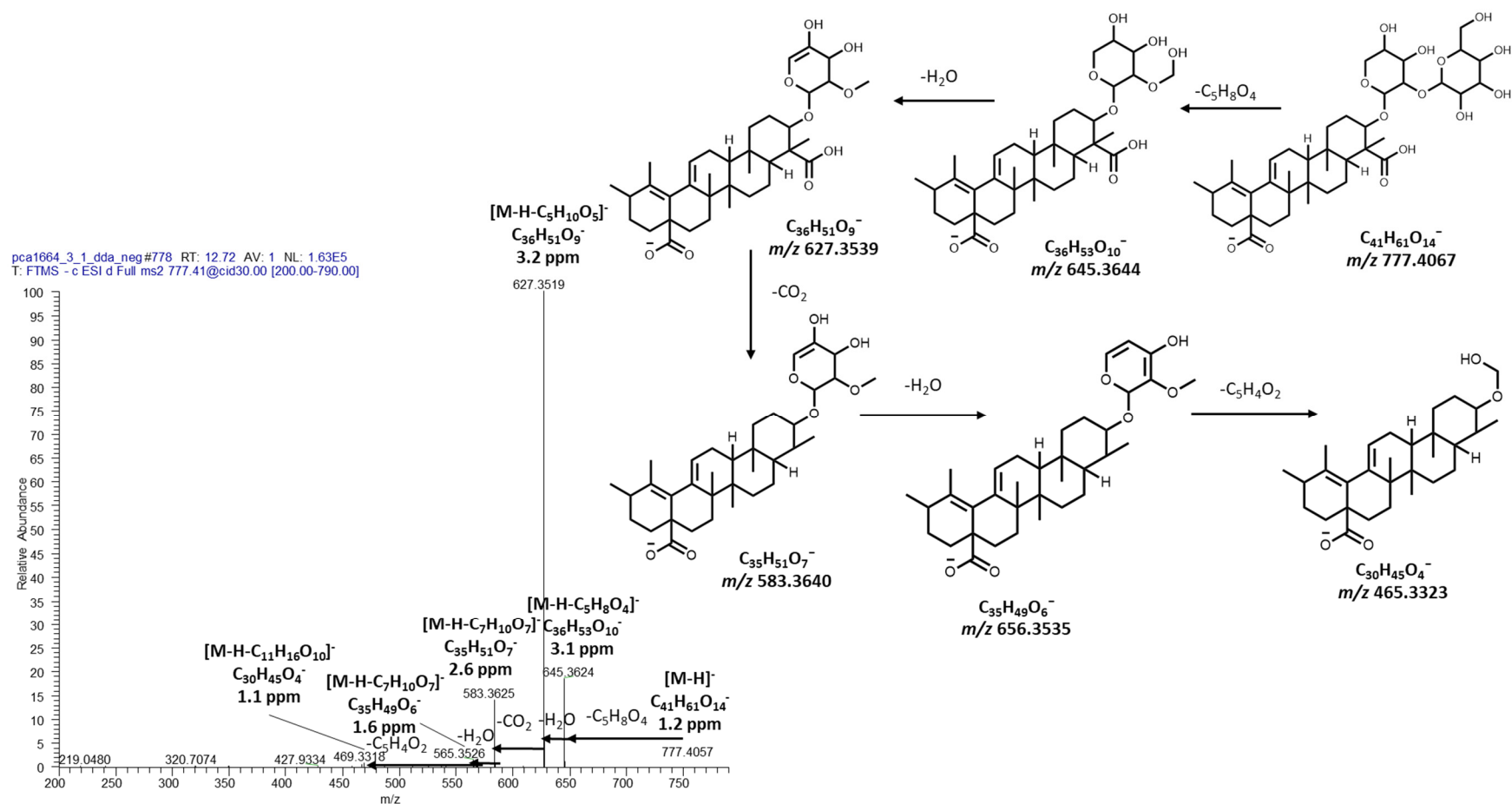
**Figure S28.** Tandem mass spectrum of  $m/z$  961.46 at  $t_R$  12.34 min corresponding to chikusetsusaponin IV (23), annotated in *Aralia elata* var. *mandshurica* (Rupr. & Maxim.) J. Wen extract. The spectrum was acquired with LIT-Orbitrap mass spectrometer operated in the negative product ion mode (collision energy 30 eV). Structures shown are suggestions.



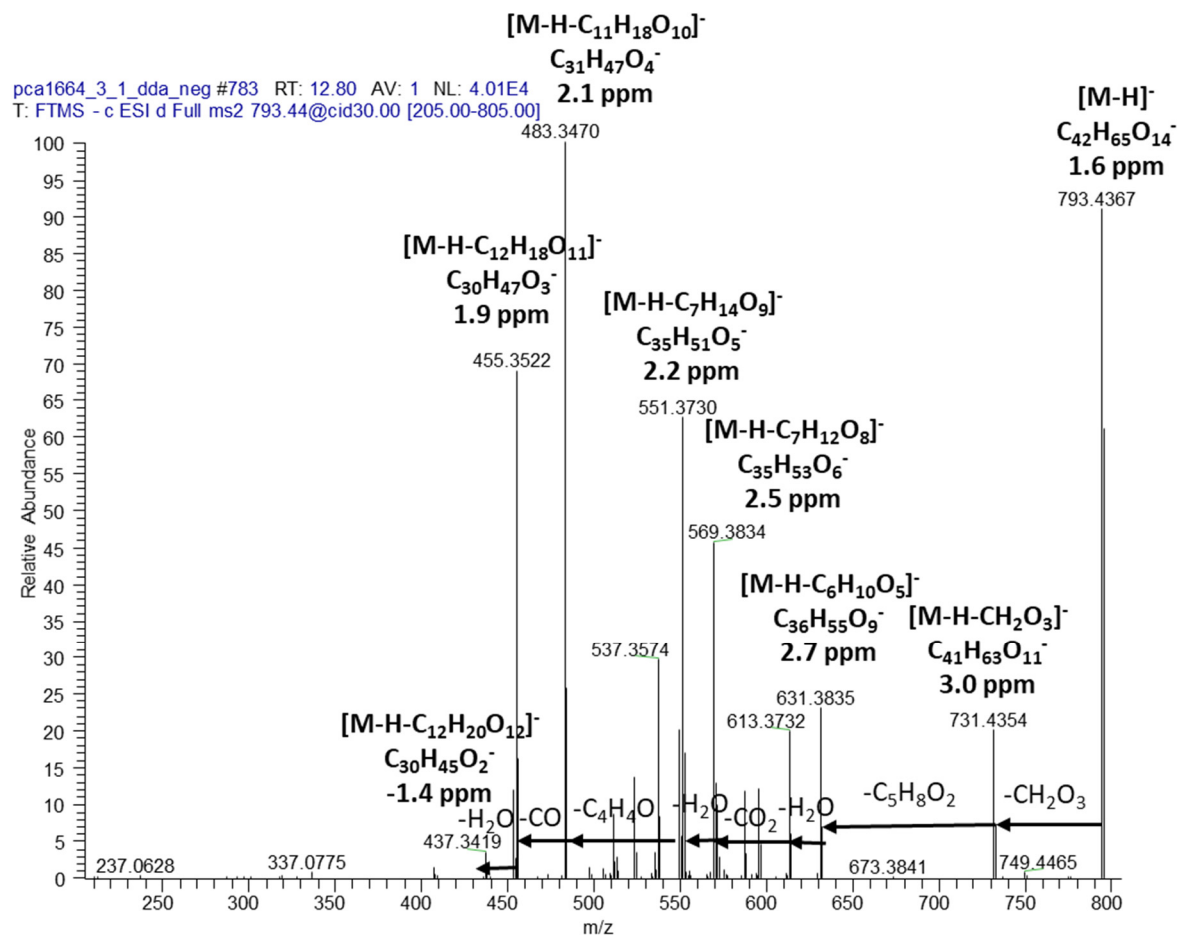
**Figure S29.** Tandem mass spectrum of  $m/z$  809.43 at  $t_R$  12.58 min corresponding to ilexoside XLVIII (**24**), annotated in *Aralia elata* var. *mandshurica* (Rupr. & Maxim.) J. Wen extract. The spectrum was acquired with LIT-Orbitrap mass spectrometer operated in the negative product ion mode (collision energy 30 eV).



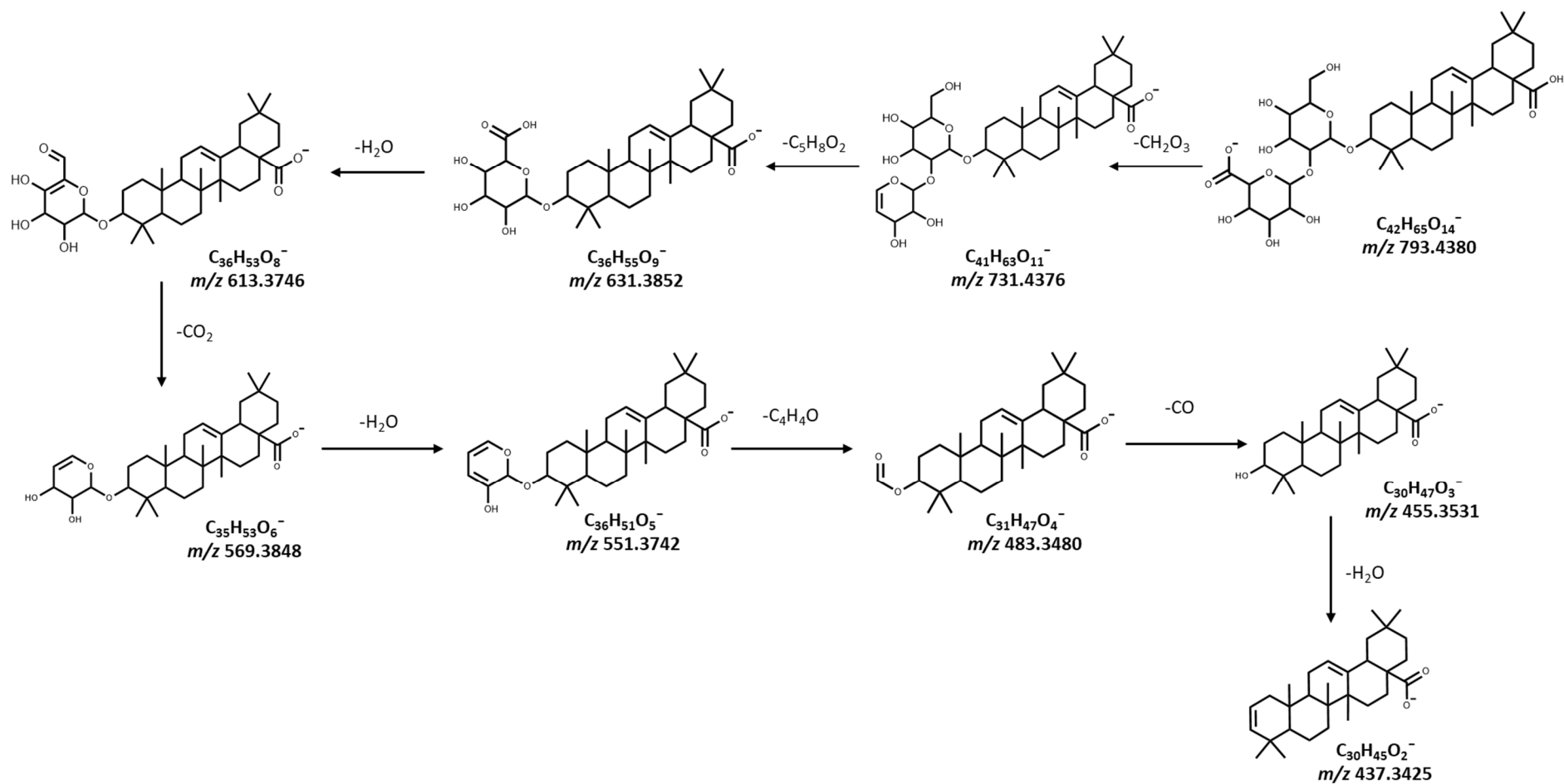
**Figure S30.** Proposed tandem mass spectrometric fragmentation patterns for the ion at  $m/z$  809.43 ( $[MHCl-H]^-$ ,  $MS^2$ ) corresponding to ilexoside XLVIII (24).



**Figure S31.** Tandem mass spectrum of  $m/z$  777.41 at  $t_R$  12.72 min corresponding to 3-*O*-hexopyranosyl-pentopyranosylurs-12,18-diene-24,28-dioic acid (**25**), annotated in *Aralia elata* var. *mandshurica* (Rupr. & Maxim.) J. Wen extract. The spectrum was acquired with LIT-Orbitrap mass spectrometer operated in the negative product ion mode (collision energy 30 eV). Structures shown are suggestions.

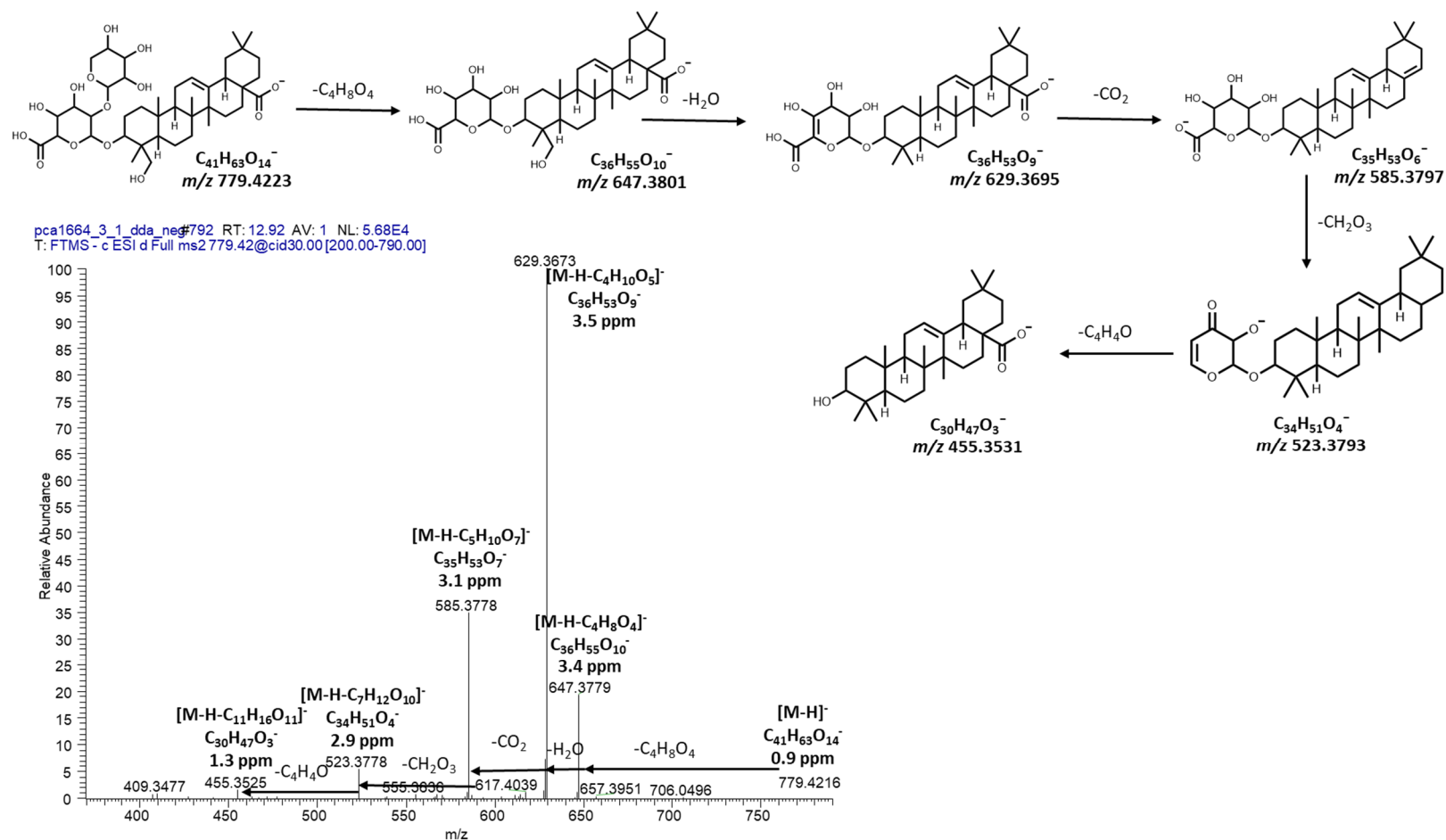


**Figure S32.** Tandem mass spectrum of  $m/z$  793.44 at  $t_R$  12.80 min corresponding to oleanolic acid-hexuronide-hexoside (**26**), annotated in *Aralia elata* var. *mandshurica* (Rupr. & Maxim.) J. Wen extract. The spectrum was acquired with LIT-Orbitrap mass spectrometer operated in the negative product ion mode (collision energy 30 eV).



**Figure S33.** Proposed tandem mass spectrometric fragmentation patterns for the ion at  $m/z$  793.44 ( $[M-H]^-$ ,  $MS^2$ ) corresponding to oleanolic acid-hexuronide-hexoside (26).





**Figure S34.** Tandem mass spectrum of  $m/z$  779.42 at  $t_R$  12.92 min corresponding to 3-*O*-[pentopyranosyl-hexuronopyranosyl] hederagenin (27), annotated in *Aralia elata* var. *mandshurica* (Rupr. & Maxim.) J. Wen extract. The spectrum was acquired with LIT-Orbitrap mass spectrometer operated in the negative product ion mode (collision energy 30 eV). Structures shown are suggestions.